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The Effect of Demographic Characteristics, Clinical and Laboratory Findings, and Treatment on Renal Damage Progression in Pauci-Immune Small Vessel Vasculitis with Renal Involvement

Renal Tutulumu Olan Pauci-İmmün Küçük Damar Vaskülitlerinde Demografik Özelliklerin, Klinik ve Laboratuvar Verilerin, Verilen Tedavinin Renal Hasar Progresyonu Üzerine Etkisi

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ABSTRACT

Objectives: To examine the demographic, clinical, and laboratory data of patients diagnosed with pauci-immune necrotizing glomerulonephritis and to reveal the effects of remission induction and maintenance treatments on these patients.

Methods: A total of 41 patients diagnosed with pauci-immune necrotizing glomerulonephritis and followed between 01.01.2009 and 30.10.2018 were included in the study. The demographic and clinical data of the patients, remission induction and maintenance treatments, effects of the treatments on survival, and treatment-related side effects were analyzed.

Results: The mean age was 54.1±16.7 years; 53.7% of the patients were female. Anti-MPO positivity was observed in 58.3% of patients, and anti-PR3 positivity was seen in 29.3%. While 95% of patients required dialysis, plasmapheresis was performed in 70.7%, and relapse occurred in 20% of the 25 patients who received maintenance treatment. Among patients needing dialysis at admission, 5 (23.8%) died, 7 (33.3%) continued to require dialysis, and 9 (42.8%) no longer needed dialysis. During follow-up, 8 out of 41 patients remained on dialysis, and 6 (14.6%) died.

Conclusion: Due to the high mortality of patients requiring dialysis at admission, immunosuppressive treatments should be prioritized, even though the treatment success rate is reduced by half in these patients.

Keywords: Anti-neutrophil cytoplasmic antibody; immunosuppressive treatment; pauci-immune necrotizing vasculitis; plasmapheresis.

ÖZET

Amaç: Çalışmamızın amacı, merkezimizde pauci-immun nekrotizan glomerülonefrit tanısıyla izlenen hastaların demografik, klinik ve laboratuvar verilerini incelemek ve verilen remisyon indüksiyonu ile idame tedavilerin hasta ve renal sağkalım üzerine etkisini ortaya koymaktır.

Yöntem: 01.01.2009 - 30.10.2018 tarihleri arasında pauci-immun nekrotizan glomerülonefrit tanısı ile takip edilen 41 hasta çalışmaya dahil edildi. Hastaların demografik ve klinik verileri, remisyon indüksiyon ve idame tedavileri, tedavilerin sağkalım üzerindeki etkileri ve tedavilere bağlı yan etkiler analiz edildi.

Bulgular: Hastaların ortalama yaşı 54,1±16,7 olup, %53,7'si kadındı. Anti-MPO pozitifliği %58,3, anti-PR3 pozitifliği %29,3 oranında saptandı. Hastaların %95'inde diyaliz ihtiyacı bulunurken, plazmaferez %70,7'sine uygulanmış; idame tedavisi alan 25 hastanın %20'sinde nüks görülmüştür. Yatışta diyaliz ihtiyacı olan hastaların 5'i (%23,8) ölürken, 7'sinin (%33,3) diyaliz ihtiyacı devam etmiş ve 9 hastanın (%42,8) artık diyaliz ihtiyacı kalmamıştır. Takipte 41 hastanın 8'i diyalize devam ederken, 6'sı (%14,6) hayatını kaybetmiştir.

Sonuç: Başvuru anında diyaliz ihtiyacı olan hastaların yüksek mortalitesi nedeniyle, bu hastalarda tedavi başarısı yarı yarıya azalsa da immünosupresif tedaviler tercih edilmelidir.

Anahtar sözcükler: Anti-nötrofil sitoplazmik antikor; immünsupresif tedavi; pauci-immun nekrotizan vaskülit; plazmaferez.

Pauci-immun vasculitides are multisystemic diseases characterized by necrotizing inflammation of small vessels and the absence of immune complex deposition in the vessel wall, and they can be anti-neutrophil cytoplasmic antibody (ANCA) positive or negative. Although it may be limited to the kidney, systemic involvement is prominent in most patients.[1] While an insidious course can be seen in a small number of patients, it usually presents with rapidly progressive glomerulonephritis in nephrology practice. Early diagnosis and aggressive treatment are extremely important, considering additional severe systemic involvement (e.g., alveolar hemorrhage). Induction therapy regimens are based on combining steroid therapy with cyclophosphamide or rituximab.

