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Amaç ve Kapsam / Aims and Scope

Türkiye Romatoloji Derneği'nin (TRD) yayın organı olan Ulusal Romatoloji Dergisi (önceki adı: RAED Dergisi) yılda üç kez, Türkçe ve İngilizce yayımlanan hakemli bir bilimsel dergidir (p-ISSN: 2651-2653; e-ISSN: 2651-2661). Dergi, romatoloji biliminin bütün konularında orijinal deneysel ve klinik araştırmaları, olgu sunumlarını, derlemeleri, tanıtım ve haberleri, yazarlara ve editöre mektupların yanı sıra romatoloji camiasını ilgilendiren duyuruları yayımlar. Bunun dışında romatoloji alanındaki yenilik ve gelişmelere yönelik toplantıların konuşma metinlerini ya da bu gelişmeleri içeren yazıları ek vererek yayımlayabilir. Derleme yazılar genellikle davetli yazı konumunda olduğundan dergiye gönderilmeden önce editör ile iletişime geçilmesi gerekmektedir. Dergi, doğrudan gönderilen derleme türü yazıları kabul etmemektedir.

Ulusal Romatoloji Dergisi **EBSCO, Gale, Index Copernicus, J-Gate, Türk Medline ve TÜBITAK ULAKBİM TR Dizin** veritabanında İndekslenmektedir.

Ulusal Romatoloji Dergisi'nin amacı ülkemizde romatoloji ile ilgilenen diğer disiplinlerin de katılımıyla romatoloji alanında güncel bir bilimsel tartışma zemini ve arşiv oluşturmaktır. Dergi bu birikimini, saygın bir biyomedikal periyodik olarak uluslararası bilimsel paylaşıma sunmayı ve böylece romatoloji biliminin gelişmesine akademik katkı sağlamayı hedeflemektedir.

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Açık Erişim, "[hakem değerlendirmesinden geçmiş bilimsel literatürün], İnternet aracılığıyla; finansal, yasal ve teknik engeller olmaksızın, serbestçe erişilebilir, okunabilir, indirilebilir, kopyalanabilir, dağıtılabilir, basılabilir, taranabilir, tam metinlere bağlantı verilebilir, dizinlenebilir, yazılıma veri olarak aktarılabilir ve her türlü yasal amaç için kullanılabilir olması"dır. Çoğaltma ve dağıtım üzerindeki tek kısıtlama yetkisi ve bu alandaki tek telif hakkı rolü; kendi çalışmalarının bütünlüğü üzerinde kontrol sahibi olabilmeleri, gerektiği gibi tanınmalarının ve alıntılanmalarının sağlanması için, yazarlara verilmelidir.

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Aims and Scope / Amaç ve Kapsam

Journal of Turkish Society for Rheumatology (formerly RAED Journal), the official organ of Turkish Society for Rheumatology, is a peer-reviewed scientific journal published quarterly in Turkish or English (p-ISSN: 2651- 2653). The journal publishes three times in a year original contributions in the form of basic and clinical research articles, case reports, reviews, news, letters to the editor and authors as well as announcements related to all topics of rheumatology. Also, abstracts or full texts of scientific meetings in rheumatology can be published as supplements of the journal. The reviews are usually invited; therefore it is necessary to contact the editor before sending them to the journal. The journal does not accept unsolicited reviews.

Journal of Turkish Society for Rheumatology is indexed in **EBSCO, Gale, Index Copernicus, J-Gate, Turkish MEDLINE and ULAKBİM.**

Journal of Turkish Society for Rheumatology aims to constitute a current scientific discussion platform and archive in rheumatology with the contribution of the disciplines related to rheumatology together. The journal intends to share its experiences with the international scientific community in a prestigious way and to provide academic contribution to the development of rheumatology science.

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Dergide yer alan bölümler aşağıda aşağıdaki gibi sınıflandırılmaktadır:

- Klinik Araştırma
- Deneysel Çalışma
- Olgu Sunumu
- Derleme
- Editöre Mektup
- Öneri
- Yazara Mektup
- Kitap Tanıtımı
- Haberler
- Özetler

ETİK VE HAKEM DEĞERLENDİRMESİ

Ulusal Romatoloji Dergisi bağımsız, önyargısız ve çift-kör hakemlik ilkeleri çerçevesinde yayın yapan süreli bir yayın organıdır. Makale baş editöre ulaşınca bilimsel kalitesi değerlendirilir ve ön değerlendirmeyi geçen yazılar yardımcı editöre gönderilir. Bölüm editörü makaleyi 2 hakeme gönderir. Hakemler 21 gün içinde kararlarını belirtmelidirler. Yardımcı editör hakem kararlarına kendi değerlendirme ve önerisini ekleyerek baş editöre gönderir ve son kararı baş editör verir. Hakemlerin kararları çatışıyorsa dergi editörü yeni hakem atayabilir.

Derginin alıntı kontrolü "Crossref Similarity Check" tarafından geliştirilen "iThenticate" programı kullanılarak yapılmaktadır. İntihal raporuna göre makale yazara geri gönderilebilir ya da reddedilebilir.

Yayınlanmak üzere dergiye gönderilen yazılar daha önce başka bir dergide yayınlanmamış veya yayınlanmak üzere eş zamanlı olarak herhangi bir dergiye gönderilmemiş olmalıdır. Bilimsel toplantılarda sunulmuş bildirilerden hazırlanan yazılar, tamamı yayınlanmamış olmak koşuluyla dergiye gönderilebilir. Gelen yazılar Yayın Kurulu tarafından ön incelemeden geçirilir. Derginin yayın amacına uygun olmayan yazılar doğrudan reddedilebilir ya da hakem değerlendirmesine alınmadan yayın amacına ve yayın kurallarına uygun hale getirilmesi amacıyla yazara geri gönderilir. Dergi kapsamına uygun görülen yazılardan klinik araştırma, deneysel çalışma, derleme ve olgu sunumu sınıfı yazılar hakem değerlendirme (eş değerlendirme/*peer review*) sürecine girerler. Yayın Kurulu, hakem yorum ve önerileri doğrultusunda dergiye gönderilen yazıların yayına hazırlanması aşamalarında gerekli gördüğü düzeltme ve değişiklikleri önermeye yetkilidir. Dil birliğini sağlamak amacıyla cümlenin bilimsel anlamını değiştirmeyen kelime değişikliklerini yapabilir. Eş değerlendirme sürecinde gerekli düzelti aşamalarını geçtikten sonra sayfa düzeni yapılıp yayına hazır hale getirilen yazıların provası, son baskı onayı için ilgili (yazışmaların yapıldığı) yazara göndeilir.

Araştırma Etiği

Yazar(lar), insanlar üzerinde yapılan çalışmalarda katılımcı bireylerden Bilgilendirilmiş Olur alındığını yazılarında belirtmeli ve çalışmanın yapıldığı kurumun Etik Kurulu veya eşdeğeri bir kuruldan alınan onay belgesini yazıyla birlikte göndermelidir(ler). Olgu sunumlarında, her olgunun kendisine ait bilgilerin yayın amacıyla kullanılacağına dair bilgilendirildiğini gösterir bir belgenin sunulması gerekir. Tüm çalışmalar Helsinki Deklarasyonu'nun son değişiklikleri işlenmiş şekline uygun yapılmış olmalıdır. Hasta bilgileri 01.08.1998 tarih ve 23420 sayılı Resmi Gazete'de yayımlanan Hasta Hakları Yönetmeliği'ne uygun olarak alınmış olmalıdır. Hayvanlar üzerindeki sonuçları bildiren deneysel çalışmaların, Hayvan Hakları Evrensel Bildirgesi, Deneysel ve Diğer Bilimsel Amaçlarla Kullanılacak Omurgalı Hayvanların Korunması Hakkındaki Avrupa Konvansiyonu (European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purpose), T.C. Tarım ve Köy İşleri Bakanlığı'nın Deneysel ve Diğer Bilimsel Amaçlar İçin Kullanılan Deney Hayvanlarının Üretim Yerleri ile Deney Yapacak Olan Laboratuvarın Kuruluş Çalışma Denetleme Usul ve Esaslarına Dair Yönetmelik, Laboratuvar Hayvanları Biliminin Temel İlkeleri (Principles of Laboratory Animal Science), laboratuvar hayvanlarının bakım ve kullanılmasıyla ilgili el kitaplarında yer alan kural ve ilkelere uygun olarak ve çalışmanın yapıldığı kurumda mevcut ise, Deney Hayvanları Etik Kurulu'ndan alacakları onay sonrasında yapılmış olması gerekir. Etik Kurul onayı yazı ile birlikte sunulmalıdır. Yazılarda, insan ve hayvanlarda yapılan çalışmalarda kullanılan ameliyat sonrası ağrı giderici tedavi yöntemleri hakkında da bilgi verilmelidir.

Yayın Etiği ve Kötüye Kullanım Bildirgesi

Ulusal Romatoloji Dergisi yayın etiğini en yüksek standartlarda uygulamayı ve Yayın Etiği ve Kötüye Kullanım Bildirgesinin aşağıdaki ilkelerine uymayı taahhüt eder. Bu bildirge Committee on Publication Ethics (COPE), Council of Science Editors (CSE), World Association of Medical Editors (WAME) ve International Committee of Medical Journal Editors (ICMJE) adlı birlik ve inisiyatiflerin, dergi editörleri için geliştirdikleri öneri ve kılavuzlar temel alınarak hazırlanmıştır. Yayımlanmak üzere dergiye gönderilen yazılar daha önce başka bir dergide yayımlanmamış (bilimsel toplantılarda sunulmuş ve tam metin yayımlanmış bildiriler dahil) veya yayımlanmak üzere eşzamanlı olarak herhangi bir dergiye gönderilmemiş olmalıdır. Dergiye gönderilen yazılar, bir editör ve en az iki danışman (hakem) tarafından incelenmek suretiyle tek-kör eş değerlendirme *(peer review)* sürecine alınır. Dergimiz gönderilen yazıların herhangi bir aşamada, amaca yönelik bir yazılım aracılığıyla intihal açısından incelenebileceği hakkını saklı tutar. Bu amaçla intihale yönelik izinsiz alıntı ya da düzmece veriler, sahtecilik (tablo şekil ya da araştırma verilerinin uydurma ya da manipüle edilmiş olması) ve araştırmada uygunsuz insan ya da hayvan denekler kullanımına yönelik incelemeler söz konusu

olabilir. Bu standartlara uygun olmayan yazılar dergide yayımlanmaz. Bu standartlara uygun olmayan yazılar dergide yayımlanmaz. Bu kural, yayımlanma sonrası aşamada saptanabilecek bu standartlarla ilgili herhangi bir uyumsuzluk durumunda da geçerlidir ve yazının yayımdan geri çekilmesini gerektirir. Yayın etiği gereği dergimiz intihal ya da duplike yayın şüphesi durumlarını rapor edecektir. Dergimiz, yayın etiğinin kötüye kullanımı ya da ihlali ile ilgili olası durumlarda COPE tarafından geliştirilen Yayın Etiği Akış Şemalarını temel alır.

Yazar Sorumluluğu

Yazarlar gönderdikleri yazıların özgünlüğünü teminat altına almalıdır. Yazının daha önce herhangi bir yerde, herhangi bir dilde yayımlanmadığı ya da yayımlanmak üzere değerlendirmeye alınmış olmadığını beyan etmelidirler. Geçerli telif hakkı sözleşme ve yasalarına uymalıdırlar. Dergimizde tablo, şekil ya da diğer katkı sunan alıntılar gibi telifli materyal ancak geçerli izin ve telif onayı ile yayımlanır. Yazarlar; başka yazarlar, katkı sağlayıcılar ya da kaynaklara uygun bir biçimde atıf yapmalı ve ilgili kaynakları belirtmelidir. Araştırma türü yazıların (kısa raporlar dahil) yazar(lar)ı "çalışmayı tasarlama", "verileri toplama", "verileri inceleme", "yazıyı yazma" ve "verilerin ve analizlerin doğruluğunu onaylama" aşamalarından en az 3 tanesine katılmış olmak ve bu durumu beyan etmek zorundadır. Yazarlar, çalışma ile ilgili bilinmesi gereken ve çalışmanın bulgularını ya da bilimsel sonucunu potansiyel olarak etkileyebilecek bir mali ilişkiyi ya da çıkar çakışması (conflict of interest) veya rekabet (competing interest) alanlarını açıklamakla yükümlüdür. Çalışmaya yapılan tüm mali katkıları, sponsorlukları ya da proje desteklerini açıklıkla bildirmelidirler. Derginin Çıkar Çakışması Politikası ile ilgili ayrıntılı bilgiyi de içeren ve olası çıkar çakışması durumunda kullanılabilecek "Çıkar Çakışması Beyan Formu"na PDF dokümanı olarak erişilebilir. Yazar yayımlanmış yazısında anlamlı bir bilimsel hata ya da uygunsuzluk saptadığında, yazıyı geri çekme ya da hatayı düzeltme amacıyla olabildiğince hızlı bir şekilde editör ile temasa geçme yükümlülüğünü taşır.

Hakem Sorumlulukları

Hakemler gelen yazıları, yazarlarının etnik köken, cinsiyet, cinsiyet tercihi, tabiyet, dini inanış ya da politik felsefelerini dikkate almaksızın bilimsel içerik açısından değerlendirir. Hakemler açısından; araştırma, yazarları ya da destekleyiciler ile ilgili bir çıkar veya rekabet çakışması bulunmamalıdır. Hakem kararları nesnel olmalıdır. Hakemler yazar tarafından atıf yapılmamış yayımlanmış ilintili yayınları belirtmelidir. Gönderilen yazı ile ilgili tüm bilgilerin gizli tutulması ve yazar tarafından yapılan telif hakkı ihlali ve intihal durumlarının farkına vardığında Editöre bildirilmesi ile yükümlüdürler. Hakem, gönderilen bir yazının içeriğinin kendi bilimsel alanı ya da birikimi ile uyumsuz olduğunu düşündüğünde ya da hızlı bir değerlendirme yapamayacağı durumlarda Editörü bilgilendirmeli ve değerlendirme sürecinden affını istemelidir.

Editör Sorumlulukları

Editörler gelen yazıları, yazarlarının etnik köken, cinsiyet, cinsiyet tercihi, tabiyet, dini inanış ya da politik felsefelerini dikkate almaksızın bilimsel içerik açısından değerlendirmelidir. Gönderilen yazıların yayımlanması için adil bir eş değerlendirme süreci sağlamalıdırlar. Gönderilen yazı ile ilgili tüm bilgilerin yayımlanana kadar gizli tutulmasını garanti altına almalıdırlar. Editörler yayının içeriği ve toplam kalitesinden sorumludur. Erratum sayfaları yoluyla gerektiğinde düzeltme yayımlamalıdırlar. Editör; yazarlar, editörler ve hakemler arasında olabilecek herhangi bir çıkar veya rekabet çakışmasına olanak vermemelidir. Ulusal Romatoloji Dergisinde hakem atamasında sadece Editör tam yetkiye sahip olup yazıların yayımlanması ile ilgili sonuç kararından da kendisi sorumludur.

YAYIN POLİTİKASI

Tüm makaleler bilimsel katkıları, özgünlük ve içerikleri açısından bilimsel komite tarafından değerlendirilecektir. Yazarlar verilerinin doğruluğundan sorumludurlar. Dergi gerekli gördüğü yerlerde dil ve uygun değişiklik yapma hakkını saklı tutar. Gereğinde makale revizyon için yazara gönderilir. Daha önce herhangi bir dilde yayınlanmış makaleler dergide yayınlanmak üzere kabul edilmeyecektir. Yazarlar bir başka dergide yayınlanmak üzere olan makaleyi teslim edemez. Tüm değişiklikler, yazar ve yayıncının yazılı izin alındıktan sonra yapılacaktır. Tüm makalelerin tam metinleri derginin www.manuscriptmodule.com/raed web sitesinden indirilebilir.

Yayın Politikası ve Makale Yazım Kuralları aşağıda belirtilen maddeler "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (ICMJE Recommendations)" (2013, http://www.icmje.org/) temel alınarak hazırlanmıştır.

Araştırma makalelerinin hazırlığı, sistematik derleme, meta-analizleri ve sunumu ise uluslararası kılavuzlara uygun olmalıdır:

Randomize çalışmalar için; CONSORT (Moher D, Schultz KF, Altman D, for the CONSORT Group. The CONSORT statement revised recommendations for improving the quality of reports of parallel group randomized trials. JAMA 2001; 285:1987-91) (http://www.consort-statement.org/).

Sistematik derleme ve meta-analizlerin raporlamaları için; PRISMA (Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 2009; 6(7): e1000097) (http://www.prisma-statement.org/).

Tanısal değerli çalışmalar için; STARD (Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, et al, for the STARD Group. Towards complete and accurate reporting of studies of diagnostic accuracy: the STARD initiative. Ann Intern Med 2003;138:40-4) (http://www.stard-statement.org/).

Gözlemsel çalışmalar için; STROBE (http://www.strobe-statement.org/).

Meta-analizleri ve gözlemsel çalışmaların sistematik derlemeleri için; MOOSE (Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting "Meta-analysis of observational Studies in Epidemiology" (MOOSE) group. JAMA 2000; 283: 2008-12).

GENEL KURALLAR

Aşağıda belirtilen özelliklerin dışında yazılarla ilgili ilkeler açısından "International Committee of Medical Journal Editors (ICMJE). Uniform Requirements for Manuscripts" dokümanları (www.icmje.org) esas alınmalıdır.

Dergiye gönderilecek yazılarda bulunması gereken bölümler sırası ile şunlardır ve her biri ayrı sayfada başlayacak şekilde sunulmalıdır:

Sayfa 1: Başlık sayfası

Sayfa 2: Türkçe Başlık, Özet ve Anahtar Sözcükler

Sayfa 3: İngilizce Başlık (Title), Özet (Abstract) ve Anahtar Sözcükler (Key words)

Sayfa 4 ve sonrası: Temel Metin

Sonraki sayfa: Kaynaklar

Sonraki sayfa: Tablo Açıklama Yazısı ve Tablo (her tablo ayrı sayfada belirtilmelidir)

Sonraki sayfa: Şekil ve Resim Alt Yazıları ve Resim/Şekiller (her şekil ayrı sayfada belirtilmelidir)

Başlık Sayfası

Başlık sayfasında aşağıdaki sıralama gözetilmelidir:

1- Yazının gönderildiği kategori (klinik araştırma, deneysel çalışma, derleme, olgu sunumu vb)

2- Yazının başlığı (başlık 80 karakteri geçmemeli ve standart dışı kısaltmalar içermemelidir)

3- Yazarların ad, soyad, iletişim adresleri ve araştırmanın yapıldığı sırada çalıştıkları kurum

4- Yazının, dergide yayınlandığında devam sayfalarının üst tarafında görünmesi arzu edilen ve 40 karakteri geçmeyen kısaltılmış başlığı

5- Varsa destekleyen kurum ve kuruluşlar

6- Yazı daha önce sunulmuşsa, sunulduğu toplantının ayrıntıları

7- İletişim kurulacak yazarın haberleşme bilgileri

8- Eğer varsa yazının içeriğiyle ilgili maddi desteğin belirtilmesi

Türkçe Özet

Araştırma yazılarında Amaç, Yöntem, Bulgular ve Sonuç bölümlerinden oluşmalı ve 250 kelimeyi geçmemelidir. Derleme ve olgu bildirilerinde yapılandırılmamış özet verilmelidir. Olgu sunumlarının özeti 100 kelimeyi geçmemelidir. Türkçe özet sayfasında en az 3 en fazla 6 anahtar kelime belirtilmelidir.

İngilizce Özet

Araştırma yazılarında "Objectives", "Methods", "Results", and "Conclusions" bölümlerinden oluşmalıdır ve 250 kelimeyi geçmemelidir. İngilizce Özet sayfasında en az 3 en fazla 6 İngilizce anahtar sözcük belirlenmeli, yazının İngilizce başlığı eklenmelidir.

Temel Metin

Giriş, Hastalar/Gereç ve Yöntem, Bulgular, Tartışma ve Kaynaklar bölümlerinden oluşmalıdır. Kısaltmalar standart olmalı ve ilk kullanıldığında parantez içinde açıklanmalıdır. Ölçümlerde uluslararası kabul edilmiş birimler kullanılmalıdır.

Tablo, Şekil ve Resimler

Metinde kullanılış sırasına göre numaralandırılmalı ve gereksiz kullanımdan kaçınılmalıdır. Olgularda kullanılan fotoğraflarda izin alınmalı ve tanınmayı önlemek için gerekli tedbirler uygulanmalıdır. Fotoğraf ve varsa çizim kalitesine özen gösterilmelidir. Yayın Kurulu yeterli kalitede olmadığı gerekçesiyle tablo, şekil ve resimlerde düzeltme veya yenileme isteğinde bulunabilir. Şekil ve resimlerin orijinal olmaları gerekir. Başka bir yayın içinde kullanılmış bulunan resim, şekil ve grafiklerin dergimizde yayımlanabilmesi için, gerekli izinler yazarlar tarafından ve makale başvurusu yapılmadan önce alınmalıdır. İznin alındığını gösterir belgenin kopyası yazıyla birlikte dergiye gönderilmelidir.

Kaynaklar

Kaynaklar güncel ve yazı için gerekli olanlardan seçilmelidir. Yazı metninde kaynaklar parantez içinde gösterilmeli ve kullanılış sırasına göre numaralandırılmalıdır. Süreli yayın adları PubMed kurallarına uygun olarak kısaltılmalı, burada yer almayan dergilerin adlarında kısaltma kullanılmamalıdır. Bildiri özetlerinin kaynak gösterilmesinden kaçınılmalıdır. Bir dergi tarafından kabul edilmiş fakat henüz yayımlanmamış olan yazılar gerektiği şekilde belgelendirilerek kaynak olarak kullanılabilir. Kabul edilmemiş yazılar da dahil olmak üzere bunun dışındaki bilgi, yazı içinde "yayınlanmamış gözlem" olduğu belirtilerek kullanılabilir. Kaynaklar aşağıdaki örneklere göre yazılmalı ve 6 yazara kadar olan kaynaklarda yazarların tamamı sunulmalı, daha fazla yazarı olan kaynak künyeleri, ilk 3 yazar ve sonuna ve ark. (yabancı dildeki kaynakların künyelerinde et al.) kısaltması gelecek şekilde düzenlenmelidir. Kaynakların doğruluğu açısından sorumluluk yazarlara aittir.

Örnekler

Türkçe süreli yayın örneği:

Göksedef D, Ömeroğlu NÖ, Denli Ş, Üreyen C, Sayılgan C, İpek G. Sistemik lupus eritematozuslu bir olguda aort yetmezliği nedeniyle aort kapak replasmanı. Cerrahpaşa Tıp Dergisi 2008;39:73-5.

Yabancı dilde süreli yayın örneği:

Wolfe F, Hawley DJ, Cathey MA. Termination of slow acting antirheumatic therapy in rheumatoid arhritis: a 14-year prospective evaluatin of 1017 consecutive starts. J Rheumatol 1990;17:994-1002.

Elektronik dergide yayımlanan süreli yayın örneği:

Yurdakul S. Is there really a higher risk for infection with anti TNF-alpha agents or is there a selection bias? Lett Ed Rheumatol 1(1):e110006. doi:10.2399/ler.11.0006

Kitap bölümü örneği:

Buchanan WW, Dequeker J. History of rheumatic diseases. In: Hochberg MC, Silman AJ, Smolen JS, Weinblatt ME, Weisman MH, editors. Rheumatology. Edinburgh: Mosby; 2003:3-8.

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Hazırlanan yazıların dergiye gönderilmeden önce aşağıdaki kontrol listesine göre gözden geçirilmesi önerilir:

1- Başlık sayfası

2- Özetler (Türkçe ve İngilizce; olgu sunumlarında en fazla 100 sözcük, diğerlerinde en fazla 250 sözcük; araştırma yazılarında yapılandırılmış)

3- Anahtar sözcükler (en az 3'er adet)

4- Temel metin (alt başlıklar)

5- Kaynaklar (ICMJE kurallarına uygunluk)

6- Şekil, tablo ve resimler (numaralandırma; alt yazılar; özgünlük/izin yazısı)

7- Başvuru mektubu

8- Telif Hakkı Devir Formu (tüm yazarlar tarafından imzalanmış)

9- Çıkar Çakışması Beyan Formu (gereğinde)

Journal of Turkish Society for Rheumatology (formerly RAED Journal), the official organ of Turkish Society for Rheumatology, is a peer-reviewed scientific journal published three times in a year in Turkish or English (p-ISSN: 2651- 2653). The journal publishes original contributions in the form of experimental and clinical research articles, case reports, reviews, news, letters to the editor and authors as well as announcements related to all topics of rheumatology. Also, abstracts or full texts of scientific meetings in rheumatology can be published as supplements of the journal. The reviews are usually invited; therefore it is necessary to contact the editor before sending them to the journal. The journal does not accept reviews which are directly submitted.

The article types in the journal are classified as below:

- Clinical Research Article
- Experimental Study
- Case Report
- Review
- Letter to the Editor
- Recommendation
- Letter to the Author
- Book Review
- News
- Abstracts

ETHICS & PEER-REVIEW

Journal of Turkish Society for Rheumatology is an independent journal based on double-blind peer-review principles. The manuscript is assigned to the Editor-in-Chief, who reviews the manuscript and makes an initial decision based on manuscript quality and editorial priorities. Manuscripts that pass initial evaluation are sent to an Associate Editor. The Associate Editor assigns the manuscript to two reviewers (internal and/or external reviewers). The reviewers must review the manuscript within 21 days. The Associate Editor recommends a decision based on the reviewers' recommendations and sends the manuscript to the Editor-in-Chief. The Editor-in-Chief makes a final decision based on editorial priorities, manuscript quality, and Associate Editor's and reviewers' recommendations. If there are any conflicting recommendations from reviewers, the Editor-in-Chief can assign a new reviewer.

All manuscripts submitted are screened for plagiarism using Crossref Similarity Check powered by "iThenticate" software. Results indicating plagiarism may cause manuscripts being returned or rejected.

Manuscripts sent to the journal for publication should not have been previously published in another journal or sent to any journal simultaneously to be published. Manuscripts prepared from papers presented at scientific meetings can be sent to the journal, provided that they are not fully published. Incoming articles are pre-examined by Editorial Board. Manuscripts that are not suitable for publication purposes may be rejected directly or sent back to the author for publication and publication rules without being evaluated by the reviewer. Among the articles deemed appropriate for the scope of the journal, clinical research, experimental study, review and case report class articles enter the peer-review process. The Editorial Board is empowered to propose the corrections and changes it deems necessary during the preparation of the articles sent to the journal in line with the comments and suggestions of the reviewers. In order to ensure language unity, he/she can make word changes that do not change the scientific meaning of the sentence. After the necessary correction steps have passed in the peer evaluation process, the proof of the articles that are made ready for publication and the page layout is sent to the relevant author (for whom correspondence is made) for the final print approval.

Research Ethics

The author(s) should indicate in their articles that Informed Consent was received from the participating individuals in the studies conducted on people and send the approval document(s) received from the Ethics Committee or equivalent board of the institution where the study was conducted. In case reports, a document must be presented, indicating that each case is informed that their information will be used for publication. All work must have been done in accordance with the final amendments to the Helsinki Declaration. Patient information should be obtained in accordance with the Patient Rights Regulation published in the Official Gazette dated 01.08.1998 and numbered 23420. The European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purpose, by the Universal Declaration of Animal Rights, which reports results on animals, for the Protection of Vertebrates to be Used for Experimental and Other Scientific Purposes, T.C. The Regulation of the Ministry of Agriculture and Rural Affairs on the Production Areas of the Experimental Animals Used for Experimental and Other Scientific Purposes and the Regulation on the Establishment Operation Control Procedures and Principles of the Laboratory to Experiment, the Principles of Laboratory Animal Science, by the care and use of laboratory animals. If it is available in accordance with the rules and principles contained in the relevant manuals and in the institution where the study is carried out, it should be made after approval from the Experimental Animals Ethics Committee. Ethics Committee approval must be submitted with the letter. In the articles, the information should be given about post-operative pain-relieving treatment methods used in human and animal studies.

Publication Ethics and Malpractice Statement

Journal of Turkish Society for Rheumatology undertakes to apply the publication ethics to the highest standards and to comply with the following principles of the Publication Ethics and Abuse Declaration. This declaration is prepared based on the suggestions and guidelines developed by the journal on editors of the Committee on Publication Ethics (COPE), Council of Science Editors (CSE), World Association of Medical Editors (WAME) and International Committee of Medical Journal Editors (ICMJE). Manuscripts sent to the journal for publication should not have been previously published in another journal (including papers presented at scientific meetings and published in full text) or simultaneously not sent to any journal for

publication. Manuscripts sent to the journal are taken into the peer review process by an Editor and at least two consultants (reviewers). Our journal reserves the right to examine the submitted articles at any stage in terms of plagiarism through a purposeful software. For this purpose, unauthorized quotations or fraudulent data regarding plagiarism, fraudulence (made up or manipulated in the form or research data of the table) and investigations may be subject to inappropriate human or animal subjects. Manuscripts that do not comply with these standards are not published in the journal. This rule also applies in case of any incompatibility with these standards which can be determined at the post-publishing stage and requires the withdrawal of the article from the publication. Due to publication ethics, our journal will report cases of plagiarism or duplicate publication. Our journal is based on Publication Ethics Flowcharts developed by COPE in possible situations related to malpractice or violation of publication ethics.

Author Responsibility

Authors should ensure the authenticity of the articles they send. They must declare that the manuscript has not been published in any language, or has been evaluated for publication. They must comply with applicable copyright contracts and laws. In our journal, copyrighted material such as tables, figures or other contributory citations is published only with valid permission and copyright approval. Authors; other authors, contributors or sources should cite appropriately and indicate relevant sources. Participating in at least three stages of research type articles (including short reports) "designing the study", "collecting data", "reviewing data", "writing the article" and "confirming the accuracy of data and analysis" must declare. The authors are responsible for disclosing a financial relationship or areas of conflict of interest or competing for interest that should be known about the study and potentially affect the findings or scientific outcome of the study. They must explicitly report all financial contributions, sponsorships or project supports to the study. The "Conflict of Interest Conflict Declaration Form", which contains detailed information about the journal's Conflict of Interest Policy and can be used in case of potential conflict of interest, is available as a PDF document. When the author detects a meaningful scientific error or incompliance in his published article, he has an obligation to contact the Editor as quickly as possible for the purpose of withdrawing or correcting the article.

