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Retroperitoneal fibrosis: Features of patients followed-up by a single tertiary rheumatology center

Retroperitoneal fibrozis: Bir tersiyer romatoloji merkezi tarafından izlenen hastaların özellikleri

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Abstract

Objective: Retroperitoneal fibrosis (RPF) is a rare autoimmune and fibro-inflammatory disorder affecting the retroperitoneum, often leading to ureteral obstruction. In this study, we analyzed the differences in demographic characteristics, clinical, laboratory, and imaging findings of patients with RPF, a rare disease followed in our clinic.

Methods: This retrospective study analyzed demographic, clinical, laboratory, imaging findings, and treatment outcomes of RPF patients aged over 18 years at Ege University Rheumatology Division. Diagnosis was based on clinical, imaging, and histopathological findings.

Results: The study included 26 patients (male/female: 17/9, mean age: 60.77 years). The most common symptom was abdominal pain, predominantly localized to the left lower quadrant. The most common cause was chronic periaortitis (CP). The majority of cases (24/26; 92.3%) had infrarenal aortic involvement. All other patients without infrarenal involvement were female. Infrarenal aneurysms were observed in 7.7%. Acute renal failure (ARF) at diagnosis occurred in 69.2% of patients, with no significant differences based on sex, age, or smoking. Immunoglobulin G4 (IgG4) related disease was identified in 19.2%, with non-IgG4 patients exhibiting higher C-reactive protein levels (p=0.082) and more frequent ARF (p=0.150). Cyclophosphamide (80.8%) and corticosteroids were the primary treatments, followed by azathioprine (61.5%), mycophenolate mofetil (34.6%), and rituximab (15.4%). None of the IgG4-related patients received rituximab.

Conclusion: In this retrospective analysis, most cases had idiopathic RPF, mainly as a complication of infrarenal CP. IgG4-related disease was the possible cause in only 19.2% of cases. The higher ARF incidence and inflammation markers in non-IgG4 along with the more frequent use of rituximab in this group suggest a more severe and treatment-resistant disease course in the non-IgG4 group. Further studies with larger cohorts are necessary.

Keywords: Retroperitoneal fibrosis, aortitis, aneurysm, periaortitis, immunoglobulin G4, IgG4

Özet

Amaç: Retroperitoneal fibrozis (RPF), nadir görülen otoimmün ve fibro-enflamatuvar bir hastalıktır. En önemli komplikasyonu üreter tıkanıklığıdır. Biz bu çalışmada kliniğimizde takipli nadir bir hastalık olan RPF'li hastaların demografik özelliklerini ve klinik, laboratuvar ve görüntüleme bulgularındaki farklılıkları analiz etmeyi amaçladık.

Yöntem: Bu retrospektif çalışmada, Ege Üniversitesi Romatoloji Anabilim Dalı'nda izlenen 18 yaş ve üzeri RPF hastalarının demografik, klinik ve laboratuvar özellikleri incelenmiştir. Tanı, klinik bulgular ve görüntüleme yöntemleriyle konmuş, bazı olgularda histopatolojik değerlendirme yapılmıştır.

Bulgular: Çalışmaya 26 hasta dahil edilmiştir (erkek/kadın: 17/9, ortalama yaş: 60,77 yıl). En sık görülen semptom karın ağrısı olup, çoğunlukla sol alt kadranda lokalizeydi. En sık neden kronik periaortit (KP) idi. Olguların 24'ünde (%92,3) infrarenal aortik tutulum vardı. Sadece infrarenal tutulumu olmayan diğer tüm hastalar kadındı. İnfrarenal anevrizmalar %7,7 oranında gözlendi. Tanı anında akut böbrek yetmezliği (ABY) %69,2 oranında görülmüş olup cinsiyet, yaş veya sigara kullanımına göre anlamlı bir fark bulunmamıştır. İmmünoglobulin G4 (IgG4) ile ilişkili hastalık %19,2 oranında tespit edilmiş olup IgG4 ilişkili hastalık olmayan hastalarda daha yüksek C-reaktif protein seviyeleri (p=0,082) ve daha sık ABY (p=0,150) görülmüştür. Siklofosfamid (%80,8) ve kortikosteroidler birincil tedaviler olup,, bunları azatioprin (%61,5), mikofenolat mofetil (%34,9) ve rituksimab (%15,4) izlemiştir. IgG4 ile ilişkili hastaların hiçbiri rituksimab almamıştır.