It is recommended to add plasmapheresis alongside immunosuppressive therapy in patients who need dialysis at the time of admission or in patients with advanced renal failure (sCre>5.8 mg/dL) or diffuse alveolar hemorrhage.[2] However, there are not enough studies investigating the efficacy of plasmapheresis treatment in patients with severe renal dysfunction. Interestingly, in this patient group, only 29% of the deaths in the first year after diagnosis were due to vasculitis itself; infections caused by immunosuppressive therapy were responsible for 50% of deaths.

In the PEXIVAS study, the results of which were reported recently, in 704 patients with an estimated glomerular filtration rate of less than 50 ml/min/1.73 m² or with alveolar hemorrhage, there was no additional benefit of plasma exchange therapy in reducing all-cause mortality or end-stage renal disease. Additionally, low-dose corticosteroid therapy has been shown to have similar effects to the standard dose on disease control.[3]

Although maintenance therapy is recommended to reduce the frequency and severity of vasculitis recurrences in patients with pauci-immun necrotizing glomerulonephritis who achieve remission with induction therapy, the choice of immunosuppressive drug for maintenance therapy and the appropriate duration remain poorly defined. Established risk factors for relapse include the persistence of PR3-ANCA positivity, a history of upper respiratory tract disease, and lower respiratory tract disease.[4]

In this study, we evaluated the demographic characteristics, clinical and laboratory data, and biopsy findings of patients with pauci-immun necrotizing glomerulonephritis. Additionally, we aimed to reveal the efficacy of induction and maintenance treatments, the effect of plasmapheresis treatment on all-cause mortality or the need for renal replacement therapy, the success rates of maintenance treatments, and the side effects of immunosuppressive drugs used.

Methods

This study was designed retrospectively and was approved by the Local Ethics Committee dated 2018, with decision no. 1359. This work was carried out in accordance with the Declaration of Helsinki (2000) of the World Medical Association. Detailed information about the study was provided to all participants, and consent forms were obtained from those who agreed to participate in the study.

The study included 41 adult patients with a diagnosis of pauci-immune type necrotizing glomerulonephritis who were followed up in the nephrology clinic of our hospital between 01.01.2009 and 30.10.2018. Clinical and laboratory data were obtained from the patients' files and the medical records in the hospital automation system. The estimated glomerular filtration rates (tGFR) of the patients were calculated using the MDRD formula:

tGFR (mL/min/1.73 m²)=175×(Scr)-1.154×(Age)-0.203×(0.742 if female)×(1.212 if African American).

Complete urine analysis and spot urine protein and creatinine levels of the patients were analyzed with the Beckman Coulter AU2700 device in the biochemistry laboratory of our hospital. In the urine analysis, the presence of ≥3 erythrocytes was accepted as hematuria. The antinuclear antibody test (ANA) was studied using the IFA method on the Helios device, and the anti-neutrophil cytoplasmic antibody

(ANCA) was studied manually using the IFA method.

The levels of anti-PR3 and anti-MPO antibodies were considered negative below the positivity limits of 12 IU/mL, borderline between 12–18 IU/mL, and positive above 18 IU/mL. Kidney biopsy findings (total number of glomeruli/number of globally sclerotic glomeruli/number of segmentally sclerotic glomeruli/number of cellular-fibrocellular-fibrous crescentic glomeruli/increase in mesangial matrix/mesangial proliferation/tubular atrophy/presence and severity of interstitial fibrosis/IgG, IgM, IgA, C3, and C4 staining intensity in immunofluorescence microscopy) were recorded.

Renal remission was defined as stabilization or improvement in serum creatinine levels along with the presence of fewer than 5 erythrocytes in the urine sediment at high magnification (40×10). Renal partial remission was defined as the presence of more than 5 erythrocytes in the urine sediment at high magnification (40×10) with stable creatinine levels, after excluding other possible causes of hematuria. Patients not meeting these criteria were considered unresponsive to renal treatment. Both partial and complete remission were categorized as "disease in remission."