Reviewer Responsibilities

Reviewers evaluate incoming articles in terms of scientific content, regardless of their authors' ethnicity, gender, gender preference, nationality, religious belief, or political philosophy. For the reviewers; there should be no conflict of interest or competition regarding research, authors or promoters. Reviewer decisions must be objective. The Reviewers should indicate the related publications that have not been cited by the author. They are obliged to keep all information regarding the submitted article confidential and inform the Editor when they become aware of copyright infringement and plagiarism by the author. The reviewer should inform the Editor and ask for forgiveness from the evaluation process when he considers that the content of a sent article is incompatible with his or her scientific field or knowledge, or when he cannot make a quick evaluation.

Editor Responsibilities

Editors should evaluate incoming articles in terms of scientific content, regardless of their authors' ethnicity, gender, gender preference, nationality, religious belief, or political philosophy. They must provide a fair peer-review process for the publication of the submitted articles. They must ensure that all information regarding the submitted letter is kept confidential until it is published. Editors are responsible for the content and overall quality of the publication. If necessary, they should publish a correction through the Erratum pages. The Editor should not allow any conflicts of interest or competition between authors, editors and reviewers. Only the Editor has full authority in the assignment of the reviewers in the Journal of Turkish Society for Rheumatology and is also responsible for the final decision on the publication of the articles.

PUBLICATION POLICY

All articles will be evaluated by the scientific committee in terms of their scientific contributions, originality and content. Authors are responsible for the accuracy of their data. The journal reserves the right to change the language and appropriate changes where it deems necessary. If necessary, the article is sent to the author for revision. Articles previously published in any language will not be accepted for publication in the journal. Authors cannot submit an article that is about to be published in another journal. All changes will be made after the written permission of the author and publisher. The full text of all articles can be downloaded from the journal's website, www.manuscriptmodule.com/raed.

The Editorial Policies and General Guidelines for manuscript preparation specified below are based on "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals (ICMJE Recommendations)" by the International Committee of Medical Journal Editors (2013, archived at http://www.icmje.org/).

Preparation of research articles, systematic reviews and meta-analyses must comply with study design guidelines:

CONSORT statement for randomized controlled trials (Moher D, Schultz KF, Altman D, for the CONSORT Group. The CONSORT statement revised recommendations for improving the quality of reports of parallel-group randomized trials. JAMA 2001; 285: 1987-91) (http://www.consort-statement.org/);

PRISMA statement of preferred reporting items for systematic reviews and meta-analyses (Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 2009; 6(7): e1000097.) (http://www.prisma-statement.org/);

STARD checklist for the reporting of studies of diagnostic accuracy (Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig LM, et al., for the STARD Group. Towards complete and accurate reporting of studies of diagnostic accuracy: the STARD initiative. Ann Intern Med 2003;138:40-4.) (http://www.stard-statement.org/);

STROBE statement, a checklist of items that should be included in reports of observational studies (http://www.strobe-statement.org/);

MOOSE guidelines for meta-analysis and systemic reviews of observational studies (Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting Meta-analysis of observational Studies in Epidemiology (MOOSE) group. JAMA 2000; 283: 2008-12).

GENERAL RULES

Apart from the features mentioned below, "International Committee of Medical Journal Editors (ICMJE). Uniform Requirements for Manuscripts" documents (www.icmje.org) should be taken as a basis.

The sections that should be included in the articles to be sent to the journal are as follows and should be presented in a way that each starts on a separate page:

Page 1: Title page

Page 2: Turkish Title, Abstract and Keywords

Page 3: Title, Abstract and Key Words in English

Page 4 and afterwards: Main Text

Next page: Resources

Next page: Table Explanation and Table (each table should be specified on a separate page)

Next page: Figure and Image Subtitles and Image / Shapes (each shape must be specified on a separate page)

Title Page

The title page should be considered in the following order:

1- The category in which the article was sent (clinical research, experimental study, review, case report, etc.)

2- Title of the article (the title should not exceed 80 characters and should not contain non-standard abbreviations)

3- Name, surname, contact addresses of the authors and the institution they work at the time of the research

4- The abbreviated title of the article, which is desired to appear at the top of the continuation pages when published in the journal and does not exceed 40 characters.

5- Supporting institutions and organizations, if any

6- If the article has been submitted before, details of the meeting it was presented

7- Communication information of the author to be contacted

8- Indicating the financial support regarding the content of the article, if any

Turkish Abstract

The research articles should consist of the "Objectives", "Methods", "Results", and "Conclusions" sections and should not exceed 250 words. An unstructured abstract should be provided in reviews and case reports. The abstract of case reports should not exceed 100 words. A minimum of 3 and a maximum of 6 keywords should be specified in the Turkish abstract page.

English Abstract

The research articles should consist of "Objectives", "Methods", "Results", and "Conclusions" sections and should not exceed 250 words. At least 3, maximum of 6 English keywords should be determined in the English Abstract page, and English title of the article should be added.

Main Text

The introduction should consist of the Patients / Materials and Methods, Results, Discussion and References sections. Abbreviations should be standard and should be explained in parentheses when they are used first. Internationally accepted units should be used in the measurements.

Tables, Figures and Images

It should be numbered in the order of use in the text, and unnecessary use should be avoided. In the photographs used in the cases, permission should be obtained, and necessary measures should be applied to prevent recognition. Attention should be paid to the quality of photographs and drawings if any. Editorial Board may request correction or renewal in tables, figures and pictures on the grounds that it is not of sufficient quality. Figures and pictures must be original. In order for the pictures, figures and graphics used in another publication to be published in our journal, the necessary permissions must be obtained by the authors and before applying for an article. A copy of the document indicating that the permit has been obtained must be sent to the journal with the article.

References

References should be selected from the ones that are up to date and necessary for the article. References in the text should be indicated in parentheses and numbered according to the order of use. Name of the journals should be abbreviated in accordance with PubMed rules, and abbreviations should not be used in the names of journals which are not included here. Citation of proceedings should be avoided. Manuscripts accepted by a journal but not yet published can be documented as required and used as a source. Information other than this, including unaccepted articles, can be used by stating that there is "unpublished observation" in the article. References should be written according to the examples below, and all the authors should be presented in references up to 6 authors, references which have more authors should be arranged in a way that ''et al.'' abbreviation will be placed at the end of the first three authors. The responsibility for the accuracy of the references belongs to the authors.

Examples

Periodical publication example in Turkish:

Göksedef D, Ömeroğlu NÖ, Denli Ş, Üreyen C, Sayılgan C, İpek G. Sistemik lupus eritematozuslu bir olguda aort yetmezliği nedeniyle aort kapak replasmanı. Cerrahpaşa Tıp Dergisi 2008;39:73-5.

Periodical publication example in a foreign language:

Wolfe F, Hawley DJ, Cathey MA. Termination of slow-acting antirheumatic therapy in rheumatoid arhritis: a 14-year prospective evaluatin of 1017 consecutive starts. J Rheumatol 1990;17:994-1002.

Example of periodical publication published in an online journal:

Yurdakul S. Is there really a higher risk for infection with anti TNF-alpha agents or is there a selection bias? Lett Ed Rheumatol 1(1):e110006. doi:10.2399/ler.11.0006

Example of book section:

Buchanan WW, Dequeker J. History of rheumatic diseases. In: Hochberg MC, Silman AJ, Smolen JS, Weinblatt ME, Weisman MH, editors. Rheumatology. Edinburgh: Mosby; 2003:3-8.

It is recommended that the prepared articles are reviewed according to the following checklist before being sent to the journal:

1- Title page

2- Abstracts (Turkish and English; maximum 100 words in case reports, maximum 250 words in others; structured in research papers)

3- Keywords (at least three each)

4- Main text (subheadings)

5- Resources (Compliance with ICMJE rules)

6- Figures, tables and pictures (numbering; subtitles; originality/ permission letter)

7- Application letter

8- Copyright Transfer Form (signed by all authors)

9- Conflict of Interest Declaration Form (if required)

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İçindekiler / Contents

Orijinal Araştırmalar / Original Article

Olgu Sunumları / Case Reports

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Sevgili Okurlarımız,

Ulusal Romatoloji Dergimiz (eski adıyla RAED dergisi) daha önce düzenli bir şekilde yayımlanarak EBSCO, J-Gate, Index Copernicus, EuroPub ve GALE indekslerine girmeyi başarmıştı. 2022 yılı itibari ile gerekli kriterleri karşılayarak ULAKBİM'e (TR dizin) de katılmış bulunuyoruz.

Dergimizin bu noktaya gelmesinde emeği geçen Editör Kurulundaki tüm arkadaşlarıma, TRD Yönetim Kuruluna, Dernek Sekreterimize ve siz yazar ve hakemlerimize yine çok teşekkür ediyorum.

Bu yeni dönemde, ULAKBİM bünyesinde kalabilmemiz için de çok önem taşıyan, orijinal araştırma sayılarımız hızla artıyor. Bu sayımızda ilk kez İngilizce olarak yayınlanan çalışmalar çoğunluğu oluşturuyor. Orijinal makalelerimizden ilkinde Berna Cafer Karalar ve ark. romatoid artrit'li (RA) bireylerde "öz bakım davranışları ölçeğinin" Türkçe geçerlilik ve güvenirliliğini değerlendiriyorlar. Sonraki iki Behçet hastalığı (BH) yazımızdan ilkinde Lütfi Akyol ve ark. hastalığın önemli bir damar tutulumu olan serebral sinüs trombozu ile ilgili deneyimlerini paylaşırken, diğer yazıda Ahmet Kor ve ark. Behçet hastalığı ile iskemi modifiye albümin ve tiyol molekülleri arasındaki ilişkiyi ve BH'ye bağlı gelişebilecek komplikasyonlarda bu moleküllerin serum düzeylerini değerlendiriyorlar. Son yazımızda da Sevtap Acer Kasman ve Mehmet Engin Tezcan RA'lı hastalarda akciğer tomografisindeki bulgular ile demografik, klinik ve komorbid risk faktörleri arasındaki ilişkiyi araştırıyorlar. Ayrıca 4 ilginç olgu sunumu da bu sayıda yer alacak.

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Validity and reliability of the Turkish version of "self-care behaviour scale" in patients with rheumatoid arthritis

Romatoid artritli bireylerde "öz bakım davranışları ölçeğinin" Türkçe geçerlilik ve güvenilirliği

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Abstract

Objective: Rheumatoid arthritis is a chronic disease that requires long-term medication, has several side effects and limits the individual's daily life that may cause self-care deficiency. Therefore, self-care behaviors of the patients should be identified systematically and self-care behaviors should be supported accordingly. This study aimed to analyze whether or not the scale of self-care behavior was a valid and reliable tool to measure self-care behaviors in the Turkish rheumatoid arthritis population.

Methods: The study was conducted between February 1, 2017 - August 30, 2017 in a rheumatology clinic of a university hospital. For language validity, the scale was translated from English and then translated from Turkish to English. For the validity of the items of the translated scale, ten expert opinions were obtained and finalized the scale and consequential form was applied to 119 patients.

Results: Cronbach's Alpha value was found to be 0.675 for internal consistency analysis in accordance with the original values of the scale. Additionally, because of expert opinions, Cronbach's Alpha value obtained by reversely scoring the first three items were 0.558.

Conclusion: Because of the validity and reliability analysis of the Self-Care Behavior scale, it is found that it is a moderately reliable and valid scale for the Turkish society; It is recommended that the items in the scale may cause misunderstandings about patients' self-care, and therefore a Turkish scale that can measure self-care behaviors in a more valid and reliable manner is recommended.

Keywords: Self-care, reliability, validity, rheumatoid arthritis, rheumatology

Öz

Amaç: Romatoid artrit, uzun süreli ilaç tedavisi gerektiren, çeşitli yan etkileri olan, kişinin günlük yaşamını sınırlandırarak kendi kendine bakım eksikliğine neden olabilen kronik bir hastalıktır. Bu nedenle hastaların öz bakım davranışları sistematik bir şekilde belirlenmeli ve buna göre öz bakım davranışları desteklenmelidir. Bu çalışmanın amacı, öz bakım davranışı ölçeğinin Türk romatoid artrit popülasyonunda öz bakım davranışlarını ölçmek için geçerli ve güvenilir bir araç olup olmadığını incelemektir.

Yöntem: Çalışma 1 Şubat 2017 - 30 Ağustos 2017 tarihleri arasında bir üniversite hastanesinin romatoloji kliniğinde gerçekleştirilmiştir. Dil geçerliliği için ölçek İngilizceden çevrilmiş ve sonra Türkçe'den İngilizceye tekrar çevrilmiştir. Çevrilen ölçeğin maddelerinin geçerliliği için on uzman görüşü alınarak ölçeğe son şekli verilmiş ve sonuç formu 119 hastaya uygulanmıştır.

Bulgular: Ölçeğin orijinal değerlerine göre iç tutarlılık analizi için Cronbach's Alpha değeri 0,675 olarak bulunmuştur. Ayrıca uzman görüşleri sonucunda ilk üç maddenin ters puanlanarak elde edilen Cronbach's Alpha değeri 0,558'dir.

Sonuç: *Self-Care Behaviour* ölçeğinin yapılan geçerlik ve güvenirlik analizleri sonucunda Türk toplumu için orta düzeyde güvenilir ve geçerli bir ölçek olduğu saptanmakla birlikte; ölçekte yer alan maddelerin hastaların özbakımları ile ilgili yanlış anlamalara sebep olabileceği ve bu nedenle öz bakım davranışlarını daha geçerli ve güvenilir bir şekilde ölçebilecek Türkçe bir ölçeğin geliştirilmesi önerilmektedir.

Anahtar Kelimeler: Öz bakım, güvenilirlik, geçerlilik, romatoid artrit, romatoloji

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Introduction

Rheumatoid arthritis (RA) is a chronic, autoimmune, inflammatory rheumatic disease of unknown etiology affecting two or more joints and systems.[1] According to a RA prevalence study conducted in 2017, it has been determined between 0.41% and 0.54%. According to the study, an increase was determined in RA prevalence in the last decade.[2] According to a recent RA prevalence study conducted in Turkey, it was determined to be 0.56% for the individuals over the age of 16.[3] The aim of RA treatment is to provide the remission of patients, reduce their pain, prevent complications and side effects, have the individuals perform their daily activities, manage symptoms and prevent the poor prognosis.[4] RA treatment is a long process including the symptom management and effective communication with healthcare professionals and the self-care process. The important matter for the patients in the treatment process is the individual's compliance to treatment. This is because the individuals will have to use drugs continuously after diagnosed. Also, they should comply with the changes in their occupational and daily lives. The compliance includes social support and complementary treatment in addition to medical treatment. It is not right to expect that the individuals comply with all these factors completely. The World Health Organization (WHO) states that the compliance to treatment problems of the individuals with a chronic disease are at a severe level and the compliance to treatment levels of the individuals receiving long-term treatment are less than 50% in the developing countries.[5]

Self-care is described as "all the activities performed by the individuals to continue well-being, life, and health status" and it has been described by Orem, a nursing theoretician, as the activities performed continuously by the individuals, which are under the control of healthcare professionals and in which the individuals exhibit appropriate and intentional behavior by themselves.[6,7] Self-care in RA may be described as being able to administer medication, recognizing/managing side-effects, knowing and managing emergency cases, going for physician checks, performing daily and occupational activities independently, performing the sports activity appropriate for the individual and jointly determined, and complying with the diet offers.

There are some behavior for the patients with RA that will affect the course of the disease and they should and should not perform. But, the people who will control this behavior of the patients are healthcare professionals. In the literature, the deficiencies have mentioned the levels at which self-care behavior performed.[8] There is no self-care behavior scale prepared for the Turkish patients with RA to perform diagnosis. For this reason, it performed a reliability and validity study of the Self-Care Behavior Scale to use for determine the level at which the Turkish patients with RA perform self-care behavior. For this purpose, hypotheses are;

- Self-Care Behavior Scale is a valid tool to measure the level of self-care behavior in Turkish patients with RA.
- Self-Care Behavior Scale is a reliable tool to measure the level of self-care behavior in Turkish patients with RA.

Materials and Methods

Study Design

The study was planned in methodological type to test the reliability and validity of the Self-Care Behavior Scale in the Turkish patient population with RA.

Research Population and Sampling

The study was conducted in the rheumatology outpatient clinic of a university hospital between May 1st and August 30th, 2017. The population of the study was composed of 119 individuals with RA who agreed to participate and complied with the inclusion criteria. The individuals who were followed for more than six months for RA agreed to participate in the study, were over the age of 18, years were without any hearing and mental disability and was able to speak Turkish included in the study. Patients who were pregnant and did not comply with the inclusion criteria were excluded from the study.

Data Collection

Self-Care Behavior Scale, Multi-Dimensional Health Assessment Questionnaire, and Patient Identification Form were used as the data collection tools. The translation from English and Turkish and back translation were performed. For the content validity of the translated scale items, the opinions of 10 experts were received and the scale was put into the final form and this form was applied to the patients.

Patient Identification Form: The Patient Identification Form was prepared by the researchers by the literature support to obtain the socio-demographic data and the data on the disease and disease activity.

Self-Care Behavior Scale (SCBS): The Self-Care Behavior Scale to be tested in terms of reliability and validity, was developed by Morowatisharifabad et al.[9], in 2011. The scale particularly measures the self-care behavior of the patients with RA. The original version of the scale is composed of 17 questions and it includes the answers of never-hardly ever-sometimes-very often-always. In the original version of the scale, there is only one negatively scored question (4th question).

The content of the scale is composed of the questions on the hot application, using joint protectors, consulting a physician, being able to perform the daily routines, receiving food supplement or avoiding some food, massage application, distraction, social and emotional support, providing stress control, providing treatment regularly, resting and exercise, etc. Additionally, the exercise time is also asked. The answers to these questions are "never-10 minutes-20 minutes-30 minutes-more than 30" (Table 1).

Multidimensional Health Assessment Questionnaire [MDHAQ]

The original version of the Multidimensional Health Assessment Questionnaire was published by Pincus et al.,[10] in 1999. The Turkish reliability and validity study of MDHAQ was conducted by Gogus et al.[11] The scale is an extended form of the Health Assessment Questionnaire. The level at which the patient individuals perform daily activities is asked in the form. The answers are "easily (0) - a bit difficult (1) - with difficulty (2) - I can't perform (3)." The symptoms specific to RA may affect, restrict and prevent the daily activities of the patients. As the additional symptoms of the patients may also affect the self-care behaviors, whether there is morning stiffness and its time are investigated with pain and fatigue scale.

Language Validity Studies of the Scale

Firstly, the language validity was tested to test whether or not the Self-Care Behavior Scale was a reliable and valid tool in assessing at what level the Turkish patient population with RA performed self-care behaviors.

• Firstly, the translation of the scale from English, the original language, to Turkish was performed by the three people, who know both Turkish and English well, and did not see the scale before.

• The scale translated to Turkish was translated into English again by the three people, who know both Turkish and English well, and did not see the scale before.

• The texts which were translated into Turkish and English by different people were compared and it was checked whether they were the same or not.

Table 1. Cronbach alpha reliability coefficients of the "Self-Care Behavior Scale" original and after item reverse scoring

	Sample size (N)	Item number	Cronbach's alpha value
Self-Care Behavior Scale (original scale)	119	17	0.657
Self-Care Behavior Scale (item reverse scoring)	119	17	0.558

• After the assessment of the scale which checked, it was sent to 10 experts to receive their opinions.

• After receiving the opinions of the experts and performing the required corrections, the final form was prepared.

• The last form of the scale, which went through all phases was put into the process to be used in the study.

As the sample size for the scale application, is recommended to be used for patients, 5-10 times of the scale item number.[12] After the scale was put into its final form, 119 individuals with RA, who agreed to participate in the study, 7 times of the scale item number, composed the research sample and the scale applied.

Content Validity Studies of the Scale

After the language validity of the scale was performed, it was sent to ten experts, including four clinicians and six academicians, to determine its content validity and the scale form put into its final form based on the experts' opinions. This form was applied to the individuals included in the study.

Reliability Studies of Scale

Test-retest method used to test the reliability of the scale. The time between the two tests should be appropriate to test the time invariance of the scale. The scale is recommended to be used again in a period of two weeks and two months. But as the remission and attack periods of the individuals with RA are very changeable, this period was limited to 24 and 72 h based on the experts' opinions. Within this time, the test was applied again by reaching the individuals again. Pearson's Correlation coefficients of these two tests were calculated. The reliability coefficient should be greater than 0.70. The fact that the value is high and it approaches +1 indicates how reliable that measurement.[13,14]

Statistical Analysis

The data were processed in a computer environment by SPSS 16. It was determined that 83.2% of the patients with RA were female, 58% were homemakers, 66.4% were unemployed, 80.7% were married and 70.6% lived in the metropolitan area. The age average of the patients was 50.60±13.79, and 35.6% were within the age range of 46-59 years. 63.9% of the individuals were primary school graduates, 77.3% had lower income than their expenses, 93.3% lived in a nuclear family, 80.7% had children and 73.9% received care from the family members. The period of the disease ranged between 6 months and 43 years and it was averagely within the range of 12.27±9.04 and similarly the period of treatment was between 6 months and 38 years

and it was averagely within the range of 10.72±8.37. In the examination of the status of having treatment for the disease, it was determined that 56.3% did not receive training, 90.8% shared their problems with their relatives and 62.2% had deformity in their joints. It was determined that 56.3% of the patients had an additional disease and 34.9% had mostly the history of cardiovascular disease. 97.5% of the patients used medicine, 46.1% used disease-modifying anti-rheumatic drugs (DMARD), 66.4% had morning stiffness and the average stiffness period was 76.05±156.73 min. The mean score of the visual pain scale in which the patients assessed their pain for the pain values they experienced in the last week was 3.33±3.15. The mean fatigue level felt in the last week was 4.87±3.47 points. Also, when the well-being of the patients was examined compared to the last two weeks, it was observed that 53.8% answered as "good."

Results

Reliability Analyses of "Self-Care Behavior Scale"

Based on the original values of the scale, Cronbach's Alpha value for the internal consistency analysis was found to be 0.675 (Table 2). The first 3 items were reversely scored based on the experts' opinions and the Cronbach's Alpha value was determined to be 0.558 (Table 2). For the test-retest used for determining the time invariance of the scale, the first 30 patients who agreed to participate in the study and accepted to be reached by phone and could be reached when called. Because of the experts' opinion, the retest period was limited to 24-72 hours. The results were determined to be statistically significant (r=0.74 p=0.000) (Table 3). Table 4 shows the split-half reliability results of SCBS. It was determined that the Cronbach's Alpha value of the first half (1-9) was 0.450 and Cronbach's Alpha value of the second half (10-17) was 0.530, and the correlation between the two halves was 0.484. Guttman Split-Half coefficient was 0.652 and Spearman- Brown coefficient was 0.653.

Assessment of the Content Validity of the "Self-Care Behavior Scale"

Experts' opinions were received for the content validity. For the statements in some of the scale items, two experts recommended changes. It was recommended in the first translation that "Used a heated pool, a bor shower" statement for the 1st item should be changed as "Going into a hot water pool"; and the "heat" statement in the 2nd item should be changed as "hot application."

The scale was put into its final form with the revisions performed based on the recommendations.

Table 2. Correlation analysis results of the test-retest scores of "Self-Care Behavior Scale"

	N	R	P
Pretest	30	0.74	0.000
Posttest	30		

Table 3. Results of "Self-Care Behavior Scale" split-half reliability analyses

The split-half correlation value	0.484
Guttman split - half coefficient	0.652
Spearman - brown coefficient	0.653
1.Half (the first 9 items) alpha value	0.450
2.Half (next 8 Items) alpha value	0.530
Number of people (N)	119

Assessment of the Construct Validity of the "Self-Care Behavior Scale"

Factor Analysis

Principal Components Analysis and Varimax method were used for construct validity on SCBS. Because of the Principal Components Analysis, 61.268% of the variation was explained with 6 components. Because of the analysis Kaiser-Meyer Olkin (KMO) coefficient and result of Bartlett's test (X^2=528.55; p=0.000) was found to be statistically significantly Kaiser-Meyer Olkin (KMO) variance value found by both factors was determined to be 0.602%.Within the scope of the study, a significant correlation was determined between the SCBS score and income status, residence, gender and educational status ($p<0.05$).

Discussion

Self-care behaviors define the actions that individuals initiate and do for the continuation of the individual's life and the continuity of health and well-being.[15,16] The key factor in successfully managing RA is the inclusion of patients in self-care behaviors.[17] In chronic diseases such as RA, self-care covers a wide spectrum such as treatment and management of symptoms resulting from the pathophysiology of the disease, coping with the disease, compliance with treatment, social life and personal relationships.[18] The European Alliance of Associations for Rheumatology stated the importance of the role of the rheumatology nurses in increasing self-management skills, developing correct behavior and patient education to increase their competence.[19] For nurses, scales are needed to determine the self-care behaviors of patients with RA and the factors affecting them. There is no scale to measure the self-care behaviors of patients with RA in Turkey. For this reason, the Turkish validity and reliability of the SCBS were examined.

Table 4. Self-care behaviour scale Turkish form frequencies of scale items

	Never (n, %)	Almost Never (n, %)	Sometimes (n, %)	Very often (n, %)	Always (n, %)
Going into a hot water pool	101 (84.9)	8 (6.7)	9 (7.6)	0	1 (0.8)
Applied hot application to parts of your body	105 (88.2)	7 (5.9)	7 (5.9)	0	0
Used joint protection, bracing or splinting	99 (83.2)	1 (0.8)	15 (12.6)	3 (2.5)	1 (0.8)
Changed the dosage of your drugs or the time of taking them without informing your physician	71 (59.7)	17 (14.3)	23 (19.3)	3 (2.5)	5 (4.2)
Adjusted your daily routine or work schedule	19 (13.4)	19 (16)	34 (20)	20 (16.8)	30 (25.2)
Taken food supplements, vitamin or eaten special foods	76 (66.4)	3 (2.5)	7 (5.9)	5 (4.2)	25 (21)
Bewared certain foods	79 (66.4)	11 (9.2)	18 (15.1)	3 (2.5)	8 (6.7)
Used massage	70 (58.8)	7 (5.9)	26 (21.8)	9 (7.6)	7 (5.9)
Done other things such as watching TV or reading to take your mind off your artrhritis (distraction)	52 (43.7)	20 (16.8)	32 (26.9)	7 (5.9)	8 (6.7)
Talked with persons who are sympathetic	33 (27.7)	15 (12.6)	47 (39.5)	4 (3.4)	20 (16.8)
Used methods to help control stress	59 (49.6)	14 (11.8)	31 (26.1)	4 (3.4)	11 (9.2)
Used relaxation methods such as meditation	95 (79.8)	4 (3.4)	11 (9.2)	3 (2.5)	6 (5)
Taken your drugs regulary and based on your prescription	1 (0.8)	2 (1.7)	12 (10.1)	8 (6.7)	96 (80.7)
Visited your physician regulary	0	2 (1.7)	9 (7.6)	2 (1.7)	106 (89.1)
Rested	7 (5.9)	8 (6.7)	25 (21)	14 (11.8)	65 (54.6)
Exercised (including water exercise)	72 (60.5)	6 (5)	21 (17.6)	4 (3.4)	16 (13.4)
	More than 30 minutes	**30 minutes**	**20 minutes**	**10 minutes**	**Never**
If you exercise, how much minutes do you exercise per day?	11 (9.2)	9 (7.6)	8 (6.7)	15 (12.6)	76 (63.9)

Because of the study of Morowatisharifabad et al.[9] in which they evaluated the reliability and validity of the original version of the scale, the Cronbach's Alpha value was found to be 0.680. The Cronbach Alpha value of the SCBS in individuals with RA in Turkey was found to be 0.657. This value shows that the scale has moderate reliability.[13]

In this study, regular drug use (80.7%) and regular doctor control (89.1%) behavior are applied more than other behaviors by patients. Similarly, in another study, the most common behaviors were; drug management, physician follow-up, and nutritional supplementation.[20] In the study of Nadrian et al.,[21] it was stated that the lowest scores were "regular exercise, especially water exercises," "using relaxation methods such as meditation" and "using a heated pool, bathtub or shower" behavior.

The least applied behavior in this study are the behaviors such as 'used a hot water pool, applied hot application parts of your body and used joint protection, bracing or splinting'. Kordasiabi et al.,[20] on the other hand, listed the least applied behavior as water exercise, diet, massage and relaxation techniques.

In this study, it was found that gender, place of residence, education level, income status and the presence of deformity in the joints affected self-care behaviors. Similar to this study, it was determined that gender, age, marital status, education, occupation, income status, duration of illness, the presence of comorbidity and health belief affected self-care behaviors. According to the research findings, it was emphasized that patients should be evaluated in a broad perspective in determining their self-care needs and that nurses should consider these factors in patient empowerment.[22,23]

Studies have shown that patients with RA exhibit different behavior. Other comprehensive studies are needed to reveal different results in patients by applying the scale in different societies and cultures.

Conclusion

Because of the reliability and validity analyses of the SCBS, it was determined to be a moderately reliable and valid scale for Turkish society, however, as the items in the scale may cause misunderstanding about the self-care of patients, and thus it is recommended to develop a Turkish

scale that can assess the self-care behavior in a more reliable and valid way.

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Ethics

Ethics Committee Approval: Ethical permission was obtained from İzmir Katip Çelebi University of Non-interventional Clinical Studies Institutionel Ethics Committee (decision number: 2016/16) and institutional permission from the hospital.

Informed Consent: Written consent was obtained from each patient participating in the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: B.C.K., Design: B.C.K., Y.T., F.Ö., Data Collection or Processing: B.C.K., Analysis or Interpretation: B.C.K., Y.T., F.Ö., Literature Search: B.C.K., Y.T., F.Ö., Writing: B.C.K., Y.T., F.Ö.

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Cerebral venous sinus thrombosis in Behçet's disease: A retrospective single-centre study

Behçet hastalığında serebral venöz sinüs trombozu: Retrospektif tek merkezli bir çalışma

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Abstract

Objective: This study aims to analyze the clinical, laboratory findings, treatments and prognosis of Behçet's disease (BD)-associated cerebral venous sinus thrombosis (CVST) and to compare the clinical features of BD patients with and without CVST.

Methods: In this single-center retrospective study, we reported a series of 24 consecutive CVST patients (20 males and 4 females; mean age 34±12 years) were diagnosed with BD according to international study group criteria. The control group included 36 (24 males and 12 females; mean age 32±8 years) consecutive patients with BD without CVST from the same center.