Sonuç: Bu retrospektif analizde, olgularımızın çoğunun idiyopatik RPF'ye sahip olduğunu ve bunun çoğunlukla infrarenal KP'nin komplikasyonu olduğunu tespit ettik. Hem KP hem de RPF'nin olası altta yatan nedeni olarak IgG4 ile ilişkili hastalık sıklığı yalnızca %19,2 idi. IgG4 olmayan grupta daha yüksek ABY insidansı ve enflamasyon belirteçleri ile bu grupta daha sık rituximab kullanımı, IgG4 olmayan grupta daha şiddetli ve tedaviye dirençli bir hastalık seyrine işaret etmektedir. Daha geniş kohortlarla yapılacak ileri çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Retroperitoneal fibrozis, aortit, anevrizma, periaortit, immünoglobulin G4, İgG4

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Introduction

Chronic periaortitis (CP) refers to a spectrum of idiopathic diseases whose common denominator is a fibro-inflammatory tissue developing in the periaortic retroperitoneum and frequently encasing neighboring structures such as the ureters and the inferior vena cava. CP includes idiopathic retroperitoneal fibrosis (RPF), inflammatory abdominal aortic aneurysms, and a combination of the two diseases, called perianeurysmal RPF.[1-3] RPF often occurs as a secondary complication of CP. While RPF with CP can be idiopathic, some cases previously classified as idiopathic may now be linked to immunoglobulin G4 (IgG4)-related disease, an autoimmune disorder first described in 2003.[3] Additionally, one-third of RPF cases are secondary to malignancies, medications (such as methysergide, hydralazine, and beta-blockers), previous radiotherapy, or certain infections. Recent studies, however, suggest that smoking and occupational asbestos exposure are also risk factors for the development of idiopathic RPF.[3-7]

The exact etiopathogenesis of the disease remains unclear; however, it is believed to result from an abnormal immune reaction to antigens present in atherosclerotic lesions of the abdominal aorta. The predominance of inflammation in the adventitia and the observation of vasa vasorum vasculitis sometimes suggests that RPF may initially occur as primary aortitis and may later cause secondary periaortic fibrosis.[3,6-10]

The clinical symptoms of RPF generally result from compression and obstruction of retroperitoneal structures. Patients may present with flank, dorsal, low back, or abdominal pain. The pain is usually constant, but colicky, if the ureter is affected. The most significant and widely recognized complication of RPF is hydronephrosis, leading to secondary renal failure due to ureteral obstruction. In addition to obstructive nephropathy, compression of retroperitoneal lymphatics and veins can result in lower extremity edema, deep vein thrombosis, scrotal swelling, varicocele, or hydrocele. Hypertension (HT) and constipation may also occur. Furthermore, RPF can be associated with systemic constitutional symptoms, including low-grade fever, fatigue, nausea, weight loss, and myalgias.[7,10,11] RPF may be associated with aortic aneurysms, however RPF does not directly cause aneurysm formation, rather CP causing RPF may also cause aneurysm formation.[1-4]

Acute phase reactants, including serum C-reactive protein (CRP) levels and erythrocyte sedimentation rate (ESR), may be elevated in 80-100% of cases. Mild to moderate anemia is commonly observed, while leukocytosis, eosinophilia, proteinuria, and microscopic hematuria occur less frequently. Antinuclear antibodies (ANA) can be found in nearly 60% of patients with idiopathic RPF. Additionally, anti-neutrophilic cytoplasmic antibodies (ANCA) and rheumatoid factor (RF) may be elevated in some cases. Although these antibody titers are generally low and nonspecific, their presence could suggest an underlying vasculitis or connective tissue disorder in some cases. Imaging techniques such as ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET) can be utilized for diagnostic evaluation.[3,7,10,11]

Different findings may change the approach to the disease and affect follow-up and treatment strategies. Therefore, we aimed to analyze the demographic features, along with the variations in clinical, laboratory, and imaging findings among patients with RPF.