Results: Headache (n=20, 83.3%) was the most common complaint at admission in patients with BD-associated CVST. In comparison between BD cases with and without CVST, extracranial vascular involvement was more frequent in the BD-associated CVST patients (p=0.03). Twenty-three (95.8%) patients received corticosteroid (CS) treatment. A total of 8 BD-associated CVST patients received anti-tumor necrosis factor-alpha (anti TNF-α) treatment. There was no significant difference in the rate of CS use before and after anti-tumor necrosis factor-α (TNF-α) treatment (p=0.345) but CS dose was significantly reduced after treatment (p=0.018). When patients with BD- associated CVST who receive or did not receive anti-TNF-α treatment compared, on cranial imaging, thrombosis was significantly less in patients received anti TNF-α treatment than who did not (p=0.02).

Conclusion: When the CVST was detected in young men patients with headache, BD should come to mind and patients should also be evaluated in this respect. As the risk of extracranial vascular involvement increases in such patients, they should be systematically evaluated in terms of vascular involvement. Although CS treatment could not be stopped completely with anti TNF-α drugs, it could be reduced. Significant radiological improvement was observed with anti-TNF-α treatment.

Keywords: Behçet's disease, cerebral venous sinus thrombosis, anti-tumor necrosis factor-α, treatment, neurobehçet

Öz

Amaç: Bu çalışmanın amacı, Behçet hastalığı (BH) ile ilişkili serebral venöz sinüs trombozunun (SVST) klinik, laboratuvar bulgularını, tedavilerini ve prognozunu analiz etmek ve SVST olan ve olmayan BH hastalarının klinik özelliklerini karşılaştırmaktır.

Yöntem: Bu tek merkezli retrospektif çalışmaya, uluslararası çalışma grubu kriterlerelerine göre BH tanısı konan 24 ardışık SVST hastası (20 erkek ve 4 kadın; ortalama yaş 34±12 yıl) dahil edildi. Kontrol grubu aynı merkezden 36 (24 erkek ve 12 kadın; ortalama yaş 32±8 yıl) SVST'si olmayan ardışık BH hastasıydı.

Bulgular: Baş ağrısı (n=20, %83,3) BH ile ilişkili SVST'li hastalarda başvuru sırasında en sık görülen şikayetti. SVST olan ve olmayan BH olguları karşılaştırıldığında, BH ile ilişkili SVST hastalarında ekstrakraniyal vasküler tutulum daha sıktı (p=0,03). Yirmi üç (%95,8) hasta kortikosteroid (KS) tedavisi aldı. Toplam 8 BH ile ilişkili SVST hastası, anti-tümör nekroz faktör (TNF-α) tedavisi aldı. TNF-α tedavisi öncesi ve sonrası KS kullanım oranında anlamlı fark bulunmadı (p=0,345), ancak tedavi sonrası KS dozu anlamlı olarak azalmıştı (p=0,018). BH ile ilişkili SVST olan ve anti-TNF-α tedavisi alan ve almayan hastalar karşılaştırıldığında, kraniyal görüntülemede, anti TNF-α tedavisi alan hastalarda tromboz, almayanlara göre anlamlı olarak daha azdı (p=0,02).

Sonuç: Baş ağrısı olan genç erkek hastalarda SVST saptandığında akla BH gelmeli ve hastalar bu açıdan değerlendirilmelidir. Bu hastalarda ekstrakraniyal vasküler tutulumu riski arttığından, vasküler tutulum açısından sistemik olarak değerlendirilmelidirler. Anti TNF-α ilaç tedavisi ile KS tedavisi tamamen kesilesemese de, dozu azaltılabilir. Anti-TNF-α tedavi ile belirgin radyolojik iyileşme gözlendi.

Anahtar Kelimeler: Behçet hastalığı, serebral venöz sinüs trombozu, anti-tümör nekroz faktör-α, tedavi, nörobehçet

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Introduction

Behçet's disease (BD) is a systemic vasculitis that can involve many tissues; patients often develop oral and genital ulcers.[1,2] Although many organs and systems can be affected, neurological involvement (neuro-BD) is uncommon. Both the central and peripheral nervous systems may be affected in such patients. The central nervous system (CNS) involvement may be parenchymal or non-parenchymal; the latter includes cerebral venous sinus thrombosis (CVST), arterial occlusion, and/or aneurysms. Although CVST is a major manifestation of non-parenchymal involvement, only a few case reports and few retrospective clinical series have described the treatment and long-term outcomes thereof. Primary treatment of neurological involvement in BD undoubtedly requires immunosuppression with or without corticosteroid (CS). Anti-tumor necrosis factor-α (anti-TNF-α) agents are now used for BD complications but experience on their effect on CVST is limited.[1,3,4]

Since data on the clinical features, disease course and outcome of BD-related CVST is limited, we tried analyzing the clinical, laboratory findings, treatments and outcomes of BD-associated CVST and compare the clinical features of patients with BD with and without CVST who were followed up in a single centre.

Materials and Methods

Patients

Between June 2014 and January 2018, patients diagnosed with BD according to the 1990 guidelines of the International Study Group or the International Criteria for Behçet's disease were included. CVST was diagnosed based on typical clinical features, magnetic resonance venography (MRV), cranial magnetic resonance imaging (MRI) features, and neurologist opinion. Patients with comorbidities (trauma, infection, malignancy, or oral contraceptive use) were excluded. The control group included thirty-six consecutive patients with BD without CVST from the same period. CVST patients were compared as patients who received and did not receive anti TNF-α treatment.

Methods

Data on 24 patients with BD-associated CVST and the 36 controls were retrieved from our electronic database and retrospectively reviewed. We recorded age at the onset of problems, and at diagnosis, along with disease duration, laboratory parameters, the cranial and extracranial locations of thromboses as revealed by imaging, and the course of cranial imaging over the years. The clinical findings were compared to those of the controls. Immunosuppressant (IS) and anticoagulant treatments prescribed at diagnosis, along with treatment duration and changes therein during follow-up, were recorded. Patients receiving anti-TNF-α treatment were examined in detail in terms of previous and ongoing treatments, treatment duration, and long-term results. The disease activity was evaluated by measuring the levels of clinical and acute phase reactants, imaging results and, patients on anti-TNF treatment, Behçet Disease Current Activity Form (BDCAF) scores. We contacted all patients by telephone.

The remission criteria were an absence of BD-related symptoms, no new vascular involvement or progression of existing vascular involvement, normal levels of acute phase reactants, and a methylprednisolone dose ≤10 mg/day for 3 months. Recurrence was defined as the development of new symptoms and/or sufficient progression of a pre-existing BD-related symptom to necessitate an increase or change in treatment. Infliximab was intravenously administered at an induction dose of 5 mg/kg during weeks 0, 2, and 6, and every 8 weeks thereafter. Adalimumab was given subcutaneously (40 mg every 2 weeks) along with etanercept (50 mg weekly).

The approval of the institutional ethical committee was obtained (University of Health Sciences Turkey, Gazi Yaşargil Training and Research Hospital, approval number: 541, date: 11.09.2020).

Statistical Analysis

Histograms and probability plots were generated. We used the Kolmogorov-Smirnov or Shapiro-Wilk test to determine whether variables were normally distributed. Continuous variables with normal distributions are expressed as mean ± standard deviation (SD); all other variables are expressed as median values (range). Categorical variables were compared using the chi-squared or Fisher's exact test. Continuous variables were compared using Student's t-test. Non-normally distributed continuous variables were compared using the Mann-Whitney U test and the Wilcoxon test. A p-value <0.05 was considered statistically significant. All tests were performed using SPSS for Windows software (ver. 22.0; IBM Corp., Armonk, NY, USA).

Results

Demographic Characteristics and Clinical Features

In total, 24 (20 males and 4 females) of 571 patients with BD (4.2%) were diagnosed with BD-associated CVST; 54

exhibited neurological involvement (9.4%), and headache [n=20 (83.3%) patients] was the most common complaint at admission. Three (12.5%) patients presented with oral aphthae and 1 (4.2%) patient with hemoptysis due to pulmonary artery aneurysm at admission.

Of the patients with CVST, the most common BD-related symptoms were oral aphthae in 24 (100%) and genital ulcers in 21 (87.5%) (Table 1).

Neurological Imaging

CVST was diagnosed using MRV and cranial MRI. A neuroradiologist (K.A.; 8 years of experience) reviewed all brain MRI scans while blinded to the clinical and laboratory data, and treatments. Multiple sinus involvement (19, 79.2%) was more common than single sinus involvement (5, 20.8%). No patient had a cerebral infarction, bleeding, or permanent neurological damage. The parenchymal involvement was observed in 32 (5.6%) patients and 2 (0.3%) exhibited both parenchymal involvement and CVST. All patients had control imaging including brain MRI and MR venography. In 10 of 23 patients at their final visit, CVST was continuing on MR venography and brain MRI.

Extracranial Thrombosis

In total, 16 (66.7%) patients exhibited extracranial vascular involvement; lower extremity deep vein thrombosis was seen in 8 (33.3%) patients, jugular vein thrombi in 7 (29.2%), and pulmonary thromboembolism in 6 (25.0%) (Table 1).

Laboratory Findings

The erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) level were elevated in 20 (83%) patients at admission. The mean ESR at presentation was 54.08 (0-20) mm/h, and the mean CRP level 66.7 (0-5) mg/dL. After 1 year, the ESR was higher in nine (39%) patients and the CRP level was higher in six (26%); the mean ESR and CRP level were 19.04 mm/h and 9.26 mg/dL, respectively. Compared to baseline, the values decreased significantly after 1 year (both $p<0.01$). Antinuclear antibody status was negative in 15 patients and weakly positive (≤1:160) in 2 patients. Anti-extracted nuclear antigen antibody status was negative in all patients. Of the 16 patients evaluated, all were negative for antiphospholipid antibodies (anticardiolipin antibody immunoglobulin G (IgG)/IgM, lupus anticoagulant, and anti-beta-2 glycoprotein (anti-ß2GPI) IgG/IgM]. HLA B51 analysis was performed in six (25%) patients; four (16.7%) were positive.

Table 1. Clinical and demographic characteristics of Behçet-associated CVST patients

Parameter	Values, n (%)
Age, mean ± SD (years)	34±12
Onset of symptoms, mean ± SD (years)	27.2±10.8
Age at diagnosis, mean ± SD (years)	27.9±10.8
Duration of the disease, mean ± SD (months)	80.7±59.1
Gender	
Male	20 (83.3)
Female	4 (16.7)
Localizations of Sinus Vein Thrombosis	
Transverse sinus	20 (83.3)
Superior sagittal sinus	18 (75.0)
Sigmoid sinus	16 (66.7)
Cavernous sinus	3 (12.5)
Symptoms	
Headache	20 (83.3)
Oral aphthae	3 (12.5)
Hemoptysis	1 (4.2)
BD-Related Clinical Findings	
Oral aphthae	24 (100)
Papuloustular lesion	14 (58.3)
Superficial thrombophlebitis	7 (29.2)
Erythema nodosum	3 (12.5)
Genital ulcer	21 (87.5)
Ocular involvement	8 (33.3)
Positive Pathergy test	6 (25)
Arthralgia	8 (33.3)
Arthritis	2 (8.3)
Localizations of Extracranial Vascular Involvement	**16 (66.7)**
Deep vein thrombosis	8 (33.3)
Jugular vein thrombosis	7 (29.2)
Pulmonary thromboembolism	6 (25.0)
Vena cava thrombosis	5 (20.8)
Iliac vein thrombosis	3 (12.5)
Pulmonary artery aneurysm	2 (8.3)
Cardiac thrombus	1 (4.2)
Treatments on CVST diagnosis	
Colchicine	16 (66.7)
Azathioprine	14 (58.3)
Corticosteroid (all)	23 (95.8)
Pulse corticosteroid	18 (75.0)
Cyclophosphamide (intravenous)	11 (45.8)
Anti TNF-α	1 (4.2)
Anticoagulant	19 (79.2)
Warfarin	16 (66.7)
Enoxaparin	19 (79.2)

BD: Behçet's disease, CVST: Cerebral venous sinus thrombosis, TNF-α: Tumor necrosis factor-alpha

Treatments and Outcomes

Treatments on CVST Diagnosis

Previous treatments included ISs and anticoagulants. In total, 16 (66.7%) patients with BD-associated CVST were prescribed colchicine and 14 (58.3%) were prescribed azathioprine. Twenty-three (95.8%) patients received CS (methylprednisolone or an equivalent) treatment. Eighteen (75%) patients received pulsed CSs and five (20.8%) received CS at a starting dose of 1 mg/kg/day, which that was gradually tapered and stopped. The pulsed protocol was methylprednisolone or an equivalent at 1 g/day for 3-5 days (induction), followed by 1 mg/kg/day (maintenance); the CS was then tapered or stopped. Eleven patients (45.8%) received pulsed cyclophosphamide (CYC) treatment (1 g per month, intravenously for 6 months, or 500 mg every 15 days). Anti-TNF-α (adalimumab) therapy was prescribed for one (4.2%) patient (40 mg subcutaneously every 2 weeks). Low-molecular-weight heparin (enoxaparin, 100 IU/kg x 2) was given during the acute period and then replaced with warfarin (used only for maintenance treatment). Before anticoagulant treatment, all patients were evaluated in terms of pulmonary artery aneurysms. Anticoagulant treatment was prescribed for 19 (79.2%) patients. All patients received enoxaparin (Table 1).

Treatment During Follow-up

Patients who received current treatments were evaluated at outpatient clinic visits every 1-3 months according to their clinical status after discharge. Ten of 16 (66.7%) patients who received colchicine treatment was switched to azathioprine and/or anti TNF-α treatment after one year because they were colchicine-resistant.

Initially, 18 (75%) patients received pulsed CS treatment. Two (8%) patients received repeat-pulsed treatments because of recurrence during follow-up. Of 23 (95.8%) patients prescribed CSs, the doses were reduced and ultimately discontinued in 16 (69.5%). At the last visit, 7 of 23 patients were receiving low dose (<10 mg/day) CS treatment.

Initially, 19 (79.2%) patients were prescribed anticoagulants, of whom 16 (66.7%) were followed up with warfarin only; 10 (43.5%) continued on both anticoagulants and warfarin. None of the 11 (45.8%) CYC-treated patients received a second CYC treatment after 6 months; all were switched to maintenance azathioprine. At the beginning, 14 (58.3%) patients received azathioprine treatment. Number of patients who were treated with azathioprine increased to 16 (66%) after one year. No patient who received colchicine, azathioprine, CYC and CS treatment developed any drug-related complications. Seven (29%) patients were switched to anti-TNF-α treatment because they were resistant to other treatments.

Analysis of CVST Patients Receiving Anti TNF-α Treatment

The mean age of eight patients (five males and three females) who received anti-TNF-α treatments was 30.6±8.3

Table 2. Clinical characteristics of Behçet's disease-associated CVST patients who received anti TNF-α treatment

Patient	Anti TNF-α treatment	Age	Previous treatment	The period before anti TNF-α treatment	The period of anti TNF-α treatment	Concomitant IS	Anti TNF-α related complication	Response at third month	Treatment at last visit
1	IFX	33	CS (pulse and maintenance) CYP, AC	5 months	64 months	CS, AZA	No	CR	IFX, AZA
2	IFX	25	CS (not pulse) CYP, AC	12 months	58 months	CS, AZA	No	CR	IFX, AZA
3	ADA	29	CS (pulse and maintenance) Colchicine, AC	4 months	70 months	CS, AZA	No	CR	ADA, AZA
4	IFX	38	Colchicine, AC	60 months	10 months	No	No	CR	IFX
5	ETN	21	CS (pulse and maintenance) Colchicine, AC	4 months	45 months	CS, colchicine	No	CR	ETA, CS, colchicine
6	IFX	21	CS (not pulse), Colchicine	108 months	24 months	CS, colchicine	No	CR	IFX, CS colchicine
7	IFX	45	CS (pulse and maintenance), Colchicine, AZA, AC	1 months	16 months	CS, AZA	No	CR	IFX, AZA
8	IFX	33	CS (pulse and maintenance), Colchicine, AZA, AC	12 months	60 months	CS, AZA	No	CR	IFX, AZA, AC

AC: Anticoagulation, ADA: Aadalimumab, AZA: Azathioprine, CR: Complete response, CS: Corticosteroid, CYC: Cyclophosphamide, ETN: Etanercept, IFX: Infliximab, IS: Immunosuppressant, TNF-α: Tumor necrosis factor-alpha

years; six of these patients were prescribed infliximab; one each received adalimumab and etanercept. The mean disease duration, which was 8.5 [minimum-maximum (min-max: 1-108)] months before anti-TNF-α treatment, increased to 51 (min-max: 10-70) months after anti-TNF-α treatment. The mean duration of CS use before anti-TNF-α treatment was 4 (min-max: 0-12) months and that after TNF-α treatment 2.5 (min-max: 0-45) months. There was no significant difference in the rate of CS use before and after anti-TNF-α treatment (p=0.345). The mean dose of CS before anti-TNF-α treatment was 34.1±22.2 mg/day, and that after anti-TNF-α treatment was 2.7±1.7 mg/day; the CS dose was significantly reduced after treatment (p=0.018). Although seven patients had received anticoagulants for an average of 3 months before anti-TNF-α treatment, this was then discontinued in six; only one patient received anticoagulants for 60 months (Table 2).

Seven of 8 CVST patients received anti TNF-α treatment had received CS treatment before anti TNF-α. At the last visit, 2 patients were continuing to receive CS treatment. When the patients received and did not receive anti TNF treatment were compared in terms of CS and anticoagulant use, there was no significant difference (p=0.679 and p=0.101, respectively) (Table 3).

During the follow-up period, all 23 patients were evaluated for CVST by MR venography and brain MRI. It was found that thrombosis continued in 10 patients. At the last visit of anti-TNF-α treatment, the cerebral venous thrombosis evident on cranial MRV disappeared in seven of the eight patients and did not recur (Figures 1 and 2). The thrombosis decreased in the other patient (Figure 3). On cranial imaging, thrombosis was significantly less in patients received anti TNF-α treatment than who did not (p=0.02)

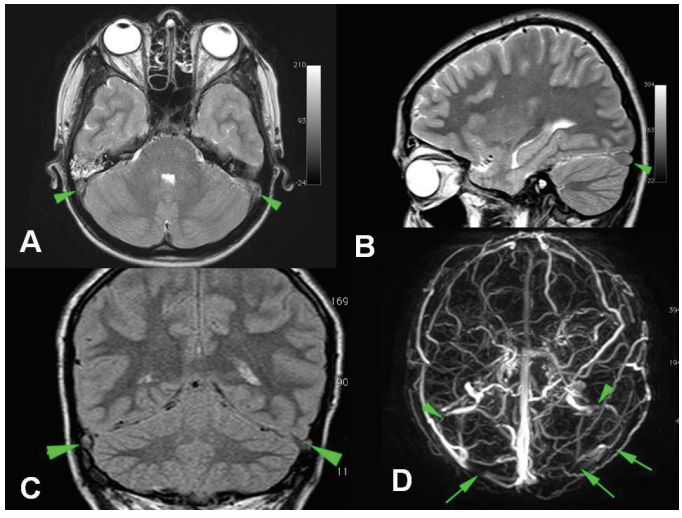

Figure 1. Magnetic resonance imaging before anti-TNF (A-D) of a 21-year-old female patient with dural venous sinus thrombus diagnosed with Behçet's. Axial T2-weighted MR (A), sagittal T2-weighted MR (B), and coronal FLAIR (C) images show thrombus in bilateral transverse sinuses (arrowhead). A magnetic resonance venography (D) shows thrombus in bilateral transverse sinuses (arrow) and sigmoid sinuses (arrowhead)

TNF: Tumor necrosis factor, MR: Magnetic resonance

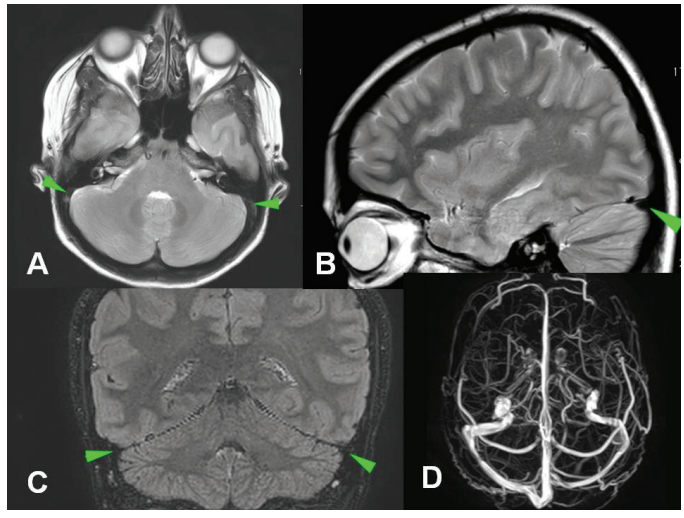

Figure 2. Magnetic resonance imaging after anti-TNF (A-D) of a 21-year-old female patient with dural venous sinus thrombus diagnosed with Behçet's. Axial T2-weighted MR (A), sagittal T2-weighted MR (B), and coronal FLAIR (C) images show no thrombus in bilateral transverse sinuses (arrowhead). A magnetic resonance venography (D) shows no thrombus in bilateral transverse sinuses (arrow) and sigmoid sinuses (arrowhead)

TNF: Tumor necrosis factor, MR: Magnetic resonance

Table 3. Comparison of the characteristics of BD-associated CVST patients in terms of anti TNF-α treatment

	BD-CVST received anti TNF treatment n, (%)	BD-CVST did not receive anti TNF treatment n, (%)	p-value
Age, mean ± SD (years)	30.6±8.3	37.2±13.5	0.222
Gender (male)	5 (62.5)	14 (93.3)	0.06
Duration of disease, mean ± SD (months)	65.3±32.6	94±67	0.271
On corticosteroid at last visit	2 (25)	5 (33.3)	0.679
On anticougulants at last visit	1 (12.5)	7 (46.7)	0.101
Thrombosis at the last cranial imaging	1 (12.5)	9 (60)	0.02
ESR (mm/h) at last visit (mean ± SD)	11±10	23.3±20	0.133
CRP (mg/dL) at last visit (mean ± SD)	3.8±3.6	12.1±20	0.267

BD: Behçet's disease, CRP: C-reactive protein, CVST: Cerebral venous sinus thrombosis, ESR: Erythrocyte sedimentation rate, SD: Standard deviation, TNF-α: Tumor necrosis factor-alpha

(Table 3). No patient who received anti-TNF-α treatment developed any permanent neurological sequelae or drug-related complications.

Comparison Between BD Cases with and without CVST

The control group included thirty-six consecutive patients with BD without CVST from the same period; they all had oral aphthae. Skin involvement was more common in the controls, while the extracranial vascular involvement was more frequent in the patients with BD with CVST (p=0.03 and p=0.03, respectively) (Table 4).

Discussion

Of all patients with BD, 9.4% showed neurological involvement. The incidence rates of CVST were 4.2% in BD and 44% in neuro-BD patients. Anti-TNF-α treatment was relatively safe and effective in patients with BD-associated CVST; most patients exhibited no recurrence. The frequency of neuro-BD ranges from 5% to 35%.[5] In an autopsy series, 20% of 170 patients with BD exhibited neurological involvement.[6] Bolek et al.[7] reported a neuro-BD rate of 18.4%. Among a cohort of 820 patients with BD, 64 (7.8%) had CVST. The prevalence of CVST in neuro-BD patients varies from 10% to 20%.[8,9] In this study, the rate of neurological involvement among all patients with BD was 9.4%. The incidence of CVST in patients with BD was 4.2%, compared to 44% in neuro-BD patients. Although some studies found that CVST was more common in males (65.6% and 68.5% of all patients), others reported no gender difference.[4,8,10] We found that the disease was significantly more common in young males (83.3%). The CVST disease duration was approximately 6.5 years. The most common initial complaint was headache; most patients presented to the neurology clinic. BD is the most common cause of CVST in some Middle Eastern countries.[11,12] The most common findings of BD-associated CVST are headache, focal neurological deficits, and changes in consciousness, which are mainly attributed to intracranial hypertension. Saadoun et al.[8] found that the initial complaint was often a severe headache that had developed a few days earlier, followed by fever and focal deficit. In an Italian study, the most common presentation of neuro-BD was an acute attack with motor symptoms and cognitive changes.[13] In contrast, most of our patients complained of sub-acute chronic and progressive headache, although some also showed behavioral changes. The parenchymal involvement was seen in only two CVST patients. No patient exhibited permanent neurological deficits, either at admission or during long-term follow-up. The headache improved in most patients. CVST patients may develop visual problems caused by neurological involvement or uveitis.[14] Eight of our CVST patients had uveitis, but none suffered permanent

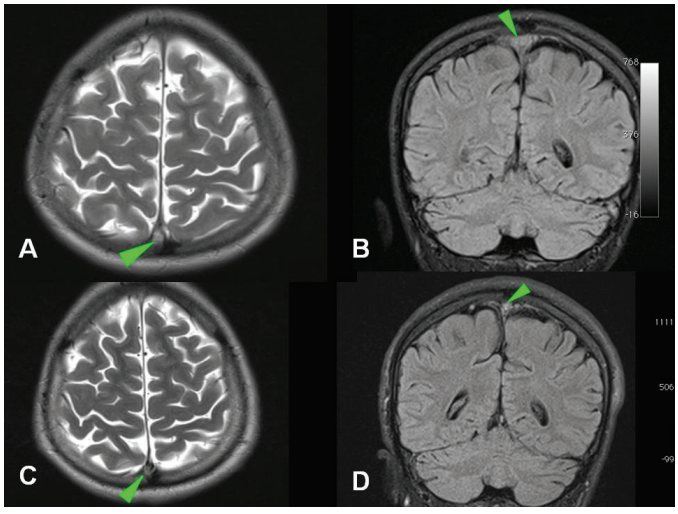

Figure 3. Magnetic resonance imaging before (A, B) and after (C, D) anti-TNF of a 21-year-old male patient with dural venous sinus thrombus diagnosed with Behçet's. Axial T2-weighted MR (A), and coronal FLAIR (B) images show thrombus in superior sagittal sinus (arrowhead). Axial T2-weighted MR (C), and coronal FLAIR (D) images show partial thrombus in superior sagittal sinus (arrowhead)

TNF: Tumor necrosis factor, MR: Magnetic resonance

Table 4. Demographics of patients with BD patients with and without CVST

	Behçet's with CVST n, (%)	Behçet's without CVST n, (%)	p-value
Age mean ± SD years	34±12	32±8	0.373
Gender (male)	20 (83.3)	24 (66.7)	0.144
Duration of the disease, mean ± SD (months)	80.7±59.1	74±40.7	0.265
Skin involvement	18 (75)	34 (94)	**0.03**
Genital ulcer	21 (87.5)	26 (72.2)	0.148
Ocular involvement	8 (33)	10 (27.8)	0.646
Positive Pathergy test	6 (25)	7 (19.4)	0.611
Arthritis	2 (8.3)	8 (22.2)	0.142
Extracranial vascular involvement	16 (66.7)	14 (38.9)	**0.03**
Gastrointestinal system involvement	0 (0)	1 (2.8)	0.309

BD: Behçet's disease, CVST: Cerebral venous sinus thrombosis, SD: Standard deviation

vision loss. As the gold standard imaging modalities, MRV and cranial MRI, which were used in this study, play critical roles in CVST diagnosis. Approximately 80% of our patients exhibited involvement of more than one sinus. The transverse sinus was the most commonly involved, followed by the superior sagittal sinus, consistent with the literature.[4,15] Two-thirds of patients exhibited extracranial vascular involvement: arterial involvement (pulmonary artery aneurysms and thrombi) was seen in eight patients, while venous and cardiac thromboses were observed in all other patients (mostly deep vein thromboses in the lower extremities). Compared to the patients with BD without CVST, extracranial vascular involvement was more common in CVST patients. As reported by Shi et al.,[4] among others, when BD is complicated by thrombosis, any vascular thrombus increases the risk of other thromboses.[16] Tunc et al.[17] found that, in BD patients with CVST, the risk of extracranial vascular involvement was high. Therefore, after the diagnosis of BD-associated CVST, all patients should be thoroughly evaluated for possible vascular involvement of other organs (including the heart). Although CSs are the cornerstone of treatment for neuro-BD, colchicine, azathioprine, and CYC serve as steroid-sparing agents that prevent relapse.[18] High-dose CS and CYC treatments are recommended for patients with BD exhibiting major organ involvement, but long-term use is limited by toxicity. In our study, five (20%) patients received high-dose CSs and 2 (8%) were given CYC before anti-TNF-α treatment.

TNF-α is a major proinflammatory cytokine that plays a critical role in the pathogenesis of BD. It is widely accepted (including by the European League Against Rheumatism) that anti-TNF-α agents (usually infliximab, adalimumab, and etanercept) are effective for treating BD.[19-21] In our study, six (25%) patients received infliximab, while one (4%) received adalimumab and another (4%) etanercept. There was no recurrence in any patient during 43 months of anti-TNF-α treatment. Significant clinical and laboratory improvements were evident by 3 months. Seven patients had received CSs for an average of 4 months before anti-TNF-α treatment, and initially remained on the CSs. However, these were discontinued after 3 months in four patients, and after 24 months in the remaining patient.

At the final follow-up, only two patients were taking ≤4 mg/day methylprednisolone or equivalent. Although the duration of CS use before and after anti-TNF-α treatment did not differ between the patients (p=0.345), the CS dose decreased significantly after anti-TNF-α treatment (mean ± SD, 34.1±22.2 to 2.7±1.7 mg/day, p=0.018). In patients with BD-associated CVST and vascular BD, it is unclear how long anti-TNF-α treatments should be given. Aksoy et al.[22] reported recurrence in two of three patients with vascular BD who discontinued anti-TNF-α treatment. Our patients were followed up for an average of 43 months; all entered remission during month 3 and none suffered recurrence. The mean BDCAF score was 2.2±1.4 at baseline and decreased significantly to 0.5±0.9 at month 3, and 0.3±0.5 at the last follow-up (both p=0.01). Cranial MRI revealed complete resolution of the thromboses of seven patients, but significant recanalization was seen in one case. No patient had any treatment-related complications. In a series of neuro-BD patients, the mortality rate was reported to be around 10%. Neuro-BD patients with CVST have better prognoses than those with parenchymal involvement.[23,24] Saadoun et al.[8] reported only 4 deaths (6%) among 64 patients followed up for a mean of 8 years; diseases other than BD (e.g. myocardial failure) or parenchymal neurological involvement attributable to BD caused the deaths. The mortality rate was similar to that of patients with CVST unrelated to BD.[25] In our study, one (4%) patient died of myocardial infarction outside the hospital. Our findings are consistent with the literature. Although the use of anti-TNF-α drugs to treat parenchymal neuro-BD has received some attention,[7,26] their use in neuro-BD patients with CVST is limited and the studies were retrospective. Although the number of patients is small, we found that long-term anti-TNF-α agents can be safely used to treat CVST, which is the best-known form of non-parenchymal neuro-BD. Although CS treatment could not be stopped completely with anti TNF-α drugs, it could be reduced.

Study Limitations

Our study was retrospective and no disease activity index was universally applied to evaluate neuro-BD activity. Therefore, we used the BDCAF index adopted in other studies to evaluate anti-TNF-α treatment efficacy. Other patients were evaluated according to the absence of CVST-related disease activity, the laboratory and imaging results, and the CS doses required.

Conclusion

As the risk of extracranial vascular involvement increases in BD-CVST patients, they should be systematically evaluated in terms of vascular involvement. Although the number of patients is small, we found that long-term anti-TNF-α treatment was safe and effective. Although CS treatment could not be stopped completely with anti TNF-α drugs, it could be reduced. Significant radiological improvement was observed with anti-TNF-α treatment.

Ethics

Ethics Committee Approval: The approval of the institutional ethical committee was obtained (University of Health Sciences Turkey, Gazi Yaşargil Training and Research Hospital, approval number: 541, date: 11.09.2020).

Informed Consent: Retrospective study.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: L.A., M.S., Design: L.A., Data Collection or Processing: L.A., K.A., C.G., Analysis or Interpretation: L.A., K.A., M.Ö., M.S., Literature Search: L.A., Writing: L.A.

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Ischemia-modified albumin levels are elevated, and thiol/disulfite homeostasis is impaired in Behçet's disease

Behçet hastalığında iskemi modifiye albümin düzeyleri yükselmiş, tiyol/disülfit homeostazisi ise bozulmuştur

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Abstract

Objective: To investigate the relationship between Behçet's disease (BD) and ischemia-modified albumin (IMA) and thiol molecules and to evaluate serum levels of this molecule in complications that may develop due to BD. BD is a vasculitic disease characterized by recurrent oral starring scarring genital ulcerated lesions and triple complex symptoms of uveitis, histopathologically involving perivascular tissues and vascular wall. It is thought that the mechanism responsible for vascular damage may be immunoregulatory system dysregulation and increased oxidative stress. In this study, serum levels of IMA and native thiol (-SH), total thiol (-SS+-SH), disulfide (-SS) were evaluated in BD and different clinical presentations of the disease.

Methods: Thirty-nine Behçet's patients and 40 healthy volunteers were included in the study. IMA, -SH, and -SS levels were measured using the spectrophotometric (Sigma-Aldrich Chemie GmbH Riedstrasse 2, Steinheim, Germany) method. Statistical analysis were performed using the SPSS version 21.0 package program.

Results: In our study, the mean IMA (p<0.001), -SS/-SH (p<0.01), and -SS/(-SS + -SH) ratios (p<0.01) were found to be significantly higher in Behçet's patients compared to the control group. In receiver operating characteristic (ROC) analysis, the highest associated value with BD was found in IMA (p:0.001, AUC:0.713). In BD, no significant difference was found between those with mucocutaneous involvement and those with organ involvement in terms of IMA and thiol/disulfide parameters (p>0.05).

Conclusion: In our study, we found that IMA serum levels were high, and -SS/-SH and -SS/(-SS + -SH) ratios were significantly low in BD.

Keywords: Behçet's disease, thiol/disulfide homeostasis, IMA

Öz

Amaç: Behçet hastalığı (BH) ile iskemi modifiye albümin (İMA) ve tiyol molekülleri arasındaki ilişkiyi araştırmak ve BH'ye bağlı gelişebilecek komplikasyonlarda bu moleküllerin serum düzeylerini değerlendirmektir. BH rekürren oral aft, skar bırakan genital ülsere lezyonlar ve üveitin üçlü kompleks semptomları ile karakterize, histopatolojik olarak perivasküler dokuları ve vasküler duvarı tutan vaskülitik bir hastalıktır. Vasküler hasardan sorumlu mekanizmanın immünoregülatör sistem disregülasyonu ve oksidatif stres artışının olabileceği düşünülmektedir. Bu çalışmada BH'de ve hastalığın farklı klinik prezentasyonlarında İMA, native thiol (-SH), total thiol (-SS+-SH) ve disülfit (-SS) serum düzeyleri değerlendirilmiştir.

Yöntem: Çalışmaya 39 Behçet hastası ve 40 sağlıklı gönüllü dahil edilmiştir. İMA, -SH ve -SS düzeyleri spektrofotometrik (Sigma-Aldrich Chemie GmbH Riedstrasse 2, Steinheim, Germany) yöntemle ölçülmüştür. İstatistiksel analizler SPSS versiyon 21.0 paket programı kullanılarak yapılmıştır.

Bulgular: Çalışmamızda Behçet hastalarında kontrol grubuna göre İMA ortalaması (p<0,001), -SS/-SH (p<0,01) ve -SS/(-SS + -SH) oranları (p<0,01) anlamlı olarak yüksek bulunmuştur. -SH (p<0,001), -SS +-SH (p<0,001) plazma seviyeleri ve -SH/İMA (p<0,01), (-SS + -SH)/İMA (p<0,01) oranlarının ise Behçet hastalarında kontrollere göre önemli düzeyde daha düşük olduğu tespit edilmiştir. Alıcı işlem karakteristiği [Receiver Operating Characteristic (ROC)] BH ile en yüksek ilişkili değerin İMA'da olduğu bulunmuştur (p:0,001, AUC: 0,713). Behçet hastalarında farklı klinik prezentasyonlar (vasküler, oküler, nörobehçet, mukokutenöz) ile çalışma parametleri arasında yapılan çoklu anova testlerinde anlamlı fark saptanmamıştır (p>0,05).

Sonuç: Çalışmamızda BH'de İMA serum seviyeleri ile -SS/-SH ve -SS/(-SS + -SH) oranlarının istatistiksel olarak anlamlı olacak şekilde hastalıkla ilişkili olduğu tespit edilmiştir.

Anahtar Kelimeler: Behçet hastalığı, tiyol/disülfit homeostazisi, İMA

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Introduction

Behçet's disease (BD) is a variable vascular vasculitis that is characterized by non-scarring recurrent oral starring scarring genital ulcers, histopathological involvement of the vascular wall and perivascular tissues.[1] Although the mechanisms causing vascular involvement have not been elucidated, it is primarily characterized by autoinflammation of the vascular wall. It is thought that immunoregulatory system dysregulation and increased oxidative stress may be associated with the development of vascular damage.[2] Bacterial and viral infections, dysregulations in humoral and/or cellular immunity are thought to affect the etiopathogenesis of the disease with genetic factors. The role of the *HLA-B51* gene, which is positive in nearly 60% of Behçet's patients, in the development of the disease is not fully known.[3,4] Since there are no specific diagnostic biochemical tests and histopathological indicators, the diagnosis of the disease is made according to clinical findings. The time required for a definitive diagnosis can usually be extended up to several years after the first symptoms appear. The prolongation of this period is due to the inconsistency of clinical findings among patients, and the prognosis of the disease depending on geographical, ethnic, and personal differences.[5] Available biomarkers in the diagnosis of BD are not yet sufficient for diagnosis and cannot predict the course of the disease and the response to treatment. There are 585 amino acids in the structure of human plasma albumin. Under physiological conditions, any metal element (cobalt, nickel, copper) can be attached to the N-terminus of the first 3 amino acids in the structure of albumin. Metal-binding capacity may vary depending on hypoxic-ischemic conditions. The form formed by hypoxia events that change the structure of serum albumin is called ischemia-modified albumin (IMA). Ischemia-reperfusion injury increases plasma IMA levels.[6,7] IMA is accepted as a sensitive biomarker as an indicator of ischemia-induced myocardial ischemia in acute coronary syndrome.[8] Additionally, increased IMA plasma levels have been shown in other diseases associated with increased oxidative stress, such as psoriasis, rheumatoid arthritis, and inflammatory bowel diseases.[9-12]

The increase in reactive oxygen species (ROS), which occurs during cellular metabolism such as sueroxide radicals, hydroxyl, and hyhydrogeneroxide, and the deterioration of the oxidative balance due to the inadequacy of the antioxidant level responsible for their neutralization causes the development of oxidative stress. The increase in ROS damages the double bond-containing areas of intracellular proteins and lipids and the double bonds of bases in the structure of DNA. Oxidative stress causes chain oxidation reactions by breaking a hydrogen atom from the double bonds. As a result, cell injury and cellular death occur due to damage to molecular structures such as intracellular proteins, lipids, and DNA.[13] In previous studies in rheumatological diseases, an increase in plasma levels of oxidant radicals secondary to autoimmunity and inflammation was found.[14,15] Similarly, it has been shown that increased oxidative stress also affects the pathophysiology of BD, and the antioxidant level decreases in the plasma of patients.[16] Thiols are one of the main reducing molecules in the human body. ROS produced in various events in the organism are converted into oxidized forms by transferring the excess electrons in their body to thiols. Thus, reversible disulfide bonds are formed. These bonds can be converted back to their old thiol forms when necessary to maintain oxidant-antioxidant hemostasis in the organism. This cycle, which is defined as dynamic thiol-disulfide homeostasis, has important roles in many events such as antioxidant protection mechanism, enzymatic activation, apoptosis, and intracellular signal transduction.[17] Thiol disulfide balance also changes in hepatic damage, cardiovascular events, central nervous system diseases, diabetes mellitus, malignancy, advanced age, and complications related to pregnancy.[18]

Although IMA levels or thiol-disulfide homeostasis have been evaluated alone in different studies in BD, the relationship of these two parameters with each other and with the complications that may develop due to the disease has not been evaluated before. This study was conducted to investigate the relationship between BD and IMA and thiol molecules and to evaluate serum levels of this molecule in complications that may develop due to BD.

Materials and Methods

Patients

A total of 39 Behçet's patients (mean age: 38.74±9.30 years) consisting of 13 females and 26 males, diagnosed according to the 1990 Behçet's Disease International Study Group criteria, followed in the rheumatology department of Ankara City Hospital, and for the control group, 40 healthy volunteers (mean age: 38.8±9.8 years) consisting of 14 females, and 26 males were included. Grouping according to clinical organ involvement patterns in Behçet's patients was made retrospectively from file scanning.

Obtaining Sample Samples and Calculating IMA and Thiol-Disulfide Values

Venous blood samples were taken into approximately 10 mL vacuum tubes and centrifuged at 1.300 g x for 10 min. The aliquoted sera were stored in Eppendorf tubes at -80 °C until the time of analysis. Thiol/disulfide homeostasis parameters were calculated using the automatic spectrophotometric method described by Erel and Neselioglu.[18] In this method,

first, sodium borohydride and disulfide bonds were reduced to free functional thiol groups. The reduced and native thiol (-SH) groups were calculated after the reaction with DTNB [5,5'-dithiobis-(2 nitrobenzoic) acid]. Half of the difference between the total thiols and -SH provides the dynamic disulfide amount. After the determination of disulfide (-SS) and -SH, total thiols (-SH+-SS) amounts, disulfide/native thiol percent ratios (-SS/-SH), disulphide/total thiol percent ratios [-SS/(-SH+ SS)] and native thiol/total thiol percent ratios [-SH/(-SH+-SS)] calculated. To calculate IMA from venous blood samples, the samples were left at room temperature for half an hour and then centrifuged at 3.500 rpm for 5 min. Samples transferred to Eppendorf tubes in aliquots were stored at -80 ºC until analysis. IMA level was measured using the Albumin Cobalt Binding test. This test was performed by mixing the patient's serum with 50 mL of 0.1% cobalt (II) chloride ($CoCl_2$,$6H_2O$) solution (Sigma-Aldrich Chemie GmbH Riedstrasse 2, Steinheim, Germany). After 10 min of incubation, 50 mL of 1.5 mg/mL dithiothreitol was added to the mixture to induce cobalt binding to the albumin. After a further 2 min incubation, 1.0 mL of a 0.9% sodium chloride solution was added to the mixture to measure the binding capacity. Absorbance determination from the samples was performed using a spectrophotometer at 470 nm. The data obtained are shown as absorbance units (ABSU). After measuring -SS, -SH and -SS + -SH levels, -SS/-SH, -SS/(-SH + -SS) and -SH/(-SH + -SS) percentage ratios were calculated.

Statistical Analysis

Kolmogorov-Smirnov test was used to determine the normal distribution of continuous variables. Independent sample t-tests and Mann-Whitney U test were used to evaluate the presence of a statistically significant difference between the patient and control groups. Pearson correlation analysis was used between parameters in the analysis of correlations. The variables' parametric and non-parametric statistical results are shown as mean ± standard deviation and median (minimum-maximum), respectively. The statistical analyses were performed using the Statistical Packages for the Social Sciences (SPSS) version 22.0 package program. The $p<0.05$ level was taken as the lower limit that was considered statistically significant. While testing the diagnostic accuracy measures of the indexes, receiver operating characteristic (ROC) analysis was used and area under the curve (AUC) was presented with 95% confidence intervals. Youden's index was used while determining the optimum cut-off value and diagnostic accuracy criteria for the cut-off value were presented.

Ethics Approval

The research protocol was approved by the Ankara Yıldırım Beyazıt University Faculty of Medicine Research Ethics Committee (approval number: 1613, date: 14.04.2021) and all patients gave informed written consent to participation in the study.

Patient Consent for Publication

Not required.

Results

Patients with Behçet's disease (n=39), 13 female and 26 male, SS and 40 healthy volunteers, 14 females, and 26 male, were included in the study ($p>0.05$). The mean age of Behçet's patients was 38.7±9.3 years, and the mean age of the control group was 38.8±9.8 years ($p>0.05$). Smoking, body mass index, and presence of comorbid diseases were found to be similar between Behçet's and control groups.

The patterns of organ involvement in the Behçet group and the data on the medical treatments used are shown in Table 1.

The relationship between drugs used with -SH, -SH+-SS, -SS, IMA levels, and -SS /-SH, -SS /(-SH+ SS) values were evaluated with multiple variance analysis ANOVA Post-hoc tests test. No statistically significant difference was observed between the different types of treatments used in Behçet's and these parameters ($p>0.05$). In the evaluation of study parameters in different organs involvement in BD, no statistically significant difference was found between clinical patterns and these parameters ($p>0.05$).

There was no significant difference in study parameters between those only mucocutaneous involvement and those organ involvement in BD (Table 2).

Table 1. Data on organ involvement patterns and medical treatments used in the Behçet group

Parameters	**n (%)**
Mucocutaneous Behçet	13 (33.3)
Neurobehçet	2 (5.1)
Vascular Behçet	13 (33.3)
Ocular Behçet	6 (15.3)
Vascular and ocular Behçet	5 (12.8)
Medical therapy	**n (%)**
Colchicine	36 (82.3)
Corticosteroids	17 (43.5)
Azathioprine	19 (48.7)
Anti-TNF	5 (12.8)
Cyclosporine	2 (5.1)
Cyclophosphamide	3 (7.6)
Interferon	2 (5.1)

Anti-TNF: Anti-tumor necrosis factor

Data on the comparison of study parameters between Behçet's and control groups are shown in Table 3. In the Behçet group -SH (488.77±46.68), -SH+-SS (549.95±69.77), -SH/IMA (511.07±67.13) and (-SH+-SS)/IMA (549.95±69.77) levels compared to the control group [-SH (529.67±55.96), -SH+-SS (629.59±104.65), -SH/IMA (589.76±98.88), (-SH+-SS)/IMA (629.59±104.65)] were found to be significantly low (p<0.001). The rates of -SD/-SH (3.84±0.87) and -SD/(-SH+-SD) (3.55±0.75) in Behçet's patients compared to the control group [-SD/-SH (3.39±0.81), -SS/(-SH+-SS) (3.16±0.71)] was found to be significantly high, while the mean of -SH/(-SH+-SS) was found to be significantly lower (p<0.01). When compared according to IMA levels, the mean of IMA was found to be significantly higher in the Behçet group (0.96±0.06) than in the control group (0.90±0.06) (p<0.001). There was no significant difference between the groups in terms of white blood cells, C-reactive protein, erythrocyte sedimentation rate (ESR), -SS (p>0.05). Figure 1 shows the distribution of IMA, s and Figure 2 shows the distribution of -SS/-SH, SS / (-SH+-SS) levels among the groups.

Table 4 shows the ROC analysis results of -SS/-SH, -SS/(-SH+-S), and IMA levels in BD. The highest value associated with BD was observed in IMA (p=0.001). When a cut-off value of 0.99 was taken for IMA in BD, it was determined that the test gave a sensitive confidence interval of 30.8% sensitivity and 97.5% specificity (AUC=0.713) Figure 3. shows the ROC analysis graph of the operating parameters in BD.

Table 5 shows the correlation between the study parameters. It has been determined that there is a statistically significant negative correlation between IMA and -SH (r:-0,504, p<0.01), -SH+-SS (r:-0,532, p<0.01) ve -SS (r:-0,249, p<0.05) levels. It was determined that there was a statistically significant positive correlation between IMA and CRP (r:0,238, p<0.05) levels.

Discussion

The etiology of BD, which is a systemic vasculitis, is not yet known. The increase in oxidative stress is thought to be an important factor in vascular injury. Stimulated neutrophils produce oxygen intermediates that cause auto-

Table 2. Comparison of patients with only mucocutaneous involvement and those with organ involvement in terms of study parameters in Behçet's patients

Parameters	Only mucocutaneous (n=13)	Organ involvement (n=26)	p-value
-SH, mean ± SD [μmol/L]	494.89±51.09	484.82±46.50	<0.05
-SH+-SS, mean ± SD [μmol/L]	530.14±48.50	523.80±48.47	<0.05
-SH/IMA, mean ± SD [%]	513.37±65.98	508.59±66.72	<0.05
(-SH+-SS)/IMA, mean ± SD [%]	550.05±66.79	549.51±71.07	<0.05

All values were expressed as mean ± SD. All values were calculated using the independent samt-test test for normal distribution. -SS: Disulphide -SH+-SS: Total Thiol, IMA: Ischemia Modified Albumin

Table 3. Comparison of study parameters between Behçet and control groups

Parameter	Behçet	Control	p-value
-SH, mean ± SD [μmol/L]	488.77±46.68	529.67±55.96	**<0.001**
-SH+-SS, mean ± SD [μmol/L]	549.95±69.77	629.59±104.65	**<0.001**
-SS, mean ± SD [μmol/L]	18.58±3.81	17.85±4.17	>0.05
-SS/-SH, mean ± SD [%]	3.84±0.87	3.39±0.81	**<0.01**
-SS /(-SH+-SS), mean ± SD [%]	3.55±0.75	3.16±0.71	**<0.01**
-SH/(-SH+-SS), mean ± SD [%]	92.88±1.51	93.66±1.42	**<0.01**
IMA, mean ± SD [ABSU]	0.96±0.06	0.90±0.06	**<0.001**
-SH/IMA, mean ± SD [%]	511.07±67.13	589.76±98.88	**<0.001**
(-SH+-SS)/IMA, mean ± SD [%]	549.95±69.77	629.59±104.65	**<0.001**
CRP mean ± SD [mg/dL]	0,007±0,0018	0.002±0.001	>0.05
ESR mean ± SD [mm/h]	11.20±7.32	10.025±5.74	>0.05
WBC, mean ± SD [x10^9/L]	7.23±1.89	6.59±1.23	>0.05
Hemoglobin, mean ± SD [x10^9/L]	13.73±1.94	14.19±2.84	>0.05
Creatinine mean ± SD [mg/dL]	0.78±0.16	0,43±0,15	>0.05
ALT mean ± SD [mg/dL]	35.02±15.52	27.30 ±13.46	>0.05

All values were expressed as mean ± SD. All values were calculated using the independent sample t-tests for normal distribution. -SS: Disulphide -SH+-SS: Total thiol, -SH: Native Thiol, IMA: Ischemia modified albumin, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, WBC: White blood cell, ALT: Alanine aminotransferase

Table 4. Specificity, sensitivity, and the cut-off levels of study parameters in Behçet.

	Cut-off	AUC (95% CI)	Sensitivity (%)	Specificity (%)	LR	p-value
-SH	524.2	0.313 (0.197-0.430)	30.8	62.5	0.82	0.004
-SH+-SS	518.7	0.329 (0.211-0.446)	61.5	72	0.82	0.009
-SS/-SH (%)	4.85	0.679 (0.560-0.798)	69.2	67.5	**2.13**	**0.006**
-SS/(-SH+-SS) (%)	4.42	0.679 (0.560-0.798)	69.2	67.5	**2.13**	**0.006**
-SH\(-SH+-SS) (%)	96.26	0.321 (0.202-0.440)	69.2	17.5	0.89	0.006
-SH\IMA (%)	534.53	0.381 (0.170-0.393)	43.6	45	0.79	0.001
(-SH+-SS)\IMA (%)	557.44	0.295 (0.181-0.408)	53.8	33.5	0.79	0.002
IMA	0.99	0.713 (0.600-0.825)	30.8	97.5	**4.10**	**0.001**

AUC: Area under the Curve, CI: Confidence interval, LR: Likelihood ratio. -SS: Disulphide -SH+-SS: Total thiol, -SH: Native thiol, IMA: Ischemia modified albumin

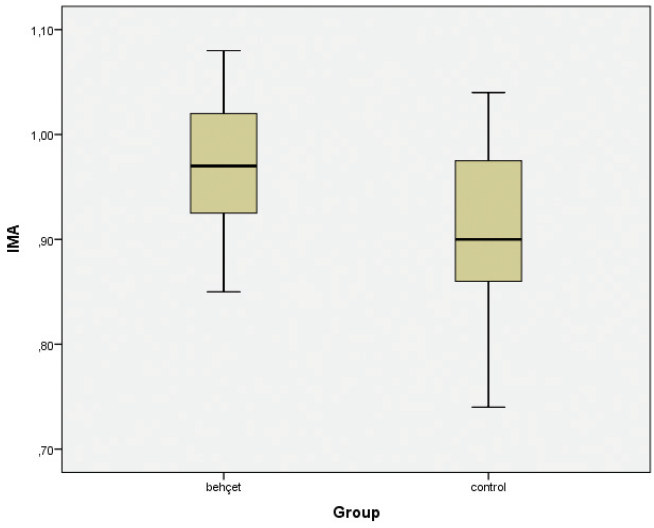

Figure 1. Showing the mean of IMA between the groups
IMA: Ischemia modified albumin

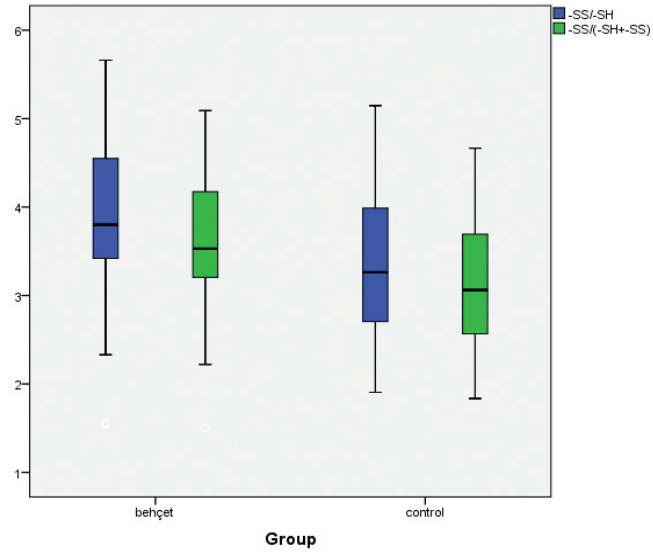

Figure 2. Showing the mean of -SS/-SH and -SS/(-SH+-SH) between the groups
-SS: Disulphide, -SH+-SS: Total thiol, -SH: Native thiol

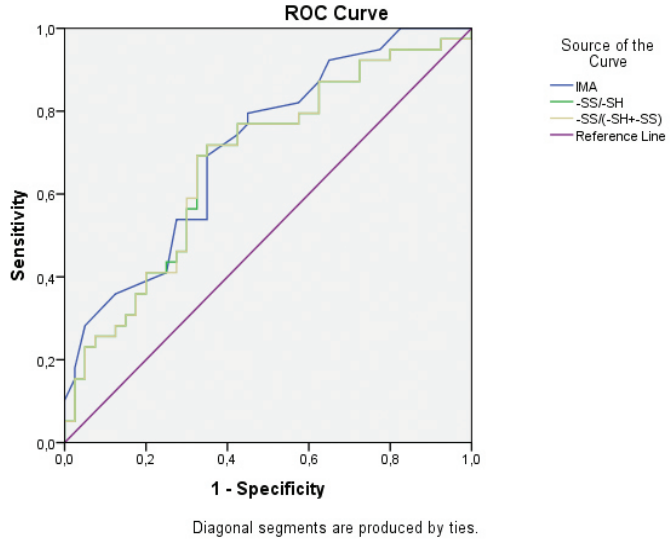

Figure 3. ROC curves of thiol-disulfide homeostasis in Behçet
-SS: Disulphide, -SH+-SS: Total thiol, -SH: Native thiol, IMA: Ischemia modified albumin

oxidative tissue damage.[19,20] It has been shown that there is an increase in oxidative stress due to inflammatory events and that the main cell involved in this increase is activated neutrophils.[21] Similarly, an increase in oxidative stress was found in BD due to excessive ROS production and a decrease in antioxidant levels.[22]

The increase in ROS resulting from the increase in oxidative stress causes many chemical changes in the albumin structure and causes the formation of IMA. It has been stated that IMA may be a new biomarker in increased oxidative stress and ischemia, and it has been shown that plasma IMA levels increase during oxidative events.[23] However, it has been determined that thiol and disulfide molecules form an important antioxidant defense system during oxidative reactions, and their plasma levels increase in case of increased oxidative stress.[24] It has been reported that deterioration in the oxidant-antioxidant balance in the body affects the emergence of various diseases.[25-27]

Table 5. Correlation between study parameters

Parameter	-SH	-SH+-SS	-SS	IMA	CRP	ESR
-SH	-	0.99**	0.036	**-0.504****	-0.148	-0.048
-SH+-SS	0.99**	-	0.170	**-0.532****	-0.185	-0.075
-SS	0.036	0.170	-	**-0.249***	-0.211	-0.186
IMA	**-0.504****	**-0.532****	**-0.249***	-	**0.238***	0.017
CRP	-0.148	-0.185	-0.211	**0.238***	-	0.071
ESR	-0.048	-0.075	-0.186	0.017	0.071	-

*All values were calculated using the Pearson correlation test. *p<0.05, **p<0.01. -SS: Disulphide, -SH+-SS: Total thiol, -SH: Native thiol, IMA: Ischemia modified albumin, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate*

It has been shown that there an increase in IMA levels in diseases accompanied by vascular endothelial dysfunction. In our study, IMA plasma levels were found to be significantly higher in Behçet's patients (0.96±0.06 ABSU) compared to the control group (0.90±0.06 ABSU) (p<0.001). Similarly, previous studies have shown that the MA level is higher in BD than in healthy individuals. In a study by Eryavuz Onmaz et al.[28] between Behçet's and the control group with 35 individuals in each group, IMA plasma levels were found to be significantly higher in Behçet's patients (0.63±0.11 ABSU) compared to the control group (0.51±0.15 ABSU) (p<0.001). In another study by Keskin et al.[29] on 45 healthy individuals and 57 Behçet's patients, IMA, total oxidant levels, total antioxidant levels (TAS), oxidative stress index (OSI), ESR and CRP levels were found to be significantly higher in BD, but it has been reported that only IMA among these markers can be a useful biomarker in distinguishing the active and inactive phase of the disease (p<0.01). In another study conducted with 26 Behçet's patients and 28 controls, IMA plasma levels were found to be statistically significantly higher in patients with active BD (0.93±0.13 ABSU) compared to individuals with inactive disease (0.82±0.14 ABSU) and control group (0.83±0.07 ABSU) (p<0.05). [30] In a study by Capkin et al.[31] consisting of 35 Behçet's patients and 31 healthy control groups, it was shown that IMA levels were significantly higher in the Behçet group (0.63±0.25 ABSU) compared to individuals in the control group (0.42±0.12 ABSU) (p<0.001). In this study, IMA was also found to be significantly higher in patients with BD (n=11) than in patients without vascular involvement (n=23) (0.78±0.37 and 0.56±0.14, respectively) (p<0.05). In our study, although IMA levels were found to be higher in BD compared to controls, they were found to be similar between the active and inactive disease stages.

Thiol groups are sulfurous protein molecules with antioxidant properties, which are found in human serum due to amino acids and albumin. Thiols can enter an oxidation reaction with reactive oxygen radicals and form disulfide bonds.[32] Disulfide bonds are covalent bonds and exist as oxidized forms. The disulfide bonds formed can be reduced back to thiol groups by a reversible reaction. The balance formed by this cycle is required for the antioxidant defense system and apoptosis control. Dysfunctions occurring in this cycle may increase reactive oxygen radicals, resulting in endothelial damage and the development of apoptosis.[33,34] In a study by Kose et al.[35], it was reported that plasma thiol levels were decreased in Behçet's patients (n=24) compared to healthy controls (n=30) (p<0.001) and that plasma antioxidant defense systems in BD might be insufficient or impaired due to the decrease in thiol levels. In another study consisting of 150 Behçet's patients and 100 healthy controls, serum -SH+-SS, -SH levels, and -SH/(-SH+-SS) ratio was found to be significantly lower in the Behçet patient group compared to the control group (p<0.001). Additionally, in this study, -SS/-SH and -SS/(-SH+SS) rates were found to be significantly higher in Behçet's patients compared to controls (p<0.001).[36] In a study by Balbaba et al.[37] in active ocular Behçet (n=20), inactive ocular Behçet's (n=20) and healthy control groups (n=20), -SH+-SS, -SH levels and -SH/(-SH+-SS) ratio were found to be significantly lower in ocular Behçet's patients compared to controls (p<0.001), whereas -SS/-SH ratio and -SS/(-SH+-SS) ratio was found to be significantly higher in Behçet's patients compared to controls (p<0.001). Similar to these studies, in our study, serum -SH+-SS and -SH levels (p<0.001) and -SH/(-SH+-SS) ratio (p<0.01) was lower in the Behçet group compared to the controls, and -SS/-SH and -SS/(-SH+-SS) ratios (p<0.01) were found to be significantly higher. In our study, no difference was found in terms of thiol groups between those with and without mucocutaneous, neurological, vascular, or ocular involvement in BD. Additionally, -SH/IMA and (-SH+-SS)/IMA ratios, which have not been evaluated before, were found to be significantly lower in Behçet's patients compared to controls (p<0.001).