Materials and Methods

This study was conducted on patients with RPF over the age of 18 who were being followed up at the Ege University Rheumatology Clinic between January 2000 and June 2024. RPF was diagnosed based on clinical findings, imaging findings such as typical irregular fibro-sclerosing lesions around the aorta, and histopathological evaluation. Demographic characteristics, clinical, laboratory, and imaging features of patients with RPF were retrospectively examined. In this study, RPF cases with and without IgG4 were included. None of the cases had any other defined systemic autoimmune disease, infection, malignancy, drug use that causes RPF. Our study included five patients with IgG4-related disease and 21 patients with non-IgG4-related disease, all with RPF. In the present study, IgG4-RD was diagnosed according to the 2020 revised comprehensive IgG4-RD diagnostic criteria.[12] The location of aortic involvement, smoking, diabetes mellitus, HT, and hyperlipidemia was evaluated in these patients. Acute renal failure (ARF) is a condition characterized by an increase in serum creatinine of ≥0.3 mg/dL (≥26.5 μmol/L) within 48 hours; or an increase in serum creatinine to ≥1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or a decrease in urine volume to less than 0.5 mL/kg/hour within 6 hours.[13] The presence and location of pain and the presence of constitutional symptoms were obtained from the data records. Laboratory parameters such as ESR, CRP, hemoglobin, serum creatinine, ANA, ANCA, were obtained from the Ege University patient registration program. Ege University Ethics Committee approved this study (approval number: 24-9.1T/40, date: 19.09.2024).

Statistical Analysis

The SPSS 21 software package was used to perform the statistical analysis. Patient characteristics were summarized using means, standard deviation (SD), ranges, and percentages as appropriate. Continuous variables were analyzed using the Mann-Whitney U test (Wilcoxon rank sum test) or t-test, and categorical data were analyzed using the χ^2 test or Fisher's exact test. A p-value of less than 0.05 was considered statistically significant.

Results

The study consisted of 26 patients, 65.4% of whom were male and 34.6% female. The mean age of the patients was 60.77 (SD: 9.2) years. The great majority of the cases, 24 (92.3%), only had infrarenal aortic involvement. One patient had infra and suprarenal fibrosis, while another patient had mediastinal, infra, and suprarenal fibrosis. All patients with more than just infrarenal involvement were female. The most common symptom was abdominal pain, mostly localized to the left lower quadrant. ARF was detected in 18 (69.2%) patients at the time of diagnosis. Double J stents had to be implanted in 15 of these patients. No statistically significant difference was found in gender, age, acute phase response, or smoking status between patients with and without ARF. However, although not significant, ESR was higher in patients without ARF than in patients with ARF (p=0.238). The most common cause was CP. IgG4-related disease was diagnosed in only five patients (19.2%) (male/female: 3/2); the mean age was 63.6 (SD: 7.0) years. The male ratio was higher in the non-IgG4 related group (p=0.580) and the mean age was higher in the IgG4-related group (p=0.461), although both were not statistically significant. While only one out of five patients diagnosed with IgG4 describes pain, 76.2% of non-IgG4 related patients initially described abdominal pain (p=0.034). Although statistically not significant, the CRP elevation was higher in the non-IgG4-related group (p=0.082). Additionally, the ESR at the time of diagnosis was higher in the non-IgG4-related group (p=0.500). ARF at the time of diagnosis was higher in the non-IgG4-related group (p=0.150). No significant differences were observed in other clinical and laboratory features between IgG4-related and non-IgG4-related diseases. Aneurysms were detected in only two (7.7%) of the patients, with diameters of 3.7 and 4.5 cm. The location of both aneurysms was infrarenal. Serum IgG4 levels were normal, and autoantibodies were negative in these patients with aneurysms.

Among the patients with IgG4 related RPF, one patient had ocular, pancreatic and lympadenopathy (LAP) involvement. One patient had bone marrow and LAP involvement Table 1.