Conclusion

The absence of specific laboratory findings in the diagnosis of BD causes inconsistencies in the diagnosis of the disease. Although some acute phase reactants such as CRP and ESR increase in BD, these markers are not specific

to the disease. Therefore, there is a need for more specific biomarkers that can be used in the diagnosis of the disease. According to the data we obtained from our study, we found that serum levels of IMA in BD are high, and the ratios of -SS/-SH and -SS/(-SS+-SH) are significantly low. The most important feature of our study is that it is the first study to evaluate IMA and thiol levels together in BD. The most important limitation of our study is that it is a cross-sectional study and only few patients were included in the study.

Ethics

Ethics Committee Approval: The research protocol was approved by the Ankara Yıldırım Beyazıt University Faculty of Medicine Research Ethics Committee (approval number: 1613, date: 14.04.2021).

Informed Consent: All patients gave informed written consent to participation in the study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.K., Design: A.K., Data Collection or Processing: A.K., Y.M., E.A., K.G., Analysis or Interpretation: A.K., E.F.O., Ö.E., Literature Search: A.K., Writing: A.K.

Conflict of Interest: No conflict of interest was declared by the authors.

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Romatoid artritte akciğer tomografisi bulguları ve klinik özelliklerle ilişkileri

Lung tomography findings in rheumatoid arthritis and their relationship with clinical features

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Öz

Amaç: Romatoid artrit (RA) hastalarını akciğer tutulumu açısından ne zaman ve nasıl taramamız gerektiği konusunda devam eden bir tartışma vardır ve hastaların komorbiditelerinin RA akciğer tutulumu için bir risk faktörü olarak önemi hakkında çok az şey bilinmektedir. Çalışmamızın amacı, akciğer tomografisinde RA tutulum bulguları varlığı ile ilişkili demografik, klinik ve komorbid risk faktörlerini ortaya koymaktır.

Yöntem: Romatoloji kliniğimizde RA tanısı ile son bir yılda muayene olan hastalar retrospektif olarak taranmıştır. Son bir yıl içinde akciğer tomografisi bulunan hastaların verileri değerlendirilmiştir. RA ile ilişkili olabilecek akciğer tomografi bulgusu olan hastalar ile tomografisinde patoloji bulunmayan hastaların demografik, klinik ve komorbid özellikleri karşılaştırılmıştır. Takiben ikili karşılaştırmada gruplar arasında anlamlı olarak farklı bulunan parametreler, regresyon analizi ile değerlendirilmiştir.

Bulgular: Çalışmaya 76 RA tanılı ve akciğer tomografisi çekilmiş hasta dahil edildi. Kırk üç hastada (%56,5) RA ilişkili pozitif tomografi bulgusu bulundu. Demografik ve klinik özelliklerden erkek cinsiyet (p=0,008), anti-siklik sitrüllenmiş peptid pozitifliği (p=0,04) ve tiroid hastalıkları varlığı (p=0,03), pozitif akciğer tomografisi bulguları olan hastalarda anlamlı olarak daha sık gözlendi. Regresyon analizinde ise erkek cinsiyet [olasılık oranı (OO) 7,79, %95 güven aralığı (GA) 1,69-35,69] ve tiroid hastalıklarının (OO 6,175, %95 GA 1,56-24,32), akciğer tomografisinde RA ile uyumlu bulgular ile birlikteliği bulundu.

Sonuç: RA kohortumuzdaki hastalarda erkek cinsiyet ve tiroid hastalıkları öyküsü ile akciğer tutulumu ile uyumlu tomografi bulguları birlikteliğini gösterdik. Bu hasta gruplarının RA-akciğer tutulumu açısından daha yakın takibi uygun olabilir.

Anahtar Kelimeler: Romatoid artrit, intertisiyel akciğer hastalığı, komorbidite, tiroid

Abstract

Objective: There is an ongoing debate about when and how we should screen rheumatoid arthritis (RA) patients for lung involvement and little is known about the importance of patients' comorbidities as a risk factor for RA lung involvement. The aim of this study is to reveal the demographic, clinical, and comorbid factors associated with positive lung computed tomography (CT) findings associated with RA.

Methods: We screened all RA patients followed at our rheumatology clinic and included those who had a thoracic CT within the past year. We divided the patients into two groups (positive or negative) according to thoracic CT findings. We compared the two groups in terms of demographic, clinical, and comorbid characteristics. We then performed multivariate analysis with a model that includes significantly different features in univariate analyses to find the amount of risk attributed to the factors for positive thoracic CT.

Results: We included 76 RA patients who had thoracic CT. Of these, 43 (56.5%) had positive findings related to RA in thoracic CT. Male gender (p=0.008), anti-cyclic citrullinated peptide antibody positivity (p=0.04), and thyroid diseases (p=0.03) were found significantly more common in the patients with positive thoracic CT findings. Additionally, multivariate analyses found male gender [odds ratio (OR) 7.79, 95% confidence interval (CI) 1.69-35.69] and thyroid diseases (OR 6.17, 95% CI 1.56-24.32) were related to positive CT findings.

Conclusion: In this study conducted in our cohort, we found that male gender and thyroid disease were risk factors for positive thoracic CT findings associated with RA. Clinicians may consider these factors when classifying RA patients for lung involvement and planning thoracic CT for screening.

Keywords: Rheumatoid arthritis, interstitial lung disease, comorbidity, thyroid

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Giriş

Romatoid artrit (RA) ilişkili akciğer hastalığı morbidite ve mortalite ile sonuçlanabilen RA'nın eklem dışı tutulumlarından biridir.[1,2] RA tüm akciğer kompartımanlarını etkileyebilir. İnterstisyel akciğer hastalıkları (İAH), romatoid nodüller, plevral effüzyon, küçük ve büyük hava yolu hastalıkları (krikoaritenoidit, konstriktif veya foliküler bronşiyolit ve bronşektazi) ve pulmoner vasküler tutulumlar RA hastalarında gözlenebilir.[3] RA'da akciğer tutulumu genelde ilk 5 yılda ortaya çıkar. Ancak akciğer tutulumu, olguların %10-20'sinde eklem semptomlarının başlangıcından önce de gelişebilir. Akciğer tutulumu, RA hastalarında tipik olarak ellili ve altmışlı yaşlarda görülmektedir.[4] Bu yüzden tanı anı eşlik eden komorbiditeler sıklıkla karşımıza çıkabilmektedir. RA'da akciğer hastalıklarının patofizyolojisi çok faktörlüdür. Yapılan çalışmalarda RA akciğer tutulumu ile genetik yatkınlık, sigara içme, kronik immün aktivasyon, çevresel faktörler, enfeksiyonlar, ilaç toksisitesi ve lokal mukozal disbiyoz arasında ilişki saptanmıştır.[5]

RA hastalarında daha önce yapılan çalışmalarda, tanı kriterlerinin ve radyografik görüntüleme yöntemlerinin farklılık gösterebildiği halde, İAH prevalansı %5-60 olarak bulunmuştur. Diğer tutulumlar ise sıklığa göre hava yolu hastalıkları, plevral efüzyon ve romatoid nodüller olarak gözlenebilmektedir.[3,4,6] RA-İAH ile ilişkili risk faktörleri arasında erkek cinsiyet, ileri yaş, tütün kullanımı, romatoid faktör (RF) veya anti-siklik sitrüllenmiş peptid (CCP) antikorlarından en az birinin pozitifliği, obezite, yüksek RA hastalık aktivitesi ve genetik faktörler yer almaktadır.[2,7,8] RA hastalarında, alt hava yollarında hava yolu aşırı duyarlılığı, küçük hava yolu hastalıkları ve bronşektazi gözlenebilmektedir. RA tanılı ancak parankimal tutulumların dışlandığı 50 hastadan oluşan bir seride, hastaların %18'inde hava yolu obstrüksiyonu, %8'inde küçük hava yolu hastalığı ve %32'sinde solunum fonksiyon testinde ve/veya akciğer görüntülemesinde hava hapsi ile uyumlu bulgular tespit edilmiştir. Bu bulgular, kadınlarda ve sigara içenlerde daha sık gözlenmektedir.[3,9] Plevrada kalınlaşma ve/veya efüzyon şeklinde kendini gösteren plevra iltihabı da RA'nın yaygın bir eklem dışı belirtisidir. Postmortem çalışmalarda, hastaların %70'inden fazlasında plevra tutulumu tanımlanmıştır. Plevra tutulumu olan hastaların ancak %3-5'i semptomatiktir.[3] Diğer yandan RA'da akciğer nodüllerinin varlığı, yüksek hastalık aktivitesi, artmış vaskülit sıklığı, hastaneye yatış ve mortalite ile ilişkili bulunmuştur.

Literatürde bildiğimiz kadarıyla hiçbir çalışmada, komorbiditelerin RA akciğer tutulumu riski veya birlikteliği ile ilişkisi araştırılmamıştır. Ayrıca önceki çalışmalarda, İAH dışı RA ile ilişkili olabilecek diğer akciğer bulgularını da dahil edecek şekilde, akciğer tomografisi gerekliliği olan RA hastalarını belirleme hedefi de değerlendirilmemiştir. Son yıllarda subklinik tutulumların belirlenebilmesinin, erken tedavi açısından faydalı olabileceği düşünülmektedir. Literatürdeki çalışmalarda akciğer tutulumu tespit edilmiş olan hastalar ile tutulum bulunmayan hastalar risk faktörü tespiti için karşılaştırılmıştır. Bu çalışmalarda tüm hastalara akciğer tomografisi çekilmediği ve takip süresi sonrası da akciğer tutulumu çıkabileceği düşünülmektedir. Bu çalışmamızda amacımız RA kohortumuzdaki hastaların akciğer tomografisinde RA ile ilişkili tutulumları bulunanların radyolojik özelliklerini ve tutulumla ilişkili demografik, klinik ve komorbid faktörleri ortaya koymaktır. Bu şekilde, akciğer tutulumları açısından tarama yapılacak RA hastalarının belirlenmesine yardımcı olmak amaçlanmaktadır.

Gereç ve Yöntem

Hastalar: Romatoloji polikliniklerinde muayene edilmiş ve RA tanısı almış erişkin hastalar çalışmaya dahil edilmiştir. Tüm hastalar, 2010 ACR/European League Against Rheumatology kriterlerini karşılamaktadır.[10] Hastane otomasyon sisteminden son 1 yıllık veriler retrospektif olarak taranmıştır. RA tanısı doğrulanan ve muayene tarihinden önce 1 yıl içinde çekilmiş akciğer tomografisi ve muayene tarihinde klinik verileri (hassas eklem, şiş eklem, komorbiditeler, kullandığı ilaçlar, eritrosit sedimentasyon hızı, C-reaktif protein, hastalık süresi) tam olarak bulunan tüm hastalar çalışmaya alınmıştır. Romatoloji polikliniklerinde hastaların muayene bulguları, hassas ve şiş eklem sayısı, komorbid durumları ve kullanmakta olduğu ilaçlar rutin olarak kaydedilmektedir. Kliniğimizde, her hastanın ilk muayenesinde sistemik hastalıkları ve kullandığı ilaçlar sorgulanmaktadır. Ek olarak e-nabız sisteminden de geçmiş tanıları taranmaktadır. Çalışmamıza bu verilerden elde edilen komorbiditeler eklenmiştir.

Çalışmamızda dışlama kriterleri tüberküloz, sarkoidoz, malignite, diğer kollajen doku hastalıkları veya otoimmün romatizmal hastalıklar, akciğer ilişkili meslek hastalıkları ve muayene tarihinde veya tomografi döneminde enfeksiyon varlığı ve gebelik/emzirme olarak belirlendi. Bu çalışma için yerel etik kuruldan onay alınmıştır (karar no: 2022/514/218/2, tarih: 28.01.2022). Bu çalışma, gözlemsel çalışmalar için Epidemiyolojide Gözlemsel Çalışmaların Raporlanmasının Güçlendirilmesi yönergeleri çerçevesinde, Helsinki Bildirgesi ile uyumlu olarak düzenlenmiştir.

Tomografi Bulguları: Herhangi bir nedenle çekilmiş toraks yüksek rezolüsyon bilgisayarlı tomografide (YRBT) ve/veya bilgisayarlı tomografide (BT) raporlanmış bulgular kaydedilmiştir. Tomografi anormallikleri şu bulguları içermektedir:[3]

İAH: Olağan interstisyel pnömoni, non-spesifik interstisyel pnömoni, lenfositik pnömoni, organize pnömoni, ilaca bağlı pnömoni

Nodüler Hastalıklar: Parankimal mikronodüller, nodüller, subplevral mikronodüller, Kaplan sendromu

Bronşiyal Hastalıklar: Bronşektazi, bronşiyolit, bronşit, bronşiyal duvar kalınlaşması, konsolidasyonlar

Plevral Hastalıklar: Plevral efüzyon, plevral kalınlaşma, plevrit

Diğer Bulgular: Mediastinal lenfadenopati, buzlu cam görünümü, bal peteği görünümü, mozaik atenüasyon, amfizem, atelektazi, vasküler hastalıklar.

İstatistiksel Analiz

Akciğer tomografisinde yukarıda sayılan bulgulardan herhangi birisi olan ve RA dışında açıklayıcı başka bir nedeni olmayan hastalar "RA tomografi pozitif" (RAT+) grubunu oluştururken, tomografisi normal hastalar "RA tomografi negatif" (RAT-) grubunu oluşturmuştur. Ayrıca, dışlama kriterlerine rağmen kalan, RA'dan bağımsız aşikar kronik obstrüktif akciğer hastalığına (KOAH) bağlı amfizem, bronşit ve atelektazi gibi bulguları olan hastalar iki romatolog ve gereklilik halinde göğüs hastalıkları uzmanı ve radyolog değerlendirmesi ile RAT- grubuna dahil edilmiştir. RAT+ ve RAT- hastalar demografik, klinik ve komorbid özellikleri açısından karşılaştırılmıştır. Devamlı değişkenler için Mann-Whitney U testi, kategorik değişkenler içinse ki-kare testi (veya Fisher Exact) karşılaştırmada kullanılmıştır. İlişkilendirme analizlerinde, RAT+ olma durumunu tahmin ettiricilerini saptamak amacıyla, gruplar arasında farklılık gösteren parametreler bağımsız değişken olarak %95 güven aralığı (GA) ile olasılık oranlarını (OO) elde etmek üzere çok değişkenli lojistik regresyon modellerine yerleştirildi. Çok değişkenli lojistik regresyon analizi modeline anlamlı farklılık gözlenen bağımsız değişkenler ile yaş parametresi eklendi. Tütün kullanımının literatürde akciğer tutulumu ile ilişkili olabileceği gösterildiği halde, tütün kullanımı durumu bilinen hasta sayısının az olması nedeniyle modele eklenmedi. Modele, RF ve anti-CCP'nin yakın ilişkisi nedeniyle RF pozitifliği eklenmedi. P değerleri <0,05 istatistiksel olarak anlamlı kabul edildi.

Bulgular

Tomografi Bulgularına Göre Gruplar: Toplam 76 hasta çalışmada değerlendirilmiştir. Hastaların 43'ü (%56,5) RAT+, 33'ü (%43,5) ise RAT- grubunu oluşturmuştur (Tablo 1). RAT+ hastaların 12 tanesinde klinik ve radyolojik olarak doğrulanmış İAH, iki tanesinde ise olası İAH mevcuttu. RAT- hastaların iki tanesinde ise klinik ve radyolojik olarak doğrulanmış uzun süreli kronik obstrüktif akciğer hastalığının tomografi bulguları gözlenmiştir.

Tablo 1. Tomografide romatoid artrit ile ilişkili akciğer bulgusu olan 43 hastada saptanan radyolojik anormallikler*

	Toplam (n=43)	İAH (n=12)	Diğer (n=31)
Nodül	15	3	12
Buzlu cam görünümü	13	12	1
Bronşiyal hastalık	12	5	7
Plevral hastalık	9	1	8
Mozaik atenüasyon	7	1	6
Mediastinal lenfadenopati	6	1	5
Bal peteği formasyonu	5	5	0
Amfizem	5	1	4
İnterstisyel fibrozis	3	3	0
Pulmoner vasküler hastalık	2	0	2

**İAH: Interstisyel akciğer hastalığı; Diğer: Klinik ve radyolojik olarak interstisyel akciğer hastalığı tanısı almamış ancak tomografisinde olası romatoid artrit akciğer tutulumu olan hastalar, n: Hasta sayısını ifade eder*

Otuz üç hastada ise RA ile ilişkili tomografi bulgusu tespit edilmemiştir.

Hastalar: Ortalama yaş 57,6±12,2 olarak tespit edilmiştir. Hastaların 58'i (%76) kadındı (Tablo 2). Gruplar arasında demografik ve klinik özelliklerden cinsiyet ve anti-CCP pozitifliği farklı bulunmuştur. RAT+ grubundaki hastaların %81,4'ünün en az bir konvansiyonel veya biyolojik hastalık modifiye edici anti romatizmal ilaç (DMARD) öyküsü mevcutken, RAT- grubundaki hastaların %100'ünün DMARD kullanım öyküsü mevcuttu.

Komorbiditeler: Hastalarda bulunan sistemik hastalıklar Tablo 3'te sıklık sırasına göre verilmiştir. RAT+ grubunda tiroid hastalığının, RAT- grubuna göre daha sık bulunduğu tespit edilmiştir (p=0,03).

RA'da Akciğer Tomografisi Bulgusunu Tahmin Ettirebilecek Faktörler: Erkek cinsiyet (OO 7,79, %95 GA 1,69-35,69) ve tiroid hastalıklarının (OO 6,17, %95 GA 1,56-24,32), akciğer tomografisinde RA ile uyumlu bulgular ile birlikteliği bulundu. RAT+ olma durumunu tahmin ettiren faktörler ve olasılık oranları Tablo 4'te verilmiştir.

Tartışma

RA hastalarında, akciğer tutulumu taraması için akciğer görüntülemesi yapılacak aday hastaların belirlenmesine yardımcı olmak için planlanan çalışmamızda, tiroid hastalıkları varlığının ve erkek cinsiyetin, akciğerde RA ile ilişkili olabilecek tomografi bulguları ile ilişkili olabileceği bulunmuştur. Ayrıca akciğer tomografilerinde sıklık sırasına göre nodül, buzlu cam görünümü, bronşiyal hastalık, plevral hastalık, mozaik atenüasyon, mediastinal lenfadenopati, bal peteği formasyonu, amfizem, interstisyel fibrozis ve pulmoner vasküler hastalık saptanmıştır. Hastaların 14'ünde ise klinik ve radyolojik olarak doğrulanmış veya olası İAH belirlenmiştir.

Tablo 2. Hastaların demografik ve klinik özellikleri

	RAT+	RAT-	p
Hasta sayısı, n	43	33	
Yaş, yıl	59,79 (SS 12,45)	54,79 (SS 11,32)	0,73
Erkek oranı, %	34,8	9,0	0,008
Tanı süresi, yıl	4 (0-24)	4 (0,1-16)	0,80
Komorbidite sayısı	2 (0-5)	1 (0-4)	0,96
Tütün kullanımı, % (n_{total}=44)			
İçiyor	29	15,4	**0,08**
Bırakmış	19,3	0	
Yok	51,6	84,6	
RF pozitifliği, %	63	55	0,20
CCP pozitifliği, %	73	50	**0,04**
Hassas eklem sayısı	0 (0, 14)	1 (0, 10)	0,51
Şiş eklem sayısı	0 (0, 8)	0 (0, 4)	0,39
ESR, mm/h	26 (2, 76)	17 (4, 57)	0,17
CRP, mg/dL	18,4 (0, 120)	12,1 (0,4, 85)	0,17
Metotreksat kullanımı, %			
Yok	58,1	39,4	0,24
Geçmişte	27,9	36,4	
Halen	13,9	24,2	
Anti-TNF kullanımı, %			
Yok	90,7	90,9	0,97
Geçmişte	2,3	3,0	
Halen	6,7	6,1	
Steroid kullanımı, %			
Yok	32,5	27,2	0,69
Geçmişte	11,6	18,2	
Halen	55,8	54,5	

CCP: Anti siklik sitrüllenmiş peptid, CRP: C-reaktif protein, ESR: Eritrosit sedimentasyon hızı, RAT+: Romatoid artrit ilişkili pozitif toraks tomografi bulgusu, RAT-: Romatoid artrit ilişkili negatif toraks tomografi, RF: Romatoid faktör, SS: Standart sapma, p<0,05 koyu olarak gösterilmiştir

Tablo 3. Akciğer tomografisi çekilmiş 76 romatoid artrit hastasında komorbiditeler

	Toplam*	RAT+*	RAT-*	p
Anemi	36	19	17	0,52
Hipertansiyon	31	15	16	0,23
Tiroid hastalıkları	20	15	5	**0,03**
Diabetes mellitus	15	10	5	0,28
Mide-bağırsak sistemi hastalıkları	12	6	6	0,61
Kronik obstrüktif akciğer hastalığı	12	6	6	0,61
Koroner arter hastalığı	6	2	4	0,22
Kronik böbrek hastalığı	5	1	4	0,10
Duygudurum bozukluluğu	4	4	0	0,09
Aritmi	2	1	1	0,68
Serebrovasküler olaylar	2	2	0	0,31
Pulmoner vasküler hastalıklar	2	2	0	0,31
Konjestif kalp yetmezliği	1	1	0	0,56
Karaciğer hastalıkları	1	1	0	0,56
Nörodejeneratif hastalıklar	1	1	0	0,56

*RAT+: Romatoid artrit ilişkili pozitif toraks tomografi bulgusu, RAT-: Romatoid artrit ilişkili negatif toraks tomografi, p: RAT+ grubu ile RAT- grubunun ki-kare (veya Fisher Exact) testinin anlamlılığı, *Hasta sayısını ifade eder, p<0,05 koyu olarak gösterilmiştir*

Tablo 4. Çok değişkenli lojistik regresyon analizi ile romatoid artritte tomografi bulgusu olma durumunu tahmin ettirici faktörler

	Olasılık oranı	%95 Güven aralığı	p
Erkek cinsiyet	7,799	1,69-35,69	**0,008**
Tiroid hastalıkları varlığı	6,175	1,56-24,32	**0,009**
Yaş	1,044	0,99-1,09	0,06
Anti-CCP pozitifliği	2,687	0,86-8,39	0,08

Nagelkerke R^2: 0.324, Hosmer Lemeshow testi: 0,704, RAT+: Romatoid artrit ilişkili pozitif toraks tomografi bulgusu, CCP: Anti siklik sitrüllenmiş peptid, p<0,05 koyu olarak gösterilmiştir

RA'nın farklı akciğer tutulumlarının açığa çıkması için risk faktörleri tanımlanmıştır. Bunlardan en çok vurgulanmış olanlar erkek cinsiyet, ileri yaş, sigara içme öyküsü, RF/anti-CCP seropozitifliği, yüksek hastalık aktivitesi ve genetik faktörlerdir.[1,2,7] Ancak literatürdeki çalışmalarda farklı sonuçlar gözlenebilmektedir. Bazı çalışmalar hastalık aktivite parametreleriyle akciğer nodülleri arasında pozitif bir ilişki gösterirken, bazılarında ise bu ilişki gösterilmemiştir.[8,11-14] RA-İAH ile C-reaktif protein ve eritrosit sedimentasyon hızı ilişkisinde de çelişkili sonuçlar bulunmaktadır.[8,11,15] Çalışmamızda literatürle uyumlu olarak akciğer tomografi bulgusuyla anti-CCP pozitifliği ve erkek cinsiyet ilişkisi bulunmuş olsa da aktivite parametreleriyle akciğer tutulumu arasında bir ilişki belirleyemedik. Çalışmamızın amacının hangi RA hastalarında İAH risk faktörlerinin belirlenmesinden ziyade kimlere tarama amaçlı akciğer görüntülemesi yapılacağının olduğu düşünüldüğünde, anlık zaman diliminde gözlenen yüksek aktivite belirteçlerinin akciğer görüntülemesi gerektirmeyebileceği düşünülebilir.

Çalışmamızda RA tedavisi ile akciğer tutulumu arasında bir ilişki saptanmamıştır. Literatürde de tedavi ile RA-İAH arasındaki ilişki konusunda çelişkili sonuçlar bulunmuştur.[8,12-15] Ancak günümüzde konvansiyonel sentetik hastalık modifiye edici ilaçların, RA akciğer tutulumu ile ilişkili olmadığı genel kabul görmektedir.

RA'da komorbiteleri inceleyen geniş örneklemli prevalans çalışmalarında hipertansiyon, diyabet, tiroid hastalıkları, anemi, depresyon, kronik obstruktif akciğer hastalığı ve koroner arter hastalıkları, RA ile beraber sıklıkla gözlenmektedir.[16,17] Çalışmamızdaki komorbidite oranları -her ne kadar prevalans çalışması olmasını engelleyen bir tomografi ihtiyacı yanlılığı olsa da- literatürle benzer saptanmıştır. Ek olarak saptadığımız, akciğer tutulumu ile tiroid hastalığı arasındaki pozitif ilişkinin dikkat çekici olabileceği düşünülmektedir. RA ve tiroid bezi arasındaki anlamlı ilişki uzun süredir bilinmektedir; otoimmün tiroid hastalığı (OİTH) olan hastalarda RA prevalansı 1-3 kat daha fazla bulunmuştur. Benzer şekilde RA'lı hastalarda da OİTH prevalansı 1-6 kat artmıştır. Eklemlerin ve tiroid bezinin eşzamanlı etkilenmesi, büyük olasılıkla, belirli bir HLA tipine, çoğunlukla HLA-DR'ye bağlı genetik yatkınlıkla ilgili olduğu düşünülmektedir.[18] İlerde bu ilişkiyi doğrulayan büyük örneklemli, neden-sonuç ilişkisini tanımlayan prospektif ve ilişki doğrulandığı takdirde tiroid hastalığının tipini açığa çıkaracak yeni çalışmalara ihtiyaç vardır.

RA'da tüm interstisyel pnömoni paternleri gözlenebilir.[19,20] Çalışmamızda 14 hastada saptanan İAH hastalığının yanı sıra kesin İAH olarak nitelendirilemeyen veya henüz nitelendirilmemiş ancak buzlu cam, bal peteği veya interstisyel fibrozis gibi olası İAH bulguları da seyrek değildir. Diğer yandan, RA'da küçük hava yolu hastalığının sık gelişiminin mekanizması ise henüz kesinleşmemiştir. Bronkoalveolar lavaj çalışmalarında, bronşiolar hastalıkları olan RA hastalarında enflamatuvar hücre sayısında artış gösterilmiştir. RA hastalarında hem hava akımı obstrüksiyonu hem de bronşiyal reaktivitenin artması, hava yolunda önceden var olan enflamatuvar değişikliklerin bronşiyal daralmaya ve hava yolu obstrüksiyonuna yol açabilecek mukozal ödemi indükleyebileceği düşünülmektedir.[21] Çalışmamızda 12 hastada bronşiyal hastalık bulguları gözlenmiştir. Ancak, bronşiyal hastalığın klinik olarak değerlendirmesi için solunum fonksiyon testlerine ihtiyaç olduğu akılda tutulmalıdır.

RA akciğer tutulumu için tanımlanmamış risk faktörlerinin de var olduğu düşünülmektedir.[7,8,22,23] Özellikle genetik faktörlerin rolü akılda tutulmalıdır. Bu genetik faktörlerin belirlenmesinin, akciğer taramasına uygun hasta seçimine ışık tutmaya yardımcı olabileceği düşünülmektedir.

Bu çalışmanın güçlü yönleri, RA için olası tüm akciğer tomografi bulgularının dahil edilmesi, tomografisi normal bir kontrol grubunun olması ve komorbiditelerin hesaba katılmasıdır. Bununla birlikte, birkaç önemli sınırlama vardır. Birincisi, kesitsel tasarımı öngörücü belirlememize engel olmuştur. İkincisi, sadece akciğer tomografisi olan hastalar dahil edilip tomografisi olmayanlar dahil olmadığından seçim yanlılığı mümkündür, ancak yine de çalışmamızın bir prevalans iddiası bulunmamaktadır. Hala, subklinik tutulumları olan ve tomografisi olmayan RA'ları almamış olma ihtimaliz olsa da bu bir olgu-kontrol çalışmasıdır. Üçüncüsü, hastaların bazısında YÇBT bazısında BT raporlarının olması standardizasyondan uzaklaştırsa da hedefe yönelik görüntüleme olmasının (örneğin; İAH için YÇBT, lenfadenopati için BT) sorunların saptanabilirliğini artırmış olduğu düşünülebilir. Son olarak, biyobelirteçler ve paylaşılan epitop ve MUC5B gibi genetik faktörler gibi başta ölçülemeyen değişkenler bu çalışmada değerlendirilmemiştir.

Sonuç

Sonuç olarak, bu retrospektif olgu-kontrol çalışmasında, RA hastalarında erkek cinsiyet ve eşlik eden tiroid hastalıklarının, RA akciğer tutulumu ile uyumlu görüntüleme bulguları ile birlikteliğini saptadık. Akciğer tutulumunun kötü prognozu ve erken tedavinin önemi göz önüne alındığında, bu bulguların, biyolojik ve genetik risk faktörlerine yönelik planlanacak gelecekteki çalışmalara yol gösterici olabileceğini düşünmekteyiz. Ayrıca bu klinik özellikteki hasta gruplarının RA-akciğer tutulumu açısından daha yakın takibi uygun olabilir.

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ANCA-associated vasculitis with temporal artery involvement: A report of two cases

Temporal arter tutulumu olan ANCA ilişkili vaskülit: Olgu sunumu

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Abstract

Antineutrophil cytoplasmic antibodies (ANCA)-associated vasculitis and giant cell arteritis are two different vasculitides that differ in their clinical presentations, treatments and prognoses. Temporal artery involvement occurs rarely in ANCA-associated vasculitis. We present two patients with ANCA-associated vasculitis with temporal artery involvement.

Keywords: Temporal artery, vasculitis, anca-associated vasculitis

Öz

Antinötrofil sitoplazmik antikor (ANCA) ilişkili vaskülit ve dev hücreli arterit, klinik görünümleri, tedavileri ve prognozları açısından farklılık gösteren iki farklı vaskülittir. ANCA ilişkili vaskülitlerde temporal arter tutulumu nadiren görülür. Bu yazıda, temporal arter tutulumu olan iki ANCA ilişkili vaskülit hastasını sunacağız.

Anahtar Kelimeler: Temporal arter, vaskülit, anca ilişkili vaskülit

Introduction

Antineutrophil cytoplasmic antibodies associated (ANCA-associated) vasculitis consists of granulomatosis with polyangiitis, microscopic polyangiitis, and eosinophilic granulomatosis with polyangiitis and causes necrotizing pauci-immune inflammation in small to medium blood vessels.[1]

Giant cell arteritis is a vasculitis of medium to large blood vessels.[2] The involvement of the branches of the extracranial carotid artery leads to the classic symptoms.[2] Giant cell arteritis can also involve the aorta and its branches. Superficial temporal artery biopsy result is the gold standard for diagnosis.[2] Typically, a granulomatous reaction is seen with mononuclear infiltration along the elastic lamina.[3]

ANCA-associated vasculitis and giant cell arteritis are two different vasculitides that differ in their clinical presentations, treatments and prognoses. The prognosis of ANCA-associated vasculitis is worse and requires more intensive immunosuppression.[3,4] Temporal artery involvement in ANCA-associated vasculitis is rare.[5-7] However, its distinction from giant cell arteritis is crucial for effective therapy. Therefore, ANCA-associated vasculitis should be considered in patients with atypical presentations of giant cell arteritis. Here, we present two patients with ANCA-associated vasculitis with temporal artery involvement.

Case Reports

Case 1

A 73-year-old man was admitted with complaints of widespread pain. He had asthma and he complained of numbness of the feet and leg weakness. He also had jaw

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claudication. There was no tenderness or induration in the temporal region. The upper and lower extremity motor strength was 3/5. Laboratory testing showed C-reactive protein (CRP) 78 mg/L, erythrocyte sedimentation rate (ESR) 55 mm/h and eosinophils 25.6×10^3/L. The 24-hour urine protein was negative and there was no hematuria. Antinuclear antibodies indirect immunofluorescence assay (ANA-IFA) was negative, while p-ANCA was positive. Doppler ultrasonography and magnetic resonance angiography (MRA) of temporal arteries were normal. Thorax and abdomen computed tomography (CT) of thorax and abdomen were normal. Electromyography (EMG) revealed sensorimotor peripheral neuropathy. Temporal artery biopsy revealed giant cells in the degenerated internal elastic lamina (Figure 1). A diagnosis of ANCA-associated vasculitis with temporal artery involvement was made and a 3-g steroid pulse was given, followed by 1 mg/kg/day oral prednisolone and 2 mg/kg/day azathioprine. The patient informed consent was obtained.

Case 2

A 55-year-old woman was admitted with fatigue and widespread pain. She had numbness of her feet, headache, night sweats, fever, and weight loss. She also had jaw claudication. The physical examination was normal. There was no tenderness or induration in the temporal region. Laboratory testing showed CRP 250 mg/L and ESR 117 mm/h. The 24-hour urine protein was negative and there was no hematuria. ANA-IFA was negative, while c-ANCA was positive. Doppler ultrasonography and MRA of temporal arteries were normal. Thorax and abdomen CT of thorax and abdomen were normal. Temporal artery biopsy revealed intense inflammation in the media, and adventitia consisting of lymphocytic infiltration with segmental involvement (Figure 2). Diagnosis of ANCA-associated vasculitis with temporal artery involvement was made and a 3 g steroid pulse was given, followed by 1 mg/kg/day oral prednisolone and 2 mg/kg/day azathioprine. One month later, she presented with leg weakness. Her right foot dorsiflexion motor strength was 2/5. Hypesthesia of the right foot was also found. EMG revealed asymmetric sensorimotor neuropathy, consistent with mononeuritis multiplex and azathioprine was discontinued, and monthly intravenous cyclophosphamide was started. The patient informed consent was obtained.

Discussion

Vasculitides are subdivided according to their clinical characteristics and the size of the affected vessels. ANCA-associated vasculitis affects small to medium vessels, while giant cell arteritis affects medium to large vessels. Upper respiratory tract, lung, and renal involvement are more frequent in ANCA-associated vasculitis, while the carotid or aortic involvement is seen in giant cell arteritis. The treatment of the two vasculitides differs, and ANCA-associated vasculitis have a poorer prognosis.[2,4]

The first patient had widespread pain, fatigue, weakness, and numbness of the hands and feet. He had asthma and eosinophilia was detected. The p-ANCA, eosinophilia, and asthma were consistent with ANCA-associated vasculitis, as was the sensorimotor peripheral neuropathy. The jaw claudication and headache were thought to indicate the temporal artery involvement. Histologically, temporal artery inflammation was detected. ANCA-associated vasculitis with temporal artery involvement was diagnosed.

The second patient had headaches and jaw claudication, which were consistent with giant cell arteritis. However, the mononeuritis multiplex is not typical of giant cell arteritis.

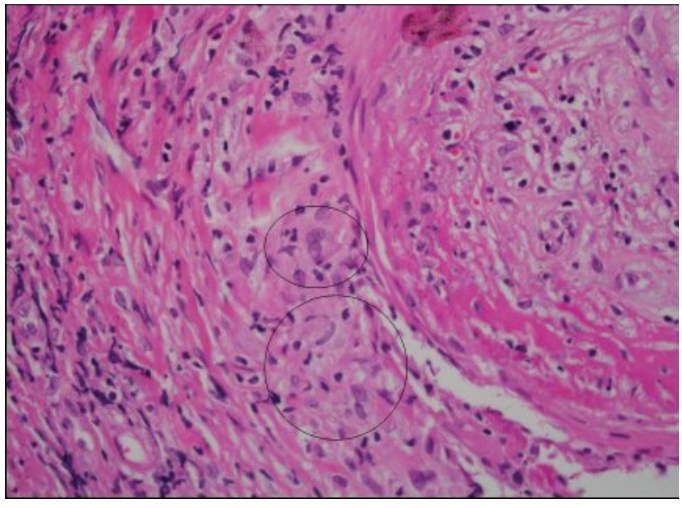

Figure 1. Histopathologic findings of the temporal arteries show giant cells at the degenerated internal elastic lamina with H&E

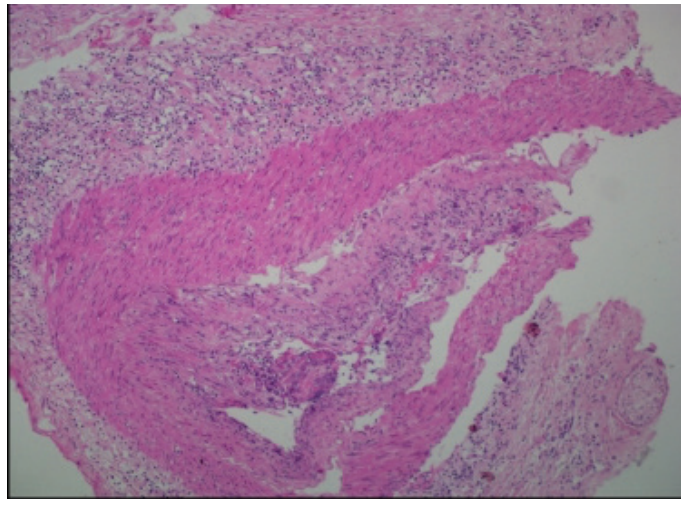

Figure 2. Histopathologic findings of the temporal artery show intimal thickening, lymphocytic infiltration and thrombosis with H&E

The c-ANCA positivity suggested a diagnosis of ANCA-associated vasculitis despite the absence of upper respiratory tract, lung, or renal involvement. Histologically, temporal artery inflammation was detected, but pathological findings were not typical of giant cell arteritis. A diagnosis of ANCA-associated vasculitis with giant cell artery involvement was made and the subsequent development of mononeuritis multiplex supported our diagnosis.

Endo et al.[7] reported a patient presenting with pain and tenderness in the temporal region in whom giant cell arteritis was diagnosed by biopsy. The clinical complaints were relieved with steroid treatment, but 9 months later the patient was admitted with bronchial asthma and peripheral eosinophilia. Although ANCA was negative, they suggested a diagnosis of eosinophilic granulomatosis with polyangiitis with temporal artery involvement. Tanaka et al.[6] reported a patient with microscopic polyangiitis with temporal artery involvement. Unlike our patient, they found necrotizing crescentic glomerulonephritis. In a cohort of 120 patients with giant cell arteritis, Hamidou et al.[8] detected different vasculitides in seven patients, including three patients with microscopic polyangiitis, two with polyarteritis nodosa, and one with granulomatosis with polyangiitis. Nishino reported that 5 of 347 granulomatosis with polyangiitis patients had temporal artery involvement, all of whom had headache and jaw claudication with loss of vision.[5]

ANCA-associated vasculitis and giant cell arteritis have different clinical presentations, treatments and prognoses. Therefore, it is important to make the correct diagnosis in a patient with temporal artery involvement. Our cases suggest that ANCA testing is beneficial in patients presenting with symptoms of giant cell arteritis but have unusual findings. ANCA positivity seems to be associated with involvement of the peripheral nervous system.

Ethics

Informed Consent: Informed consents were obtained from the patients.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: Ö.V., B.G., Design: Ö.V., B.G., A.T., Data Collection or Processing: Ö.V., H.K., A.T., Analysis or Interpretation: B.Ö., A.D., Literature Search: Ö.V., Writing: Ö.V.

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Morfea ve ellerde fasiit gelişen bir olgu

Morphea and a case with fasciitis in the hands

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Öz

Lokalize skleroderma (morfea), aşırı kollajen birikimine bağlı olarak deri ve deri altı dokusunun kalınlaşması ve endürasyonu ile karakterize bir hastalıktır. Nedeni tam olarak bilinmemektedir. Lokalize skleroderma, deri ve deri altı dokuya sınırlı bir hastalık olarak bilinmesine karşın iç organ tutulumu olan nadir olgular da bildirilmiştir. Burada morfea ile izlenmekte iken, ellerde sinovit ve fasiit gelişen genç bir olgu sunulacaktır.

Anahtar Kelimeler: Lokalize skleroderma, sinovit, fasiit, tedavi

Abstract

Localized scleroderma (morphea) is a disease characterized by thickening and induration of the skin and subcutaneous tissue due to excessive collagen accumulation. The reason is not known exactly. Although localized scleroderma is known as a disease limited to the skin and subcutaneous tissue, rare cases with internal organ involvement have also been reported. Herein a young case with synovitis and fasciitis in the hands will be presented while being followed up with morphea.

Keywords: Localized scleroderma, synovitis, fasciitis, treatment

Giriş

Morfea, lokalize sklerodermanın bir deri tutulumudur. Sıklıkla yalnızca deriyi etkileyen, uzun seyirli bir deri hastalığıdır. Nadir görülmesi ve klinik açıdan heterojen olması nedeniyle, hastalığın patogenezi hala tam olarak aydınlatılamamıştır. Günümüzde travma, radyasyon, ilaçlar, enfeksiyonlar, genetik ve otoimmünite üzerinde durulmakta, nedeni ne olursa olsun hastalık sürecinin damarsal hasar ve deride elastikiyeti sağlayan kollajen üretiminin artışı ve yıkımının azalmasıyla ilerlediği bilinmektedir.[1]

Klinik bulgulara ve tutulan dokunun derinliğine göre alt gruplara ayrılır: Plak, jeneralize, büllöz, lineer ve derin morfea. Lokalize skleroderma deride yalnızca birkaç leke ile sınırlı olabileceği gibi tüm vücudu kaplayan yaygın lezyonlar ile karşımıza gelebilir. Hastalığın başlangıcı genellikle sessiz olmasına rağmen, seyri hızlı olabilir.[2] Hastalık başlangıç yaşı ortalama 40'lı yaşlar olup, kadınlarda 2-3 kat daha fazla görülür. En sık belirtileri deride sertleşme ve ağrısız renk koyuluğu, aktif evrede leylak rengi, kronik evrede kahverengimsi renk değişikliğidir. Morfea yıllar içinde kendiliğinden gerileme gösterebilir. Nadir olarak dirençli seyredip, özellikle kollarda ve bacaklarda kalıcı değişiklikler oluşturabilir.[1]

Deriyi ilgilendiren birçok hastalık lokalize sklerodermayı taklit edebilir, hatta derinin primer maligniteleri ile karışabileceğinden ayırıcı tanı için mutlaka deri biyopsisi yapılmalıdır.[3] Lokalize skleroderma tedavisinde deri alanları sınırlı tutulmuşsa sıklıkla steroidli krem-merhemler, immün sistemi düzenleyici krem-merhemler (takrolimus/pimekrolimus) gibi lokal tedaviler tercih edilirken, yaygın veya şiddetli tutulum durumlarında sistemik immünosüpresif tedaviler kullanılmaktadır.[1,2,4]

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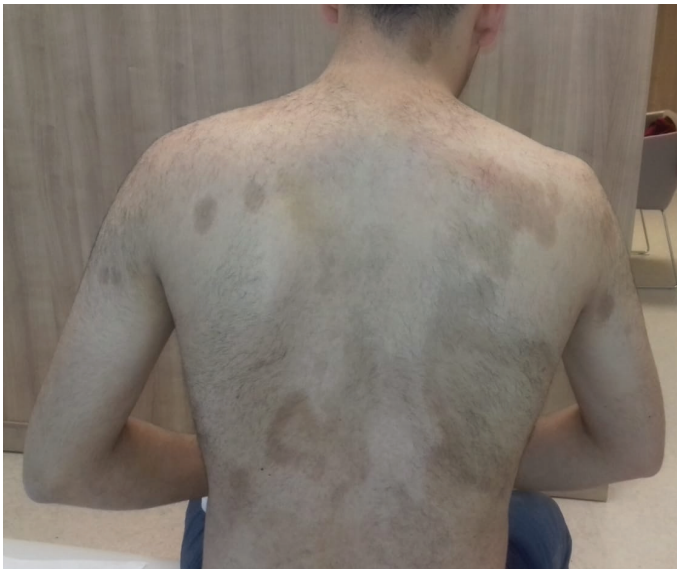
Bu bildiride morfea tanısı ile takip edilmekte iken ellerde sinovit ve fasiit tespit edilen, iç organ tutulumu olmayan genç bir erkek olgu sunulacaktır.

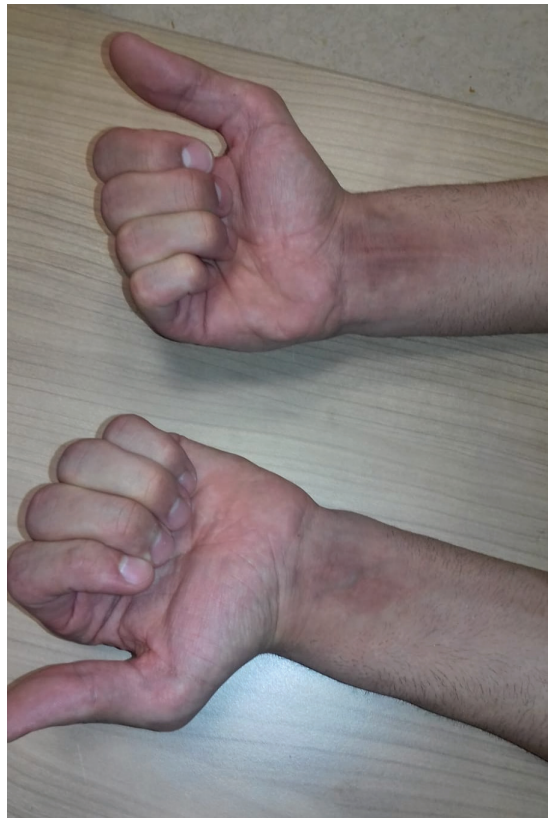
Olgu Sunumu

El parmaklarını kapamada zorluk, her iki el parmakları proksimal interfalangiyal (PİF) eklemlerde şişme şikayetleriyle romatoloji polikliniğine başvuran 27 yaşında erkek hasta, garson olarak çalışmaktaydı. 2012 yılında kolda ve sırtta siyah renk değişikliği olmuş, dermatoloji bakısı ve 2014 yılında sırttaki deri lezyonlarından 2 yerden yapılan biyopsi sonucu deri eklerinde azalma, kollajen demetlerde azalma, deri ekleri çevresinde fibroz, süperfisiyal perivasküler alanda lenfosit ve polimorfonükleer lökositlerde artış bulguları ile morfea tanısı almıştı. Morfea tanısından 2 yıl sonra (2016) dizlerde, ayak ve ellerde hafif ağrıları ve sabah katılığı başlamıştı. Ellerini kapatmada zorluk oluyormuş. Aynı süreçte el bileğinin iç yüzünde deride kızarıklık ve sertleşme farketmişti. Şüpheli ağız-göz kuruluğu tarifliyordu. 2016'da hidroksiklorokin 200 mg/gün verilmiş, 2017'de kolşisin tb 2*1 eklenmişti. İki ay kullandıktan sonra kolşisini kendisi kesmişti. Hasta Kasım 2019'da el 2. ve 3. PİF'lerde şişlik, hareket kısıtlılığı, ellerini kapatamama, yumruk yapamama yakınmalarıyla başvurdu. Özgeçmişinde morfea dışında özellik yoktu. Fizik muayenesinde sırtta ve kollarda yaygın morfea plakları vardı (Resim 1). Ellerde 2.-3. PİF'ler şiş, sıkmakla hafif ağrılıydı, ellerini yumruk yapamıyordu. El bilek iç yüzlerinde lineer sert plaklar mevcuttu (Resim 2,3). Sklerodaktili yoktu, diğer sistem muayeneleri olağandı. Laboratuvar tetkiklerinde ise; hemogram, karaciğer ve böbrek fonksiyon testleri, rutin idrar tetkiki ve tiroid fonksiyon testleri normal bulundu. C-reaktif protein: 0,54 mg/dL (normal 0-0,5 mg/dL), eritrosit sedimentasyon hızı: 16 mm/saat (normal 0-15 mm/h) idi. Serolojik tetkiklerde; anti-nükleer antikor 1/100 titrede zayıf pozitif- benekli paternde-, Ekstraktabl nükleer antikor profilinde anti SS-A antikoru +1 pozitiflik dışında anormallik yoktu. Anti-siklik sitrüline peptid antikor (anti-CCP) ve romatoid faktör (RF) negatifti. El grafileri doğal bulundu. Göz muayenesi sonucu Schirmer testi 15 mm, gözyaşı kırılma zamanı (BUT testi) ise 10 sn olup, normaldi. Sağ ve sol el manyetik rezonans raporunda musküler fasyalarda yağ baskılı T2 sekanslarda hiperintens görünümde lineer tarzda hafif dereceli sinyal artışları izlendi. Fleksör tendon kılıfları çevresi, el dorsumu düzeyi, özellikle proksimal interfalangiyal düzeyde tendon kılıfları çevresi ve sinovyumda non-spesifik ödematöz sinyal artışları görülmekte olup, bulgular 2. ve 3. parmakta kısmen daha belirgin izlenmekteydi. El bileği seviyesinden karpal tünel bitimine kadar tüm ekstensör ve volar yüzlerde yer yer vasküler yapıları da içine alan yaygın subkütan non-spesifik ödem mevcuttu.

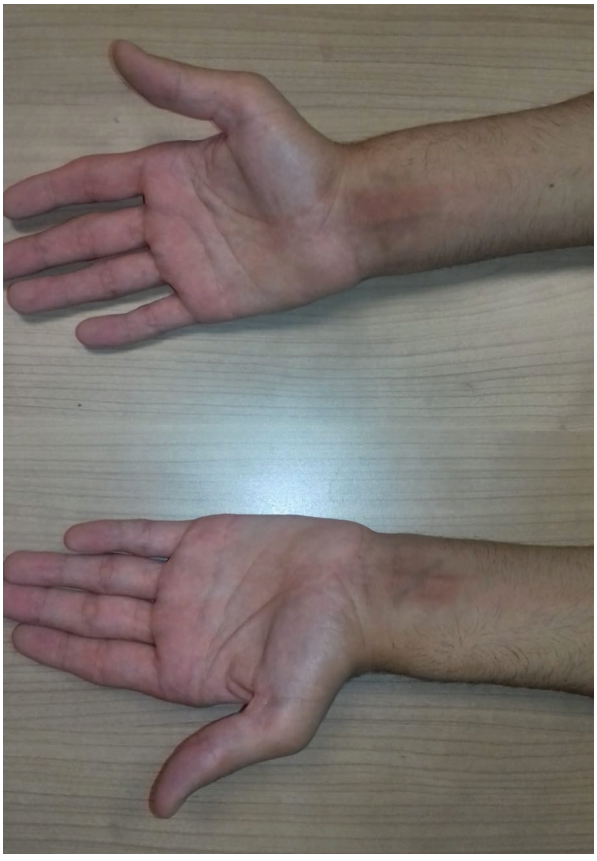
Hasta hidroksiklorokin 400 mg/gün ve kolşisin 0,5 mg 1*2 almakta idi. Bu tedavilerle yakınmalarında değişiklik olmadığını ifade ediyordu. Deri bulgularına ek olarak elde sinovit ve fasiit mevcuttu. Öykü, fizik muayene ve laboratuvar tetkiklerine dayanılarak herhangi bir iç organ tutulumu yoktu. Nadir görülen morfea ile ellerde sinovit ve



Resim 1. Sırtta yaygın morfea plakları



Resim 2. El bileklerinde morfea lezyonları



Resim 3. Ellerde PİP şişliği ve el bileklerinde morfea

fasiit birlikteliği olduğundan hastaya Ocak 2020 tarihinde metotreksat (MTX) 10 mg/hf (titre edilerek artırılacak), folik asit ve prednizolon 30 mg/gün başlandı. Birinci ay kontrolünde 15 mg/hf MTX ve 30 mg/gün prednizolon ile görüldü. Belirgin değişiklik olmamakla beraber el şişliğinde azalma ve fleksiyonda hafif düzelme saptandı.

Tartışma

Skleroderma derinin fibrozuna neden olan bir hastalıktır. Sadece deri tutulumu ile sınırlı olabileceği gibi iç organ tutulumunun da eşlik ettiği daha ciddi hastalık formlarında da görülebilir. Skleroderma, sistemik skleroz ve lokalize skleroderma olarak iki majör gruba ayrılır. Lokalize skleroderma yalnızca deri ve derialtı dokuya sınırlıdır ve Raynaud fenomeni, akroskleroz ve iç organ tutulumunun olmaması ile sistemik formdan ayrılır.[1] Morfea ile lokalize skleroderma eşanlamlıdır ve heterojen bir grup hastalığı içermektedir. Lokalize sklerodermalar lezyonun şekli, genişliği ve derinliğine göre sınırlı, yaygın, derin ve lineer şeklinde 4 gruba ayrılmaktadır. Ekstremitelerin lineer lokalize sklerodermaları, en coup de sabre lokalize sklerodermaları ve progresif fasiyal hemiatrofi (Parry-Romberg sendromu) lineer lokalize sklerodermalardır. Diğer lokalize sklerodermalardan farklı olarak, lineer lokalize sklerodermalar sıklıkla çocukluk çağında başlamakta ve tutulan deriye komşu deri altı yağ tabakası, kas ve kemikler etkilenebilmektedir. Sonuçta, hastalığa özgü deformiteler oluşmaktadır. Lineer lokalize skleroderma sıklıkla alt ekstremiteyi tutar.[5] Ardından sırasıyla üst ekstremiteler, frontal bölge, göğüs ön kısmı, karın ve kalçaları etkiler.[2] Bizim olgumuzda önce gövde ve kollar plak morfea şeklinde tutulmuş, ardından el bileklerinde lineer tarzda deri lezyonları ve elde kas-fasya-tendon etkilenimi şeklinde seyretmiştir. Ve bu tutulum ödem sonucu yumruk yapamama sorununa yol açmıştır.

Erişkin ve çocuklarda en sık görülen lokalize skleroderma türü lineer sklerodermadır. Bu tür tutulum, altındaki kaslar ve kemikleri etkileyebilen kalınlaşmış bir deri hattından oluşmaktadır. Bu yüzden de lezyonlar etkilenen eklem veya kasın hareketini kısıtlayabilir.[6] Vücudun tek bir tarafını tutma eğilimindedir.[2]

Lokalize sklerodermanın etiyolojisi tam olarak bilinmemektedir. Pek çok araştırmaya göre anormal kollajen sentezine yol açan immünolojik sebepler bulunmaktadır. Bazı çalışmalar fibroblast ve kollajen sentezini artırdığı bilinen TGF-~ ve PDGF gibi büyüme faktörlerinin ve sitokinlerin, lokalize sklerodermada arttığını göstermiştir.[7] Hastalığın etiyolojisinde otoimmüniteyi destekleyen kanıtlar da vardır.[2] Özellikle jeneralize morfea alt tipinde antinükleer antikor, antihiston antikor, anti-fosfolipid antikor, romatoid faktör ve lupus eritematozus hücresi gibi otoantikorların varlığı gösterilmiştir.[8-10] Fakat maalesef bu antikorların hiçbiri hastalığa özgün değildir. Son zamanlarda, lokalize sklerodermaya yüksek oranda özgün olduğu iddia edilen Cu/Zn süperoksit dismutaza karşı gelişen bir antikor tanımlanmıştır.[11]

Bu hastalığın öncelikle sistemik sklerozdan ayırıcı tanısının yapılması ve lokalize sklerodermayı taklit edebilen pek çok deri hastalığının da düşünülmesi gerekmektedir. Fakat lokalize skleroderma ve sistemik skleroz arasında her zaman histopatolojik ayrım da pek mümkün olmayabilmektedir. Bu iki hastalığın histopatolojik olarak enflamatuvar infiltratın dağılımı ve yoğunluğuna veya papiller dermis tutulumuna göre ayrılabileceğini bildiren çalışmalar vardır. Bu araştırmacılar lokalize sklerodermada enflamatuvar değişikliklerin sistemik skleroza göre daha belirgin olduğunu ve sistemik formda olmayan papiller dermiste sklerozun sıklıkla görüldüğünü gözlemlemişlerdir.[12]

Lokalize sklerodermanın sistemik forma dönüşmesi çok nadirdir. Böyle bir durumla karşılaşıldığında öncelikli olarak ilk tanıda bir hata olduğu düşünülür. Bununla birlikte lokalize

sklerodermanın sistemik formla birlikteliği de bildirilmiştir.[2,13,14] Olgumuzda sistemik tutulum bulgusu olmamakla birlikte morfeanın yanı sıra ellerde fleksiyonda kısıtlılık bulunmaktaydı, el-parmak derisinde sertlik-sklerodaktili yoktu, fakat hasta ellerini yumruk yapamamakta idi. Nadir de olsa böyle olgular iç organ tutulum olasılığı açısından dikkatle izlenmelidirler.

Bu hastalığın tedavisinde pek çok güncel bilgiler olgu sunumlarına ve kişisel deneyimlere dayanmaktadır. Bu nedenle günümüzde kullanılmakta olan tedavilerin başarısı hala sınırlıdır. Plak morfealı hastalar 3-5 yılda spontan remisyona girebildikleri için özel bir tedavi gerektirmezken yaygın, lineer ve derin morfealı hastalar yüksek morbiditeleri nedeniyle daha agresif tedaviye ihtiyaç duyarlar.[2,15] Plak morfea lezyonları kozmetik sorunlara yol açabilir. Hafif lezyonlarda kortikosteroidli krem veya pomadlar, lokal tedavilere cevap vermeyenlerde lezyon içi steroid, topikal kalsipotrien ve tokoretinat uygulanırken yaygın ve ilerleyici lezyonlarda sistemik kortikosteroidler, D-penisilamin, metotreksat gibi ilaçlar verilir.[1,2]

Literatürde morfea ile eozinofilik fasiit birlikteliğini konu alan olgu-çalışma ve derleme yazıları[16,17] olmakla beraber morfea ile fasiit-yaygın deri altı ödem birlikteliğine dair güncel yazı bulunamadı. Bu olgunun yazılması, tartışılması ve bilimsel katkı için sunulması için hastadan onam alınmıştır.

Sonuç

Lokalize sklerodermada fibroz genellikle deride sınırlı gözlenirken, nadiren deri altı doku, fasya ve alttaki kaslar ve hatta kemik dokuyu içerebilir. Bazı olgularda iç organ anormallikleri ile sistemik manifestasyonlar oluşabilir.[18] Bu nedenle morfea ile izlenmekte olan hastaların sinovit-fasiit ve nadiren iç organ tutulumları açısından dermatoloji ile romatoloji kliniklerinin iş birliği ile takip edilmesi, erken tanı ve tedavi açısından çok önemli gözükmektedir.

Etik

Hasta Onayı: Bu olgunun yazılması, tartışılması ve bilimsel katkı için sunulması için hastadan onam alınmıştır.

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Case Report / Olgu Sunumu

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Is it a liver abscess or liver infarction? Diagnostic dilemma in a patient with systemic lupus erythematosus and antiphospholipid syndrome: a case-based mini review

Karaciğer apsesi mi yoksa nekrozu mu? Sistemik lupus eritematoz ve antifosfolipid antikor sendromu olan hastada tanısal ikilem: Olgu eşliğinde kısa bir derleme

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Abstract

Thromboses in hepatic and portal veins are the most common problems affecting the gastro-hepatic system in antiphospholipid syndrome (APS), but hepatic artery thrombosis has been rarely reported especially during pregnancy or the postpartum period. We have reported a 26-year-old female patient with a previous diagnosis of systemic lupus erythematosus and APS manifested by fever and severe abdominal pain. Based on clinical and laboratory findings, diagnosis of liver abscess was initially considered. The final diagnosis was confirmed as liver infarction due to APS based on liver biopsy. After treatment with intravenous immunoglobulin, anticoagulation, plasmapheresis, and steroid, the clinical and laboratory improvement were observed. Here, our aim is to attract attention that hepatic necrosis may mimic liver abscess in terms of clinical symptoms and laboratory findings.

Keywords: Systemic lupus erythematosus, antiphospholipid antibody syndrome, hepatic necrosis, liver abscess

Öz

Hepatik ve portal ven trombozları antifosfolipid antikor sendromunun (AFAS) en sık gastrointestinal tutulum şeklidir. Hepatik arter trombozları ise özellikle gebelik veya postpartum dönemde nadir de olsa bildirilmiştir. Burada ateş ve şiddetli karın ağrısı ile başvuran 26 yaşında sistemik lupus eritematoz ve AFAS tanıları ile takip edilen kadın bir hasta sunduk. Klinik ve laboratuvar bulgular ile öncelikle karaciğer apsesi düşünülen hastaya karaciğer biyopsisi sonrası AFAS ilişkili karaciğer nekrozu tanısı kondu. İntravenöz immünoglobulin, antikoagülasyon, plazmaferez ve steroid tedavisi sonrası klinik ve laboratuvar iyileşme sağlandı. Amacımız nadir de olsa karaciğer nekrozunun klinik ve laboratuvar olarak karaciğer apsesini taklit edebildiğine dikkat çekmektir.