ANCA was negative in all patients with RPF. Four (14.8%) patients had ANA positivity above 1/160 dilution. Among them, ENA profiles were negative in two patients, only AMA was positive in one patient, and PM-Scl, Mi-2, and DFS-70 were positive in one patient. Two (7.4%) patients were positive for lupus anticoagulants. Three of the ANA positive cases were in the IgG4-related group. Neither the patients with idiopathic RPF nor the patients with IgG4-related diseases had additional symptoms and clinical signs of connective tissue disease, and none of these patients met the classification criteria for connective tissue diseases.

RPF was demonstrated in 8 patients with MRI, in 17 patients with CT, and in 1 patient with PET CT. Fibrosis was seen in 3 patients, who underwent retroperitoneal biopsy. Among the patients in the study, one patient underwent eye biopsy and two patients underwent minor salivary gland biopsy. Except for the two biopsies that were performed retroperitoneally and one minor salivary gland biopsy, other biopsies showed IgG4- related disease findings.

Most of the patients received cyclophosphamide (80.8%) as initial treatment together with corticosteroids. The mean initial daily dose of methylprednisolone was 49.0 mg. Maintenance therapy consisted mostly of azathioprine (61.5%). Mycophenolate mofetil (34.6%) and rituximab (15.4%) were other agents used as alternative therapies. None of the patients with IgG4-related disease required rituximab treatment.

Clinical and laboratory parameters of these six patients with IgG4 related disease were given in Table 1. Comparison of laboratory, clinical and treatment features of patients with IgG4-related and non-IgG4-related RPF was given in Table 2.

Discussion

The incidence of RPF reported in the literature is 0.1-1.3/100,000, being more common in men and most frequently seen in the 40-60 age group.[3,5,7,10,14-17] In this study, the mean age of RPF patients was higher than reported in the literature. The mean age was higher in the IgG4-related group than in the non-IgG4-related group, in accordance with the literature.[14-20] The male ratio was higher in the non-IgG4 related group (p=0.580). Although some publications in the literature state the opposite,[14-17] studies by Kim et al.[18], Khosroshahi et al.[19], and Poddar et al.[20] similarly mentioned an increase in male dominance in the non-IgG4 related group.

CP can affect multiple vascular regions. In the study conducted by Kim et al.[18], the abdominal aorta was the most frequently affected site (84%), with the thoracic aorta

Table 1. Clinical and laboratory characteristics of patients diagnosed with IgG4-related disease

Patient	Gender	Age	Involvement	Acute renal failure	Cigarette	Pain location	ESR (mm/h)	CRP (mg/L)	IgG4 (g/L)	Involvement side	Biopsy
1	Male	52	Infrarenal	-	Quit smoking	No pain	5	1.4	6.2	Eye, LAP, pancrease	Eye
2	Male	65	Infrarenal	-	Quit smoking	Abdomen	22	2	2.41	-	
3	Male	64	Infrarenal	+	Smoking	No pain	4	5	4.69	-	
4	Female	71	Mediastinal and abdomen	-	No smoking	No pain	119	3	5	Lung, bone marrow	MSG
5	Female	66	Infrarenal	+	No smoking	No pain	18	7	1.03	-	Retroperitoneal

CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, Hb: Hemoglobin, LAP: Lympadenopathy, MSG: Minor salivary gland biopsy

Table 2. Comparison of laboratory, clinical and treatment features of patients with IgG4-related and non-IgG4-related retroperitoneal fibrosis