Anahtar Kelimeler: Sistemik lupus eritematoz, antifosfolipid antikor sendromu, karaciğer nekrozu, karaciğer apsesi

Introduction

Antiphospholipid syndrome (APS) is an autoimmune disease characterized by arterial and venous thrombosis due to antiphospholipid antibodies. Obstetrical APS is another entity that may affect both mother and fetus during the entire pregnancy with high morbidity.[1] The syndrome can be primary when happening in patients without identified autoimmune disease or associated with autoimmune diseases, particularly systemic lupus erythematosus (SLE).[2] Although mesenteric ischemia or portal and hepatic vein thrombosis can be seen during APS, liver ischemia and necrosis can rarely occur.[3] Here, we reported a case with SLE, and APS presented with fever and abdominal pain mimicking liver abscess. In this case-based review, we would like to emphasize that APS-induced liver infarction can mimic a liver abscess radiologically and clinically.

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Case Presentation

A 26 -year-old female with a previous diagnosis of SLE, APS, type 1 diabetes mellitus presented to emergency department with new onset dyspnea and vague abdominal pain. Past medical history was remarkable for deep venous thrombosis (DVT), pulmonary thromboembolism (PTE) and transient ischemic attack (TIA). Her medications included warfarin, insulin detemir, insulin aspart and oral cyclophosphamide for resistant immune thrombocytopenia. However, the patient indicated not receiving the drugs in the last three days for unknown reasons. Pathologic findings on physical examination were as follows: Mild tachycardia, tachypnea, and mild abdominal tenderness in the right upper quadrant on palpation. Blood pressure was normal, and no pathologic sounds were found during lung examination. Laboratory findings including hemoglobin 12.4 g/dL, platelet count 24.000/mm^3, lymphocyte count 450/mm^3, C-reactive protein 322 mg/L (normal range; 0-5 mg/L), erythrocyte sedimentation rate 82 mm/hour, aspartate aminotransferase 450 U/L (normal range; 0-40 U/L), alanine aminotransferase 311 U/L (normal range; 0-40 U/L), lactate dehydrogenase 760 U/L (normal range; 135-214 U/L), pro-calcitonin 2.1 ng/mL (normal range; <0.046 ng/mL), D-dimer 3.59 mg/L (normal range; 0-0.5 mg/L), serum fibrinogen 699 mg/dL (normal range; 170-420 mg/dL), prothrombin time 15 (normal reference; 10.5-14.5), partial thromboplastin time 130 (normal range; 24-40), lupus anticoagulant 3.87 (normal reference; 0.8-1.2), anticardiolipin IgG antibody 27.8 UI/mL (normal reference; 9.9-10 UI/mL) were found. Pulmonary computerized tomographic (CT) angiography revealed thrombus formation in the left pulmonary artery branches. During follow-up with anticoagulation, on day 2 of hospitalization, fever (39 °C) was developed, and pain in the right upper quadrant of abdomen intensified mimicking acute abdomen. Contrast enhanced CT evaluation of abdomen demonstrated non-specific findings such widespread hypoechoic lesions in the liver (Figure 1). Doppler imaging showed normal blood flow in the portal and hepatic systems was remarkable for evidence of acute thrombus formation of inferior vena cava (IVC) below the junction of hepatic veins. The liver abscess was initially considered based on fever, abdominal pain, and highly elevated acute phase parameters. Antibiotics and intravenous immunoglobulin (IVIG) were administered due to marked decrease in platelets with newly developed ischemia in the thumb finger of right hand and strong evidence of infection. However, microbiologic studies were found negative. Anticoagulation with enoxaparin was re-administered following elevation in platelets by IVIG. Dynamic magnetic resonance imaging (MRI) demonstrated lesions with T1W hypointense with peripheral enhancement and diffusion restriction observed along the right-middle hepatic vein traces (Figure 2). Liver biopsy was performed. Based on histopathologic evidence showing coagulation necrosis in the liver (Figure 3a, b), the diagnosis of APS related hepatic infarction was concluded and combination regimen of plasmapheresis and steroid was initiated. The patient was discharged with oral, cyclophosphamide, steroid, and subcutaneous low-molecular-weight heparin after complete clinical and laboratory improvement.

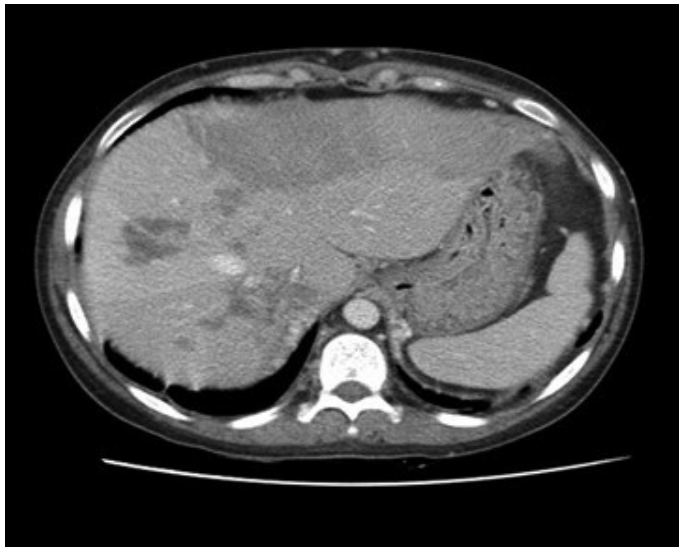

Figure 1. Widespread hypoechoic lesions detected by abdominal CT imaging

CT: Computer tomography

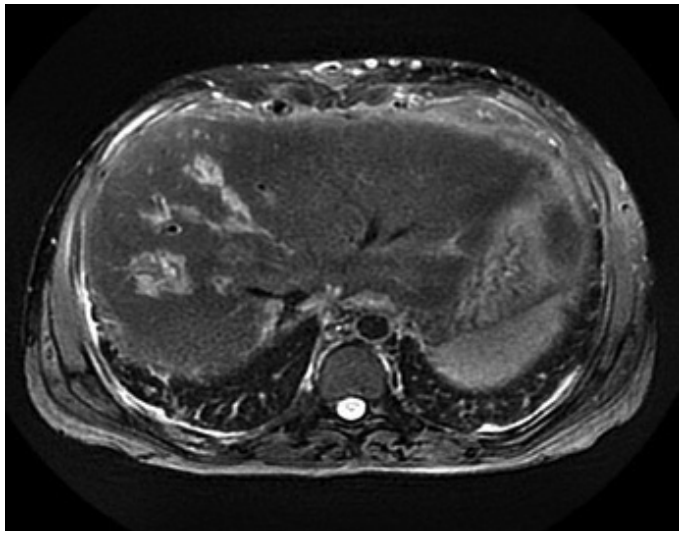

Figure 2. Lesions with T1W hypointense with peripheral enhancement and diffusion restriction observed along the right-middle hepatic vein traces on dynamic MR imaging of abdomen

MR: Magnetic resonance

Discussion

Liver is the most common affected organ among APS associated gastrointestinal involvement. The hepatic involvement generally manifests by clinical features of thrombosis of the hepatic veins, portal veins and rarely IVC.[3] Among those, hepatic infarction is rather uncommonly seen due to dual blood supply to liver by hepatic artery and portal system.

Gastrointestinal manifestations of SLE, such as nausea, vomiting and insignificant abdominal pain are generally mild. However, in the presence of acute severe abdominal pain in a patient with SLE, mesenteric vasculitis, hepatobiliary disease, and acute pancreatitis should be considered in the differential diagnosis.[4] In a study a study based on liver biopsy findings of patients with SLE, hepatic congestion was found the most common histopathologic feature followed by fatty changes, arteritis, peliosis hepatis, nodular regenerative hyperplasia, and rarely hepatic necrosis.[5]

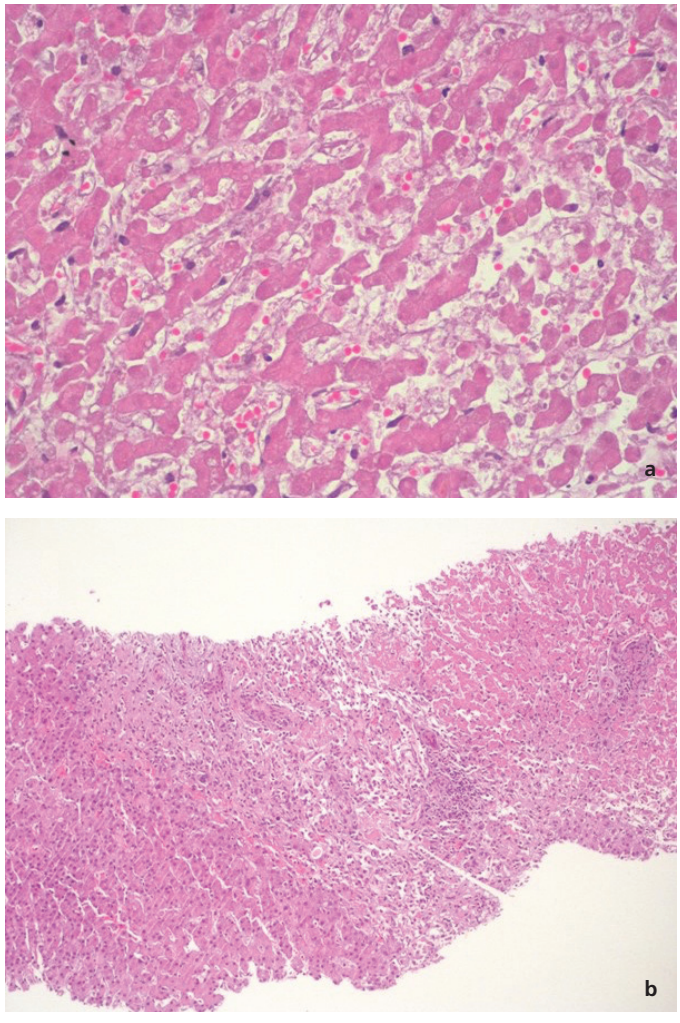

Figure 3a. Left side of the picture demostrated preserved liver parenchyma, liver necrosis is seen in the right side (HE x 100), **b.** Hepatic cell nuclear loss in the necrotic areas and intact trabecular structure and sinusoids in liver parenchyma. (HE x 400)

The first case possibly representing the association of hepatic infarction with high lupus anticoagulant titer in the literature was described in a 31-year-old female patient manifested with fever, right upper abdominal pain, thrombocytopenia, and elevated liver function tests following termination of 26-week pregnancy. The diagnosis of hepatic infarction was considered based on multiple hypoechoic lesions in liver upon CT imaging and the presence of high titers of lupus anticoagulant. The clinical improvement was documented after administration of steroid and heparin.[6] To date, nearly all cases of hepatic necrosis and/or infarction were reported during pregnancy and/or in the postpartum period due to APS itself or related to HELLP (H: Hemolysis, EL: Elevated Liver enzymes, LP: Low Platelets) syndrome.[7-9]

In the literature, the first case of hepatic infarction in a patient with SLE was identified in a 24-year-old male receiving hemodialysis presented with complaints of fever and right abdominal pain. Antibiotic treatment was initiated for a presumed diagnosis of acute cholecystitis. Thereafter, diagnostic laparotomy was required due to lack of response to antibiotics and deterioration in abdominal pain. The diagnosis of hepatic infarction was confirmed by multiple scattered necrotic foci appeared on laparotomy, histopathologic evidence of multiple micro-thrombosis in hepatic artery and portal venous branches and accompanied high lupus anticoagulant titers.[10]

What makes our case unique is that it is the first in the literature to demonstrate hepatic infarction in a non-pregnant female patient diagnosed with SLE and APS.

Of note, in our patient, we also should consider two other situations affecting the liver structure. Budd-Chiari syndrome (BCS), which is characterized by hepatomegaly, abdominal pain, and ascites, can be seen during APS due to hepatic vein occlusion.[3] In this study, the hepatic veins were patent and IVC thrombosis did not extend to the orifice of the hepatic veins. No evidence of ascites and hepatomegaly was also observed. As a result, we excluded the possibility of BCS in this case using radiological imaging tools. Another situation which should be taken into account is the catastrophic anti-phospholipid syndrome (CAPS). CAPS is a devastating condition characterized by multi-organ failure within a short time.[11] The patient had a history of thrombotic events such as TIA, DVT, and PTE developed in previous periods. In the last admission, we observed liver infarction, digital ischemia in her right-hand finger thumb and IVC thrombosis. However, digital ischemia may have stemmed from SLE-related vasculitis. Unfortunately, we did not perform a skin biopsy to confirm whether digital ischemia was due to APS or vasculitis. Additionally we cannot entirely rule out that IVC thrombosis may have already developed. If IVC thrombosis has developed in the

last week, CAPS should be considered in this case. However, the predominant vessel involvement in CAPS is in the form of small vessel thrombosis.[11]

The involvement of large vessels during CAPS is rarely observed. Therefore, we did not consider CAPS at the beginning of evaluation of our patient. However, we cannot deny that our patient may have definite CAPS. Whether it is a reflection of CAPS or not, what we want to specify in this case is that hepatic infarcts can mimic a liver abscess.[10-12]

As reported by Li et al.[12], in this patient, a diagnosis of the liver abscess was initially considered based on hypoechoic lesions on imaging and other clinical features. Liver biopsy, which was performed following a lack of response to antibiotics and negative microbiological studies, showed coagulation necrosis in the liver. As is well-known, marked increase in liver function tests is expected to occur in hepatic infarction. Moderate elevation in LFTs was found only in in our case, in contrast to the other two cases. Although no histopathological evidence of micro-thrombosis was demonstrated we considered APS-related arterial thrombosis and liver necrosis based on clinical and laboratory improvement after plasmapheresis and steroid treatment.

The differential diagnosis of these two entities is of great importance because of the completely different therapeutic management. Ultrasonography and CT imaging may not suffice to confirm a precise diagnosis. Of note, the enhancement seen along hepatic vascular structures and perivascular intensity on MRI are highly suggestive findings for hepatic infarction.[13] In this case, Doppler imaging and abdominal CT evaluation were inconclusive, therefore MRI was performed. Despite strong evidence suggesting hepatic necrosis in MRI, an accurate diagnosis was confirmed by liver biopsy.

Conclusion

Albeit rarely seen, hepatic infarction should also be considered in the differential diagnosis in SLE, and patients with APS presented with fever, abdominal pain, elevated liver function tests that mimics liver abscess. Thus, liver biopsy should be considered as an option to eliminate diagnostic ambiguities in selected cases.

Ethics

Informed Consent: Written consent was taken from the patient.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: R.Y., C.K., Design: R.Y., D.Ü.C., M.D., C.K., Data Collection or Processing: R.Y., M.D., D.A., C.K., Analysis or Interpretation: R.Y., D.Ü.C., M.D., D.A., C.K., Literature Search: R.Y., D.Ü.C., M.D., C.K., Writing: R.Y., D.Ü.C., C.K.

Conflict of Interest: No conflict of interest was declared by the authors.

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Case Report / Olgu Sunumu

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Relapsing polychondritis with pituitary adenoma

Hipofiz adenomu ile tekrarlayan polikondrit birlikteliği

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Abstract

Relapsing polychondritis (RP) is an autoimmune disease with unknown etiology, and mainly affects cartilaginous and non-cartilaginous organs. The RP is also associated with some solid tumors such as lung cancer, Kaposi sarcoma, and prostate cancer. There is no single effective treatment for alleviating symptoms or prevention of disease progression. However, corticosteroids are the main choices of RP treatment. The other drugs included immunosuppressive agents. Here, we present a new case of a patient who was diagnosed with relapsing RP along with pituitary adenoma and showed the effectiveness of etanercept [anti-tumor necrosis factor (TNF) agent] in the control with arthritis. Pituitary adenoma can develop following relapsing RP and should therefore be considered in the RP diagnostic procedure, and it could be affected on the patient's visual field test. Also, immunosuppressive agents such as anti-TNF agents can be used to control the disease.

Keywords: Relapsing polychondritis, cancer-related polychondritis, polychondritis, pituitary adenoma, anti-TNF

Öz

Tekrarlayan polikondrit (TP), etiyolojisi bilinmeyen ve esas olarak kıkırdaklı ve kıkırdaksız organları etkileyen otoimmün bir hastalıktır. RP ayrıca akciğer kanseri, Kaposi sarkomu ve prostat kanseri gibi bazı solid tümörlerle de ilişkilidir. Semptomları hafifletmek veya hastalığın ilerlemesini önlemek için tek bir etkili tedavi yoktur. Bununla birlikte, kortikosteroidler TP tedavisinin ana seçimidir. Diğer ilaçlar, immünosüpresif ajanları içerir. Burada, hipofiz adenomu ile birlikte tekrarlayan RP tanısı alan ve artrit kontrolünde etanerseptin [anti-tümör nekroz faktör (TNF) ajan] etkinliğini gösteren yeni bir olguyu sunduk. Hipofiz adenomu nükseden TP sonrası gelişebilir ve bu nedenle RP tanı prosedüründe düşünülmelidir ve hastanın görme alanı testinden etkilenebilir. Ayrıca hastalığı kontrol altına almak için anti-TNF ajanları gibi immünosüpresif ajanlar kullanılabilir.

Anahtar Kelimeler: Tekrarlayan polikondrit, kansere bağlı polikondrit, polikondrit, hipofiz adenomu, anti-TNF

Introduction

Relapsing polychondritis (RP) is a rare autoimmune disease with unclarified etiology, mainly affecting the cartilaginous tissues of the body. Nevertheless, other non-cartilaginous and proteoglycan rich tissues may also be affected. RP is a relatively rare disease without an animal model, making it more difficult to the assess the pathophysiology of the disease. RP is a life-threatening disease because it is often difficult to diagnose and treat.[1] The disease is a heterogeneous phenotype with different episodes and progressive.[2] The most common clinical presentations of RP are seronegative arthritis, laryngotracheal symptoms, nasal chondritis, ocular inflammation, and auricular chondritis.[1,3] Additionally, respiratory problems, infection, and cardiac complications with valvular involvement are the most common causes of morbidity and mortality in RP patients.[1]

Less commonly, RPs also associated with some benign and malignant solid tumors. Cancer-related RPs are reported, including lung cancer,[4,5] Kaposi sarcoma,[6] prostate cancer, malignant fibrous histiocytoma, soft-tissue sarcoma, breast cancer, urothelial carcinoma, and vocal cord tumor (glottis).[4,7]

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There is no uniformly effective treatment for alleviating symptoms or the prevention of disease progression. Meanwhile, corticosteroids are the main choice of RP treatment.[4] Other treatment strategies are dapsone, non-steroidal anti-inflammatory drugs, and colchicine, which have been proposed for mild RP patients.[7,8] Immunosuppressive agents, such as mycophenolate mofetil, cyclosporine, azathioprine, cyclophosphamide,[7] and anti-tumor necrosis factor (anti-TNF),[9] have also been applied to patients with severe symptoms of refractory or relapsing RP cases. The current study presented a new case of a patient diagnosed with RP along with pituitary adenoma and showed the effectiveness of etanercept (an anti-TNF agent) in control with refractory arthritis.

Case Report

A 52-year-old Iranian woman who presented with a 10-year history of joint pain and recurrent attacks of episcleritis was referred to the rheumatology clinic due to pain and swelling in the joints of the hands and wrists. Based on the patient's medical history, she had controlled mild hypertension with losartan tablets (25 mg/day) and due to the red retina has been examined several times by an ophthalmologist. She had complained of recurrent attacks of earlobe redness recurring every two to three months at the same time with the redness of the eye and was accompanied by pain and swelling of the earlobe.

On examination, she had arthritis of the right wrist and metacarpophalangeal 2 and 3 in both hands and other joints were normal. In complete ENT examination (inspection of the face, ears, nose, throat, and neck), only chondritis of the earlobe was observed (Figure 1). The only abnormal laboratory findings (Table 1) were high C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR).

Due to recurrent attacks of chondritis, episcleritis, and arthritis with relapsing polychondritis diagnosis, she was treated with prednisolone (5 mg/day) and methotrexate (10 mg/weekly). The symptoms of arthritis completely improved and recurrent attacks of the eyes and earlobes were not repeated. ESR was reduced from 43 to 12 mm/hour. After eight months of treatment, she again complained of arthritis attacks in the joints of the shoulders, knees, and ankles. Therefore, the doses of prednisolone and methotrexate were increased (50 mg/day and 20 mg/weekly, respectively). After reducing the dose of prednisolone, the symptoms recurred and the severity of symptoms and pain led to her hospitalization. The patient's ESR increased from 12 to 80 during a recent relapse. Malignancy was assessed due to the association of recurrent polychondritis with some tumors.

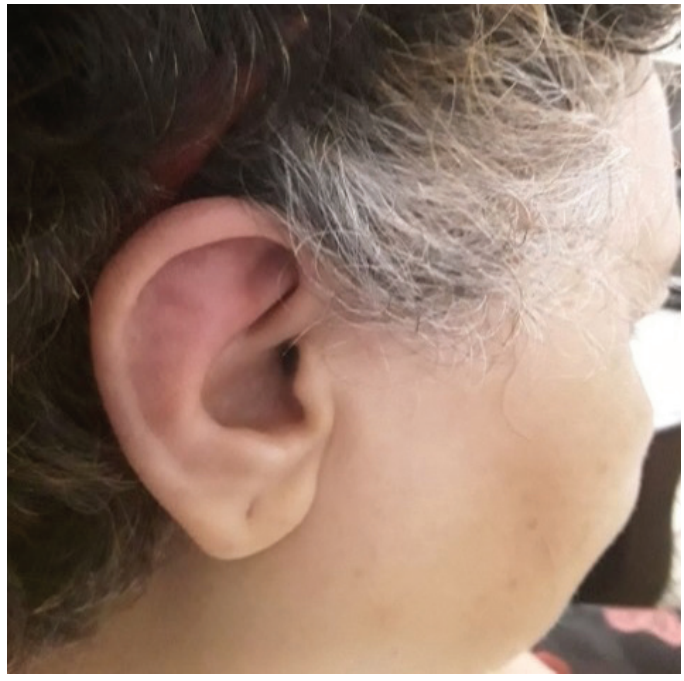

Figure 1. An ENT examination was observed chondritis of the earlobe

Table 1. Laboratory findings

Laboratory test		Results
Hematology	White blood cells (WBC)	8700
	Red blood cell (RBC)	4100000
	Hemoglobin (Hb)	12 g/dL
	Hematocrit (HCT)	39
	Mean corpuscular volume (MCV)	81
	Mean corpuscular hemoglobin (MCH)	29
	Mean corpuscular hemoglobin concentration (MCHC)	32
	Platelet (Plt)	326×10^3/mL
	Erythrocyte sedimentation rate (ESR)	43 mm/hour *
Serology	C-reactive protein (CRP)	32.0 mg/L *
	Anti-cyclic citrullinated peptide antibody (anti-CCP)	Negative
	Anti-neutrophil cytoplasmic antibodies (ANCAs)	Negative
	Rheumatoid factor (RF)	Negative
	ANA (anti-nuclear antibody)	Negative
Biochemistry	AST	17
	ALT	23
	BUN	0.9
	Urine analysis (UA)	Normal
Microbiology	Tuberculin test for tuberculosis (PPD)	Negative
	HBV markers	Negative
	HCV antibodies	Negative
	Brucellosis antibodies	Negative
	Chest X-rays (for ruled out tuberculosis)	Normal

* Abnormal range

CT scans of the lungs, abdomen, pelvis, ear, throat, and nose were normal. Digital mammography was normal.

Following relapsing RP, the patient was treated with subcutaneous etanercept (50 mg/weekly), prednisolone (15 mg/day), and methotrexate (20 mg/weekly). The patient's symptoms significantly improved and the pain was controlled. The ESR was reduced to 23 after two months, during which the dose of prednisolone was reduced to 5 mg/day. In the third month of etanercept therapy, the patient complained of headaches and laboratory tests demonstrated a slight increase in prolactin and the visual field test showed temporal hemianopia (Figure 2). Magnetic resonance imaging of the pituitary gland and Sella turcica revealed the enhancing intrasellar mass with extended to supraspace containing high signal area on T1 weighted (hemorrhage) and cystic change, which was suggested to be pituitary macroadenoma with a compression effect on optic chiasma and displacement of pituitary infundibulum (Figure 3). The patient underwent surgery and pathological examinations confirmed non-functioning pituitary adenoma (Figure 4). The patient's headache and visual field test improved following surgery. Finally, the treatment was continued with prednisolone (5 mg/day), methotrexate (15 mg/weekly), and etanercept subcutaneously (50 mg/week).

Discussion and Conclusion

Relapsing polychondritis (RP) is a rare recurrent auto-inflammatory disorder attacking cartilage and non-cartilage tissues, particularly the ear, nose, and tracheobronchial. The diagnosis of RP is commonly based on clinical features without specific serologic tests.[1] RP diagnosis is according to McAdams's criteria and three of the six following signs are essential: Audio-vestibular damage, respiratory tract chondritis, ocular inflammation, nasal chondritis, non-erosive seronegative inflammatory arthritis, and bilateral auricular chondritis. Damiani and Levine modified McAdams's criteria as following: McAdam criteria along with patient's response to corticosteroids or having McAdam criteria with tissue diagnosis.[7] Another criterion for RP diagnosis is the Michet criteria, including

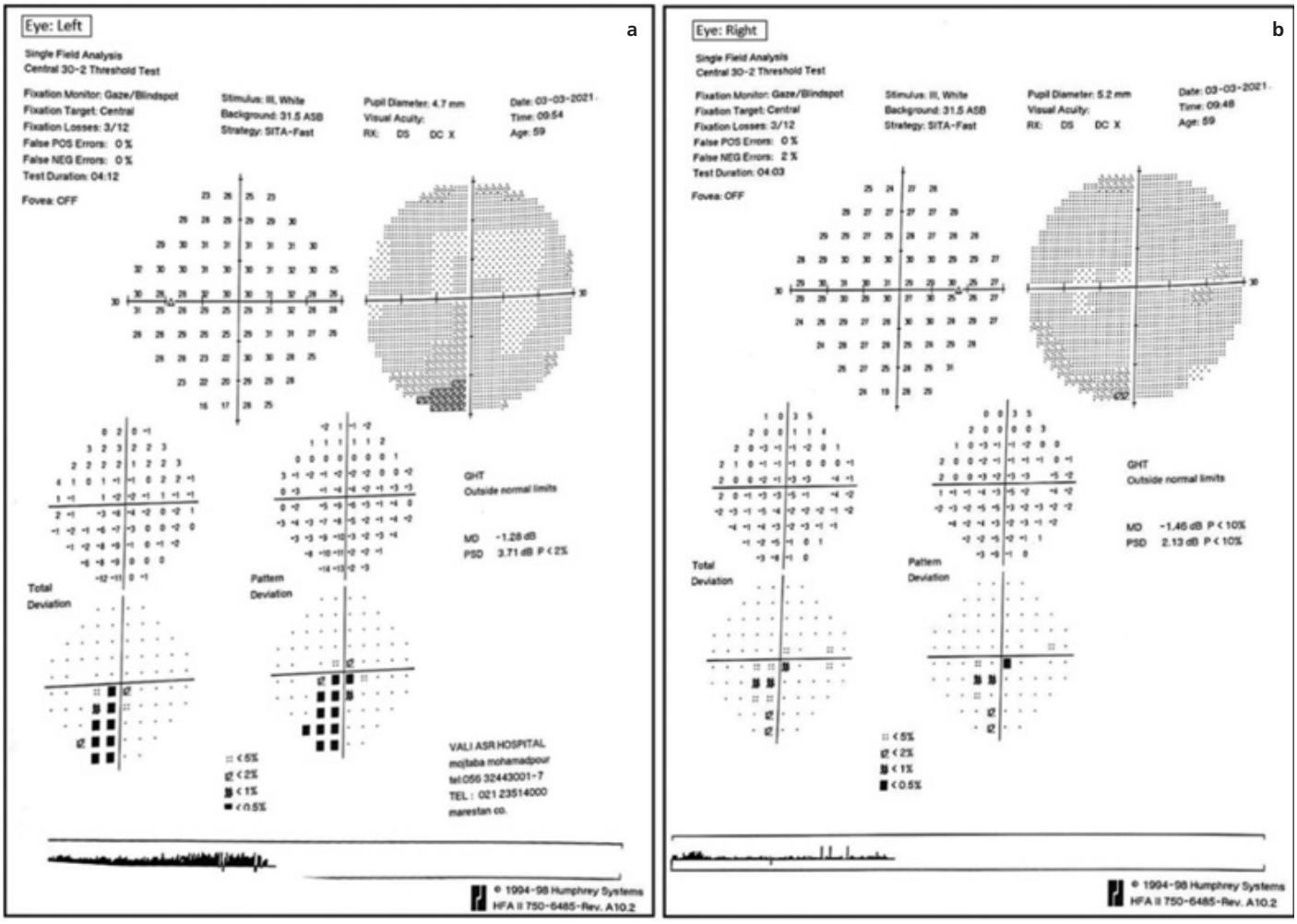

Figure 2a. The visual field test showed temporal hemianopia in left eye, **b.** and right eye

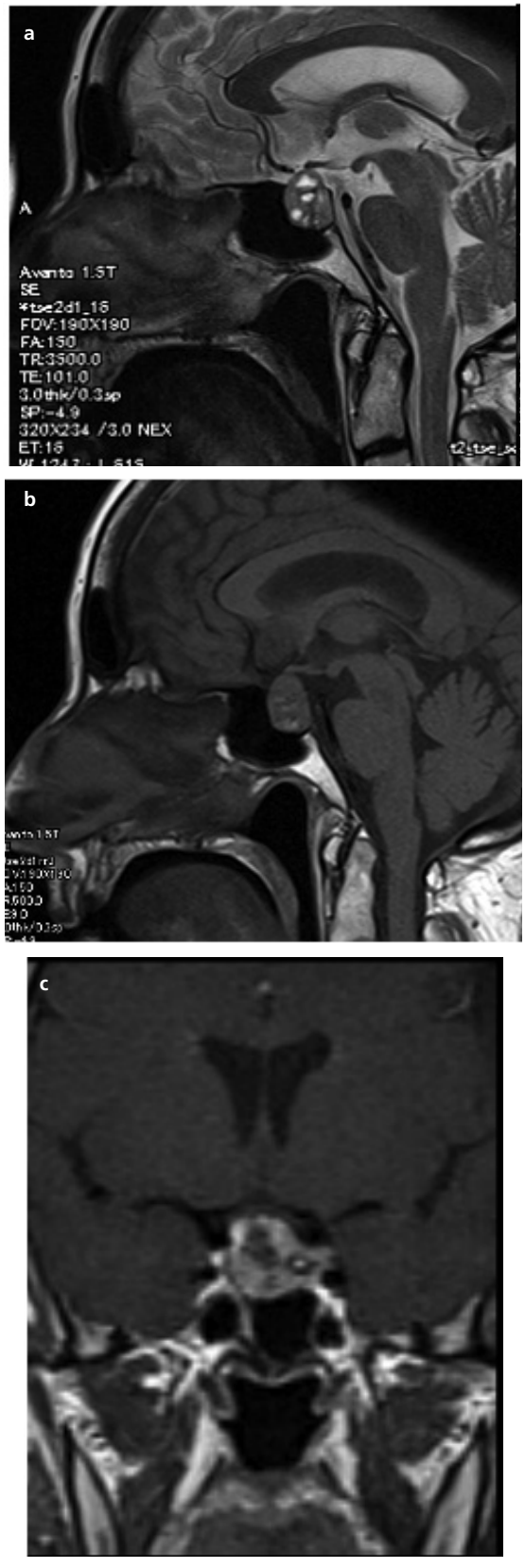

Figure 3. MRI of the pituitary gland and Sella turcica showed the enhancing intrasellar mass with extension to supra space (23×12×16 mm) containing high signal area on T1 weighted (a & b) hemorrhage and cystic change. c) pituitary macroadenoma with compression effect on optic chiasma

MRI: Magnetic resonance imaging

proven inflammation in two of the three parts of the body (laryngotracheal cartilages, nasal, and auricular) along with two manifestations, namely, hearing loss, seronegative arthritis, vestibular dysfunction, and ocular inflammation.[1] Here, our patient had recurrent chondritis, episcleritis, and arthritis with the diagnostic criteria of Michet in the absence of evidence of another disease.