		CP (n=26)	IgG4-CP (n=5)	Non-IgG4-CP (n=21)	p-value
Male, n (%)		17 (65.4)	3 (60)	14 (66.7)	0.580
Mean age n (SD)		60.7 (9.3)	63.6 (7.0)	60.1 (9.8)	0.461
Pain n (%)		17 (65.4)	1 (20)	16 (76.2)	**0.034**
Pain location	Abdominal n (%)	8 (30.8)	1 (20)	7 (33.3)	NA
	Back n (%)	4 (15.4)	0 (0)	4 (19.0)	
	Left flank n (%)	8 (30.8)	0 (0)	8 (38.1)	
	Right flank n (%)	1 (3.8)	0 (0)	1 (4.8)	
Renal failure n (%)		18 (69.2)	2 (40.0)	16 (76.2)	0.150
Doble J stent n (%)		15 (57.7)	2 (40.0)	13 (61.9)	0.346
Constitutional symptoms n (%)		6 (23.1)	2 (40.0)	4 (19.0)	
Hypertension n (%)		9 (34.6)	2 (40.0)	7 (33.3)	0.580
Diabetes mellitus n (%)		7 (26.9)	2 (40.0)	5 (23.8)	0.411
Hyperlipidaemia n (%)		4 (15.4)	1 (20.0)	3 (14.3)	0.600
Smoking history n (%)		11 (42.3)	3 (60)	8 (38.1)	0.346
ESR n (25-75)		20.5 (8.5-43.2)	18 (4.5-70.5)	26.0 (18.7)	0.749
High ESR n (%)		13 (50.0)	2 (40)	11 (52.4)	0.500
CRP n (25-75)		5.5 (1.8-14.7)	2.0 (0.9-5.0)	13.5 (17.3)	0.185
High CRP n (%)		15 (57.7)	1 (20)	14 (66.7)	0.082
Localization	Infrarenal n (%)	26 (100)	5 (100)	21 (100)	NA
	Mediastinal n (%)	1 (3.8)	1 (20)	0 (0)	
	Suprarenal n (%)	2 (7.7)	1 (20)	1 (4.8)	
Aneurysm n (%)		2 (7.7)	0 (0)	2 (9.5)	0.646
Treatments	CYC n (%)	21 (80.8)	3 (60)	18 (85.7)	0.236
	AZA n (%)	16 (61.5)	3 (60)	13 (61.9)	0.657
	MMF n (%)	9 (34.6)	1 (20)	8 (38.1)	0.420
	Rtx n (%)	4 (15.4)	0 (0)	4 (19.0)	0.400

AZA: Azathioprine, CP: Chronic periaortitis, Constitutional symptoms (malaise, fatigue, weight loss), CRP: C-reactive protein, CYC: Cyclophosphamide, ESR: Erythrocyte sedimentation rate, MMF: Mycophenolate mofetil, NA: Non-available, Rtx: Rituximab

(46%) being the next most commonly involved, while 38% of patients had an accompanying aortic aneurysm. Another study reported thoracic vascular involvement in about 35% of 77 CP patients.[7] In comparison to patients with isolated abdominal CP, those with diffuse CP were more likely to be female, older, and show systemic symptoms, along with back or abdominal pain.[7] In a cohort of 51 patients studied by Yardimci et al.[5], 43 patients (84.3%) had infrarenal abdominal aortitis, while nine (17.6% re-evaluate percentage based on accurate patient data) had suprarenal involvement-eight of whom also had infrarenal periaortitis. Additionally, three patients (12%) had inflammatory abdominal aortic aneurysms.[5] Patients with diffuse CP had a higher prevalence of aneurysmal disease.[5] Similarly, a study from the Netherlands found that 25% of 53 consecutive patients with idiopathic RPF had aneurysmal

dilatation.[21] In this study, 24 (92.3%) of the patients with RPF had only infrarenal involvement, while one patient had infra and suprarenal fibrosis, and one patient had mediastinal, infra, and suprarenal fibrosis. Aneurysms were detected in two patients (7.4%), both of whom had infrarenal aneurysms. Interestingly, all other patients without exclusive infrarenal involvement were female, suggesting a potential difference in disease distribution based on sex. Given this, female patients may benefit from a full abdominal and thoracic scan. However, it is important to scan the infrarenal area for aneurysm involvement.

In the study, the median age of patients involving more than just infrarenal involvement was higher, but there was no significant difference (p=0.812). Similarly, patients with aneurysms and those diagnosed with IgG4-related disease tended to be older, but again, the differences were not significant (p=0.554, p=0.447). There were no significant differences in disease-related symptoms between patients with or without aneurysms or across different locations of involvement. To make more accurate analyses about this subject, research should be conducted with a larger number of patients.

In the literature, chronic CP has been frequently associated with IgG4-related disease. Yardimci et al.[5] diagnosed IgG4-related CP in 31 of 51 CP patients, while Kim et al.[18] identified 10 cases of IgG4-related CP in their cohort of 61 CP patients. Li et al.[22] reported that 77 of 105 CP cases belonged to the IgG4-related group, with no significant differences in age or disease course between IgG4-related and non-IgG4-related groups. However, the male-to-female ratio was significantly higher in the IgG4-related group. Similarly, Ozawa et al.[23] found periaortitis in 65 of 179 patients with IgG4-RD, with periaortitis predominantly affecting the abdominal aorta below the renal artery. In a study from China involving 587 IgG4- related disease patients, large vessel involvement was observed in 15.2%, and renal failure occurred in 48.3%.[24] Serum IgG4 levels may be high in both aneurysmal and non-aneurysmal types of CP.[7] In the study by Poddar et al.[20] 6 of 33 RPF patients were diagnosed with IgG4-related disease, while in the study by Hu et al.[17] 47 of 117 RPF patients were diagnosed with IgG4-related disease. In the study by Wang et al.[14] the rate of IgG4-related disease was 35.6%. In this study, IgG4-related disease was diagnosed in only five patients (19.2%). The most common cause was CP. Among these five patients, four had only infrarenal involvement, and one had both thoracic and abdominal involvement. No accompanying aneurysms were observed in these patients. The male ratio was higher in the non-IgG4-related group (p=0.580). CRP elevation was significantly higher in the non-IgG4-related group (p=0.082); in addition, ARF at diagnosis was also more common in this group (p=0.150). No significant differences were found in other clinical and laboratory features between the two groups. As a result, the higher CRP levels in the non-IgG4-related group suggest a more pronounced inflammatory response. In contrast, Li et al.[22] reported that ARF due to ureteral obstruction was more common in the IgG4-related group, which also exhibited higher ESR and CRP levels and recurrence rates.[22] Choi et al.[15] reported more ARF in the IgG4-related group; however, acute phase responses were similar, although slightly higher in the non-IgG4 group. Hu et al.[17] found higher CRP levels and higher ARF in IgG4-related disease patients. Conversely, Kim et al.[18] found no differences in laboratory findings, treatment, or outcomes between IgG4-related and non-IgG4-related CP cases and Wang et al.[14] found that the proportion of high CRP patients in the non-IgG4-related group was higher than that in the IgG4-related RPF group but there was no difference in ARF rates. In this study, the rate of IgG4-related disease was lower; CP was found to be the most common cause of RPF. In addition, the higher rates of ARF and high CRP levels in patients with non-IgG4-related RPF, and the need to use rituximab in this group, while it was not used in the IgG4-related group, suggest that more severe, aggressive, and treatment-resistant disease was observed in the group with non-IgG4-related RPF.

In the literature, low back pain was found to be the most frequent symptom in RPF patients.[6,8] In the present study, 65.4% of patients had pain at the beginning of the disease. The majority of these patients described abdominal pain (reported by 29.6% of patients) and left flank pain (reported by 29.6% of patients). In patients with IgG4-related disease, four out of five reported no pain, while only one experienced abdominal pain. In contrast, 76.2% of non-IgG4-related patients initially presented with abdominal pain. In the study by Kasashima et al.[25] abdominal or back pain was more prevalent in non-IgG4-related CP patients. In the study by Wang et al.[14], 48.4% of patients had lower back pain, which was more common in non-IgG4 related patients. In this study, the rate of abdominal pain was low in patients with IgG4-related disease. This may lead to delayed recognition and diagnosis of these patients. More attention should be paid to this respect.