In RP disease, the laboratory findings could be indicative of inflammation or sometimes tissue damage, urinalysis, and liver function tests are useful to detecting renal and liver function disorders, respectively.[7] Other laboratory tests, such as anti-phospholipid antibodies, anti-nuclear antibody, rheumatoid factor, and complement serum levels, could be helpful to diagnose RP or prove the presence of concurrent diseases.[10] In our patient, increased CRP and ESR were observed and other tests were negative.

Several studies have shown a significant association of RP with some malignancies and RP and cancer could occur at the same time. For example, myelodysplastic syndrome (MDS) has been reported in correlation with RP and it can occur after, simultaneously, with/or before RP, and in patients with MDS with RP, mortality is high.[11-13] In a study by Francès et al.,[14] on 200 patients with RP, the MDS was diagnosed in 22 cases. In this regard, with several published cases occurring in males' patients, also there may be strong sex priority. Also, Hodgkin and non-Hodgkin have been described in RP patients.[13,15,16] Although, there is a high association with a large number of patients with both diseases, its basis is unknown. In a study by Tomomatsu et al.,[17] a patient with simultaneously MDS and RP has reported following a transplantation of non-myeloablative allogenic bone marrow from a sibling donor, suggesting that the RP in this case may have been a paraneoplastic complication of the hematologic disorder. In several reports, the diagnosis of malignancies often occurred after RP in 10 cases with active disease (mean duration of 30 months).[4] Less commonly, RP is also associated with some benign and malignant solid tumors. The association of colorectal cancer with RP is rather uncommon and has been detected in three RP patients.[7] In a study by Gning et al.,[18] a 30-year-old female patient was reported with rectal cancer with RP and no special associated features were recorded. Lung cancer has also been reported in three RP patients.[5] Other tumors reported include vocal cords tumor (glottis), Kaposi sarcoma,[6] breast cancer, prostate, soft-tissue sarcoma, urothelial carcinoma, and malignant fibrous histiocytoma.[4,7] Additionally, cutaneous features and the variety of skin lesions are reported in cancer-related RP, such as pyoderma gangrenosum, dermatomyositis, and musculo-aponeurotic fibromatosis.[4] Hence, cutaneous-related RP could be a

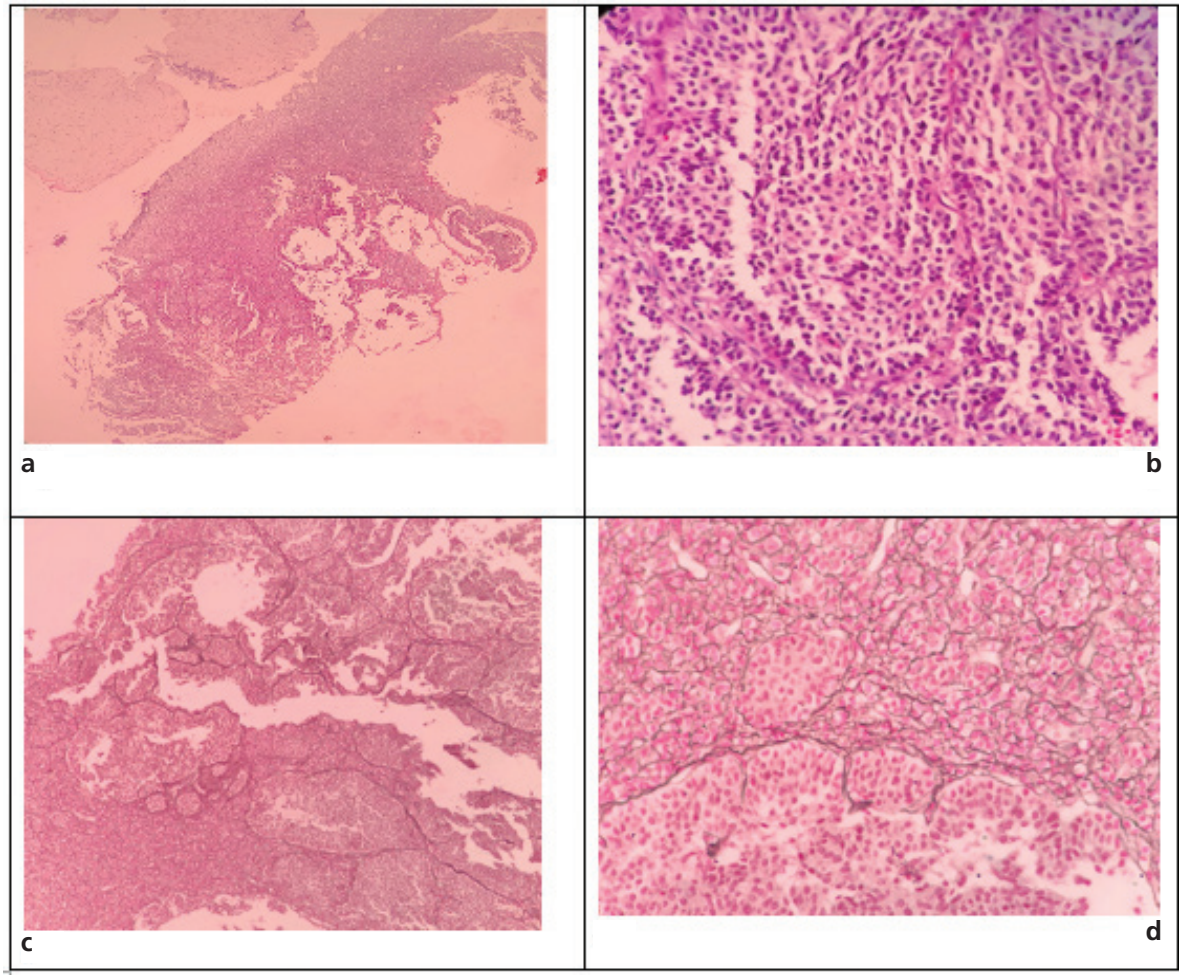

Figure 4. Histopathological image of non-functioning pituitary adenoma. **a & b.** Proliferation of monomorphal cells with round nuclei and vesicular chromatin and acidophilic cytoplasm (Hematoxylin & eosin stain), **c & d.** Reticulin-specific staining: Lack of usual acinar design

potential predictor of further cancer in RP cases. In our patient, detected pituitary adenoma was observed after several temporary remissions were presented without any cutaneous manifestation. A pituitary adenoma is usually associated with increased prolactin levels. In a study by Ahmed et al.,[19] five cases of pituitary adenoma with elevated PRL levels were reported and in this regard, our case also demonstrated an increase in prolactin levels.

No uniformly effective treatments for alleviating symptoms or the prevention of disease progression exist yet. Studies have shown that RP is mostly treated with corticosteroids, such as prednisolone.[4] Immunosuppressive agents, such as cyclosporine A, methotrexate, azathioprine, and cyclophosphamide also approved for patients with severe symptoms of refractory or relapsing RP.[4,7] In 2010 a study reported an RP therapy with TNF-α-antagonists, such as etanercept, resulting in a significant alleviate disease activity. In our case, the patient's symptoms significantly improved with subcutaneous etanercept (50 mg/weekly), prednisolone (15 mg/day), and methotrexate (20 mg/weekly). These results may alter the part of immunosuppressive therapy in RP pathogenesis.[20]

Pituitary adenoma can develop following relapsing RP and should therefore be considered in RP diagnostic procedure and it could affect the patient's visual field test. Additionally, immunosuppressive agents, such as anti-TNF agents, can be used to control the disease. It is also suggested that RP patients should be followed up for tumors thorough physical examination, radiological and laboratory investigations, physical examination, and history. RP patients should also be screened more carefully even in the remission of disease for early detection of tumors.

Ethic

Informed Consent: This case report was presented to the ethics committee of Birjand University of Medical

Sciences and approved with the following code: IR.BUMS.REC.1400.123. Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: N.N., Z.S., Design: Z.S., Data Collection or Processing: Z.S., Analysis or Interpretation: Z.S., Literature Search: Z.S., Writing: N.N., Z.S.

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Hazırlayan: Gülay Koca

2021 YILINDAN HABERLER

Acı Kaybımız

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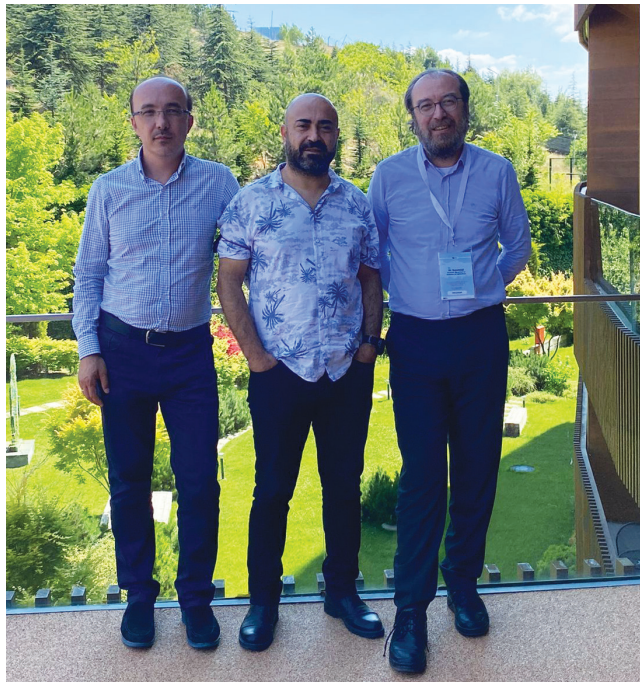
Romatolojinin Türkiye'de gelişmesine ve çok sayıda romatoloğun yetişmesine katkıda bulunmuş olan hocamızı sevgi ve saygı ile anıyoruz.

2021 yılının ilk etkinliği

"XV. Romatoloji Uzmanlık Öğrencileri ve Uzmanları İçin Eğitim Kursu & VII. Romatolojide Yaklaşımlar ve Profesörler ile Yuvarlak Masa Toplantıları"



COVID-19 salgını nedeniyle 2021 yılında 6 ay ertelenerek 8-11 Temmuz 2021 tarihinde Dr. Umut Kalyoncu, Dr. Timuçin Kaşifoğlu ve Dr. Cemal Bes başkanlığında, Eskişehir'de düzenlenen kursa 32 konuşmacı ve 145 katılımcı katkıda bulundu.

Kursumuza katılan meslektaşlarımıza, verdikleri destekler için ilaç endüstrisine ve başarılı organizasyonu için DEvent firmasına teşekkürlerimizi sunarız.

2021 yılının son etkinliği

“21. Ulusal Romatoloji Kongresi”

2020 yılında pandemi nedeniyle ertelenen “21. Ulusal Romatoloji Kongresi” 29 Eylül - 3 Ekim 2021 tarihleri arasında Prof. Dr. Fatoş Önen ve Prof. Dr. Servet Akar başkanlığında Antalya’da 625 katılımcı ile başarıyla tamamlanmıştır.

Kongrede sunulan 250 bildiri Ulusal Romatoloji Dergisi’nde yayınlanmıştır.

Kongreye katılan meslektaşlarımıza, verdikleri destekler için ilaç endüstrisine ve başarılı organizasyonu için DEvent firmasına teşekkürlerimizi sunarız.

Türkiye Romatoloji Derneği, Türkiye Futbol Federasyonu ve Trabzonspor kulübü işbirliği ile Dünya Ankilozan Spondilit Günü farkındalık aktivitesi gerçekleştirildi. Ankilozan spondilit hastalığına dikkat çekmek amacıyla 8 Mayıs 2021 Dünya AS Günü'nde "Ankilozan spondiliti erken tanıyın, ağrıya boyun eğmeyin" sloganı ile hayata geçirdiğimiz farkındalık kampanyamız, MediaCat Felis Ödülleri tarafından "Sağlık İletişimi Bölümü Gerilla Projesi" ödülüne layık görüldü.

Basın Bülteni

Ankilozan spondiliti erken tanıyın, ağrıya boyun eğmeyin!

İstanbul, Mayıs 2021 - Toplumsal farkındalık yaratmak amacıyla her yıl Mayıs ayının ilk Cumartesi günü Dünya Ankilozan Spondilit (AS) Günü olarak kabul ediliyor. Halk arasında iltihaplı bel romatizması olarak bilinen AS hastalığına dikkat çekmek amacıyla 8 Mayıs Dünya AS Günü'nde **"Ankilozan spondiliti erken tanıyın, ağrıya boyun eğmeyin!"** sloganı ile yeni bir farkındalık kampanyası hayata geçirildi.

8 Mayıs Cumartesi günü oynanan Trabzonspor - Antalyaspor maçı esnasında gerçekleştirilen farkındalık etkinliğinde futbolcular maça çıkarken her zamanki gibi koşarak değil, yere yakın bir körükten eğilerek sahaya çıkarak AS hastalığına dikkat çekti. Maçın spikeri ise; "Değerli futbolseverler, bugün her iki takım da gördüğünüz gibi sahaya biraz zorlanarak çıkıyor. Nedeni ise omurgada hareket kısıtlılığı yaratan iltihaplı bel romatizması Ankilozan Spondilit'e dikkat çekmek.1 Eğer 3 aydan uzun süren bel ağrınız varsa; ağrınız dinlenmeyle artıyorken hareketle azalıyor ve sabahları 30 dakikadan fazla süren bel tutukluluğunuz varsa mutlaka doktorunuza danışın.1,2 Ankilozan spondiliti erken tanıyın, ağrıya boyun eğmeyin!" anonsu ile hastalıkta erken tanının önemini vurguladı.

Kampanya ile ilgili açıklamalarda bulunan **Türkiye Romatoloji Derneği Başkanı Prof. Dr. Fatoş Önen;** "Ülkemizde her 200 kişiden birinde görülen AS hastalığında erken tanı büyük önem taşıyor. Toplumu doğru şekilde, doğru yollardan bilgilendirmeyi ve hastalığın geniş kitleler tarafından duyulmasını hedefleyen kampanyanın bu anlamda başarıya ulaşmasından ötürü son derece mutluyuz." dedi.

3 aydan uzun süren bel ağrısı AS hastalığı olabilir

Hastalıkla ilgili bilgiler veren Prof. Dr. Fatoş Önen; "AS vücutta birçok sistemi tutan enflamatuvar bir hastalık. Günümüzde enflamatuvar bel ağrısı sıklıkla mekanik bel ağrısıyla karıştırılıyor. Enflamatuvar bel ağrısını mekanik bel ağrısından ayıran önemli farklılıklar bulunmaktadır. Enflamatuvar bel ağrısı ağırlıklı olarak 40 yaşın altındaki kişilerde başlamakta, ağrılar üç aydan uzun sürmekte ve istirahatla geçmemektedir. Bel ağrısının özellikle gecenin ikinci yarısından itibaren hastaları uyandırması ve sabahları 30 dakikadan uzun süren tutukluğa neden olması da enflamatuvar bel ağrısının belirtileri arasında yer almaktadır." diye konuştu.

AS erkeklerde, kadınlara oranla 2-3 kat daha fazla görülüyor

Prof. Dr. Fatoş Önen ayrıca; "AS'nin nedeni halen bilinmemekle beraber, güçlü bir genetik bağ söz konusudur. AS yetişkin nüfusun yaklaşık %0,5'ini etkiler ve her yaşta görülebilse de çoğunlukla genç yaşlarda ortaya çıkar. Hastalık erkeklerde, kadınlara oranla 2-3 kat daha sıktır." dedi.

AS hastalığının yönetilmesinde, erken tanı büyük önem taşıyor

AS'nin enflamasyon sonucunda bel, sırt, boyun ve kalçanın arka kısımlarında ağrı ve tutukluğa neden olduğunu belirten Prof. Dr. Fatoş Önen "İlerleyen dönemlerde, bazen kamburluk ve omurgada kalıcı hareket kısıtlılığı gelişebilir. Ankilozan spondilitte göğüs kafesinde, daha çok diz ve ayak bileği gibi büyük eklemlerde ve topuk gibi kas kirişleri ile bağların yapıştığı kemik bölgelerinde de ağrı ve şişlikler ortaya çıkabilir. Ayrıca gözde kızarıklık ve ağrı (üveit), sedef hastalığı veya iltihaplı bağırsak hastalığı AS'ye eşlik edebilir." diye konuştu. Prof. Dr. Fatoş Önen; "Erken teşhis, egzersiz ve uygun müdahale ile hastaların daha sağlıklı ve kaliteli bir yaşam sürmesi mümkündür." diye açıklamalarına devam etti.

22 Mayıs 2021 tarihinde Gut Hastalığı Farkındalık Günü öncesinde hastalığın erken teşhisine ve düzenli hekim kontrollerine dikkat çekmek amacıyla "Geç Olmasın, Gut Olmasın" farkındalık kampanyası hayata geçirildi.

Basın Bülteni

TÜRKİYE ROMATOLOJİ DERNEĞİ GUT HASTALIĞINA DİKKAT ÇEKİYOR

Son yıllarda dünyada ve Türkiye'de görülme sıklığı artan gut hastalığı, beslenme düzeninden dolayı halk arasında "Kralların Hastalığı" veya "Hastalıkların Kralı" olarak biliniyor. Özellikle ayak baş parmağında ortaya çıkan ve vücudun birçok farklı eklemlerinde görülebilen gut hastalığı, Türkiye'de önemli bir toplum sağlığı problemi olup yaklaşık olarak her 300 kişiden birini etkilemektedir.

22 Mayıs Gut Hastalığı Farkındalık Günü'nde düzenlenen "Geç Olmasın, Gut Olmasın" farkındalık kampanyası çerçevesinde açıklama yapan Türkiye Romataloji Derneği Başkanı Prof. Dr. Fatoş Önen ve Türkiye Romatoloji Derneği Üyesi Prof. Dr. İsmail Sarı; gut hastalığının ülkemizde yeterince bilinmediğine ve gutun özellikle 40 yaş üstündeki erkekler arasında yaygın olduğuna dikkat çekerek hastalığın erken teşhis ve tedavisinin daha sonra gelişecek komplikasyonların önlenmesinde önemli olduğunu vurguladı.

Türkiye Romatoloji Derneği'nin desteklediği "Gut Hastalığı Farkındalık Çalışmaları" ile gut hakkında bilgilendirmeler yapılacak, erken tanı, yaşam şekli değişiklikleri ve tedavinin, atakları önleme ve hastalığın seyrini düzeltmedeki önemli rolü anlatılacak ve gut belirtileri görülmesi halinde hemen uzman bir hekime başvurulmasının önemi vurgulanacak.

21 Mayıs 2021 – 22 Mayıs Gut Hastalığı Farkındalık Günü öncesinde hastalığın erken teşhisine ve düzenli hekim kontrollerine dikkat çekmek amacıyla "Geç Olmasın, Gut Olmasın" farkındalık kampanyası hayata geçirildi.

Gut hastalığına dikkat çekerek, toplumu gut hastalığına yönelik bilgilendirmeye, sağlıklı yaşam seçimlerine yönlendirmeye ve hekim kontrollerini ihmal etmemeye davet eden farkındalık kampanyası çerçevesinde açıklama yapan Türkiye Romataloji Derneği Başkanı Prof. Dr. Fatoş Önen, Türkiye Romatoloji Derneği olarak gut hastalığı farkındalık çalışmalarını desteklediklerini belirterek, gut hastalığı, tedavisi ve risk grubundaki kişiler hakkında bilgi verdi. Gut hastalığının başlıca eklemleri tuttuğu ancak diyabet gibi pek çok hastalıkla birliktelik gösterebildiği, tedavi edilmediğinde, eklemlerde kalıcı hasardan böbrek yetmezliğine kadar birçok komplikasyona yol açabildiğini belirten Prof. Dr. Önen "Kanda ürik asit fazlalığı ile ortaya çıkan gut hastalığı, en sık görülen iltihaplı romatizmalardan biridir. Genellikle ayak başparmağında veya ayakta başlayan bu hastalık, belli bir süre sonra düzelen ataklar halinde seyreder. Atakları yaşayan hastalarımız, ağrının şiddetini tanımlarken, ağrı nedeniyle yürüyemediklerini, yatakta yorganın bile ayaklarına değmesini istemediklerini belirtiyorlar" dedi.

Gut, gelişiminde birden fazla etmenin rol aldığı bir hastalıktır

Gut hastalığı gelişiminde pek çok risk faktörü olduğunu belirten Türkiye Romatoloji Derneği Üyesi Prof. Dr. İsmail Sarı; yaş, cinsiyet, genetik yatkınlık, eşlik eden hastalıkların varlığı, kullanılan ilaçlar ve batı tarzı beslenme alışkanlığının gut gelişiminde önemli role sahip olduğunu söyledi. Öte yandan gutu tek başına bir eklem hastalığı olarak düşünmenin doğru olmadığını gerek diyabet gerek yüksek kan basıncı gibi hastalıkların guta sıklıkla eşlik ettiğini ve gut hastalarında kalp krizi riskinin artmış olduğunu vurguladı.

Gut tedavi edilebilen bir hastalıktır

Prof. Dr. Sarı sözlerine şöyle devam etti: "Gut tedavisi olan bir hastalıktır. Yaşam tarzı değişiklikleri ve uygun ilaç kullanımı ile hastalık tedavi edilebilir. Tedavi edilmemiş gut hastalarında tekrarlayıcı iltihaplı eklem atakları gelişir, eklemlerde hasar ve fonksiyon kaybı ortaya çıkabilir. Eklemlerinde, özellikle ataklar şeklinde yakınmaları olan hastalar gut tanısı ve tedavisi için mutlaka bir romatoloji uzmanına başvurmalı, daha sonraki dönemde de hastalığın ve tedavinin izlenmesi için 3-6 ay aralarla hekimlerine kontrole gitmelidirler. Gut tedavi edilebilen bir hastalıktır. Uygun ilaç kullanımı ve yaşam tarzı değişiklikleri ile tedavi edilir.

Türkiye'de her 300 kişiden biri gut hastası

Türkiye Romatoloji Derneği Başkanı Prof. Dr. Fatoş Önen, erken tanının ve düzenli hekim kontrollerinin altını çizerek "Gut en sık görülen iltihaplı romatizmalardan biridir. Sıklığı, ülkelere göre değişmekle birlikte %0,9 ile %2,5 arasındadır. Türkiye'de de çok sayıda gut hastası bulunmaktadır. Dengesiz beslenme ve yaşam tarzı nedeniyle son yıllarda, gut sıklığı giderek artış göstermektedir. Özellikle ailesinde gut bulunan ve diğer risk faktörlerini taşıyan kişilerin yaşam tarzı değişiklikleri ve doğru beslenme ile ileride gutsuz bir yaşam sürebilmeleri mümkün" dedi.

"Geç Olmasın, Gut Olmasın" projesinde gut hastalığına yeni karakter

Gut Hastalığı Farkındalık Günü kapsamında hayata geçirilen "Geç Olmasın Gut Olmasın" farkındalık kampanyası çerçevesinde gut hastalığında kişinin yaşadığı ağrı ve hassasiyet hissini yansıtmak adına yeni bir gut karakteri de yaratıldı. Bu karakter ile verilmek istenen mesaj gut hastalığına yakalanmış bireyin ataklar döneminde hissettiği acıyı vurgulamak oldu. Yapılan çalışma ile hastalığın önlenebilir ve tedavi edilebilir olduğuna dikkat çekildi. Söz konusu çalışma için Türkiye'nin uluslararası tasarım dünyasında öne çıkan yeteneklerinden Onur Can Çaylı ile iş birliği yapıldı. Dünya çapında geniş izleyici kitlesi olan film ve dizilerin görsel tasarım ekibinde yaptığı başarılı çalışmalarla adını duyuran Çaylı, yarattığı karakterle farkındalık çalışmalarına destek verdi.

12 Ekim 2021 tarihinde Dünya Artrit Günü etkinlikleri kapsamında Derneğimiz ve Novartis Türkiye işbirliği ile hazırlanan AS ve BEN platformunda romatizmal hastalıklara dikkat çekmek ve romatizmalı hastalarımızın daha sağlıklı bir yaşam sürdürmesine katkı sağlamak amacıyla Yetkin Dikinciler ile Dünya Artrit Gününe özel hazırlanan Podcast serisi yayınlandı.

Hazırlayan: Gülay Koca

2022 YILINDAN HABERLER

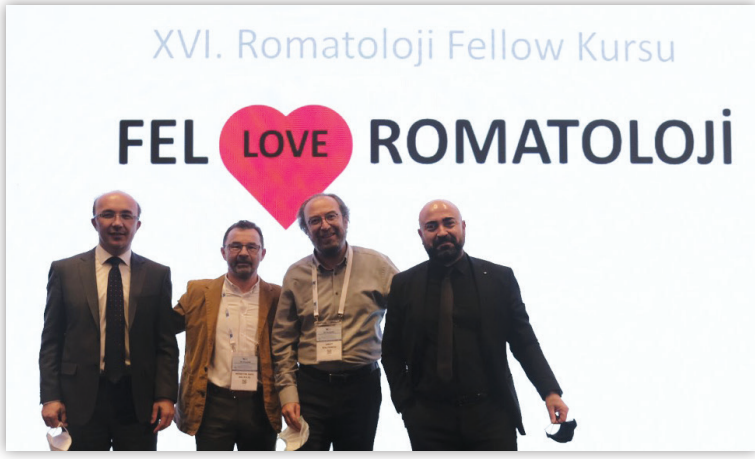
Ulusal Romatoloji Dergisi Ulakbim'de indekslenmektedir

Ulusal Romatoloji Dergisi Ulakbim'de indekslenmektedir

Derneğimizin kurucu üyesi ve İstanbul Üniversitesi Cerrahpaşa Tıp Fakültesi İç Hastalıkları A.D. Romatoloji Bilim Dalı emekli öğretim üyesi Prof.Dr.Hasan Yazıcı, ülkemizde Romatoloji'nin Bilim Dalı olarak kuruluşunda ve yaygınlaşmasındaki değerli çalışmaları, uluslararası alanda Türkiye'deki çalışmaların tanınmasına öncülük etmesi ve etik kuralların yürekli bir savunucusu olması nedeniyle, her yıl İstanbul Tabip Odası tarafından verilen Dr. Türkan Saylan 14 Mart Tıp Hizmet Ödülü'ne layık görüldü.

Derneğimiz üyesi ve İstanbul Üniversitesi-Cerrahpaşa, Cerrahpaşa Tıp Fakültesi, İç Hastalıkları Anabilim Dalı Romatoloji Bilim Dalı Öğretim Üyesi Prof. Dr. Gülen Hatemi, yayınlarının uluslararası yüksek etki faktörü olan dergilerde yayınlanması, uluslararası işbirliğinin geliştirilmesi, Behçet hastalığı tedavisinde sunduğu yeni değerlendirmelerin fikir lideri olması nedenleriyle İstanbul Tabip Odası 14 Mart etkinlikleri kapsamında Dr. Türkan Saylan Tıp Bilim Ödülü'ne layık görüldü.

XVI. Romatoloji Uzmanlık Öğrencileri ve Uzmanları İçin Eğitim Kursu & Romatolojide Yaklaşımlar ve Profesörler ile Yuvarlak Masa Toplantıları, 200 katılımcı ile 13-16 Ocak 2022 tarihlerinde Dr. Umut Kalyoncu, Dr. Timuçin Kaşifoğlu ve Dr. Cemal Bes başkanlığında Antalya'da başarı ile düzenlendi.



12-15 Mayıs 2022 tarihinde Gürcistan Romatoloji Derneği ve Türkiye Romatoloji Derneği tarafından Dr. Maia TSUTSKIRIDZE ve Prof. Vedat HAMURYUDAN'ın başkanlığında düzenlenecek olan Black Sea Rheumatology toplantılarının ilki Gürcistan'ın Batum kentinde düzenlenecektir.

Black Sea Rheumatology toplantıları, Karadeniz ülkelerindeki romatolojiye ilgi duyan klinisyenler ve bilim insanları arasında bilimsel köprüler kurmayı ve ileri dönemlerdeki ortak çalışmaları teşvik etmeyi amaçlamaktadır. Bu doğrultuda, bilimsel program dahilinde temel ve klinik araştırmalar üzerine konuşmaların yanı sıra yaygın ve bölgesel romatizmal hastalıkların tedavileri üzerine de konuşmalar, sözel sunumlar ve tartışmalar yer alacaktır.

Son yıllarda yalnızca yan dal uzmanlık öğrencilerimizin ve genç uzmanlarımızın sayısı giderek artmakla kalmıyor romatoloji bilim alanında da baş döndürücü bir hızla yenilikler, gelişmeler ortaya çıkıyor.

Romatoloji'ye yeni başlayan ve her geçen gün sayıları artan fellowların eğitim ihtiyacını karşılamak için destekleyici nitelikte bir içeriğe sahip olacak TRD Yaz Okulu 30 Haziran - 3 Temmuz 2022 tarihleri arasında Çanakkale'de düzenlenecektir.

Düzenleme Kurulu

Dr. Fatoş Önen,

Dr. Servet Akar,

Dr. Timuçin Kaşifoğlu,

Dr. Gökhan Keser,

Dr. İsmail Sarı

XXII. Ulusal Romatoloji Kongresi bu yıl Türkiye Romatoloji Derneği Yönetim Kurulu Başkanı Prof. Dr. Yasemin Kabasakal başkanlığında 26-30 Ekim 2022 tarihlerinde Antalya'da düzenlenecektir.