ANA may be positive in 25-60% of patients with RPF. In addition, anti-thyroid antibodies have been reported to be positive in 31% of patients, RF in 14% of patient and ANCA in 10% of patients with RPF. Their presence is often associated with the accompanying autoimmune disease, although not always.[10,12] In this study, ANCA was found to be negative in all patients. Four patients

had ANA profiles with positivity above a 1/160 titer, and two patients had negative ANA profiles. One patient had AMA-M2 positivity; one patient had DFS-70, PM-SCL, and Mi-2 positivity. Two patients were positive for lupus anticoagulant. None of the patients had thromboembolic events. None of the patients with idiopathic RPF and patients with IgG4-related diseases had additional symptoms and clinical signs of connective tissue disease, and none of these patients met the classification criteria for connective tissue disease. Antibody positivity was considered a tendency to systemic autoimmunity in patients with RPF. One patient with RPF. who was not included in the study, was diagnosed with Erdheim-Chester disease. In the study conducted by Hu et al.[17] on 117 RFP patients, ANA positivity was observed in 32 patients, RF positivity in 17 patients, and anticardiolipin antibody positivity in 23 patients.[18] For differential diagnosis, it is important to screen for different autoimmune events and other diseases that may develop in patients with RPF.

Glucocorticoids, mycophenolate mofetil, cyclophosphamide, azathioprine, methotrexate, cyclosporine, rituximab, and tocilizumab can be used in the treatment of RPF.[6] In the present study, most patients (80.8%) were given cyclophosphamide as initial treatment, and azathioprine was the most commonly used maintenance treatment (61.5%). Rituximab (15.4%) and mycophenolate mofetil (34.6%) were used as alternative treatments. Rituximab is generally the treatment regimen of choice in resistant patients and patients with severe conditions. The preference for rituximab in non-IgG4-associated patients, but not in IgG4-associated patients, suggests that IgG4-associated cases may respond better to induction therapies, whereas non-IgG4-associated patients may be more resistant to treatment. Furthermore, the fact that high serum CRP levels and ARF were more frequent in the non-IgG4-related group may suggest more severe inflammation, and an aggressive disease course in this group. While Kim et al.[18] reported similar treatment responses between the IgG4-related and non-IgG4-related groups, Li et al.[22] found a higher probability of relapse in the IgG4-related group compared to the non-IgG4-related group.

Surgery is considered for CP patients with aneurysms. In a single-center study analyzing 1,555 aortic surgeries, periaortic RPF was identified in 1.09% of cases. Among these 17 RPF patients, 11 received only optimal medical treatment, while six underwent endovascular abdominal aneurysm repair after medical treatment failure, achieving a 100% technical success rate.[24] Additionally, one study reported that RPF patients with aortic aneurysms smaller than 5 cm did not require endovascular intervention, as regression occurred with corticosteroid treatment.[7] In this study, surgery was not performed for two patients with aneurysms, and the mean maximum aneurysm diameter was 4.1 cm.

Study Limitations

In this article, we present single-center data on patients with RPF. Given that RPR is a rare disease, a small number of cases seem acceptable. Another main limitation of the study is the retrospective design. Additionally, a potential limitation is that IgG4 levels were assessed in some patients after they had received immunosuppressive treatment and entered remission. This might have led to an underestimation of IgG4-related RPF cases, as prior treatment could have influenced IgG4 levels and involvements.

Conclusion

This study analyzed demographic, clinical, and laboratory data, imaging findings, and treatment outcomes of RPF patients, which is a rare disease. Patients with non-IgG4-related RPF showed more severe disease, with higher rates of ARF and elevated CRP levels, suggesting a more aggressive and treatment-resistant form of the disease. On the other hand, there was no difference between patients with and without ARF that could distinguish these patients or predict ARF. Additionally, all non-infrarenal RPF cases were female, indicating possible sex-based differences in disease distribution. The study calls for further research with larger patient populations to clarify these findings and improve management strategies.

Ethics

Ethics Committee Approval: Ege University Ethics Committee approved this study (approval number: 24-9.1T/40, date: 19.09.2024).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Concept: G.K., K.A., Design: G.K., K.A., Data Collection and Processing: F.T., D.K., S.K., G.K., Y.K., K.A., Analysis or Interpretation: F.T., G.K., Y.K., K.A., Literature Search: F.T., D.K., S.K., Writing: F.T., D.K., S.K., G.K.

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