During the follow-up of the patients, data were collected on whether plasmapheresis was performed after diagnosis, the number of sessions if performed, immunosuppressive drugs used in remission induction and maintenance therapy, clinical and laboratory response to treatment, treatment duration, and side effects of immunosuppressive drugs. Creatinine levels, tGFR, proteinuria, hematuria, and antibody titers were recorded at the 1st, 2nd, 3rd, 4th, 5th, 6th, 9th, 12th months (and at 15th, 18th months in 3-month intervals, if applicable), as well as at the final control visit.

For each patient, the primary outcomes recorded were the survival status at the last follow-up, the need for renal replacement therapy (hemodialysis, peritoneal dialysis, transplantation) at admission and at the last visit, treatments received, and renal remission status.

Statistical Analysis

SPSS 17.0 for Windows was used for statistical analysis. Descriptive statistics were expressed as numbers and percentages for categorical variables and as means and standard deviations for numerical variables. Comparisons between two independent groups were made using the Mann-Whitney U test, as numerical variables did not show normal distribution. Chi-square analysis was used to compare rates in independent groups. A statistical alpha significance level was accepted as $p<0.05$.

Results

The files of 41 patients who were followed up with the diagnosis of pauci-immun vasculitis with renal involvement in our Nephrology Clinic were analyzed retrospectively. Of the 41 patients, 22 (53.7%) were female, 19 (46.3%) were male, and 10% of the patients were of Syrian origin. The mean age at diagnosis was 54.1±16.7 years (range: 19–78). While constitutional complaints were present in 31 (75.6%) patients, macroscopic hematuria was detected in 14 (34.1%) patients. Although renal involvement was present in all included patients, pulmonary involvement was detected in 59% of the patients, upper respiratory tract involvement in 36.6%, neurological involvement in 14.6%, and eye involvement in 5%. Peripheral neuropathy detected by EMG was observed in 5 of 6 patients with neurological involvement.

At the time of admission, 39% of the patients had hypertension, and 12% described a recent upper respiratory tract infection before admission. The frequency of autoimmune disease was found to be 24%. The number of patients who needed dialysis at the time of diagnosis was 21 (51.2%). While the majority of the patients constituted the Anti-MPO positive group, 12% were followed up with a diagnosis of ANCA-negative pauci-immun vasculitis (Table 1).

The median tGFR at admission was 16 ml/min/1.73 m², and the median proteinuria level was 2210 mg/day. Hematuria was present in 85% of the patients at admission. Biopsy data were available for 30 of the 41 patients included in the study. Crescents were detected in the biopsy of 27 of 30 patients.

During the follow-up period, creatinine, hematuria, proteinuria, antibody titer, and tGFR levels were analyzed separately at the 1st, 2nd, 3rd, 4th, 5th, 6th, 9th, 12th, 15th, 18th, 21st, 24th months, and at the last visit. The median follow-up period was 7 months (IQR: 2–31.8).

Plasmapheresis was performed in 70.7% of the patients during induction treatment. The mean number of plasmapheresis sessions was 38. All of the patients who continued to need renal replacement therapy (RRT) had received plasmapheresis during remission induction treatment. It was observed that 11 of the 21 patients who required RRT at the time of diagnosis no longer needed RRT after remission induction therapy. Plasmapheresis was performed in 10 of these 11 patients who no longer required RRT.

Table 1. Demographic and clinical characteristics at admission

	n (%)
Gender (female)	22 (53.7)
Race	
Turkish	36 (87.8)
Syrian	4 (9.8)
Kazakhstan	1 (2.4)
Age of diagnosis(year)*	54.1±16.7
Height (m)*	161.8±9.1
Weight*	72.1±15.1
BMI*	27.8±5.6
Smoking	
Never smoked	26 (65)
Ex smoker	11 (27.5)
Active smoker	3 (7.5)
Cigarette (packet/year) **	20 (IQR 12.5-40)
Drug abuse	0
Hypertension	16 (39)
Diabetes Mellitus	9 (22)
Ischemic heart disease	6 (14.6)
Peripheral arterial disease	2 (4.9)
Cerebrovascular disease	1 (2.4)
Chronic liver disease	0
Family history of Pauci-immune necrotizing glomerulonephritis	2 (4.9)
Presence of autoimmune disease	10 (24)
Hypothyroidism	5 (12)
Romatoid artrit	1 (2)
Ankylosing spondylitis	1 (2)
Other autoimmune diseases	3 (7)
Application complaint	
Constitutive symptoms	31 (75.6)
Hemoptysis	13 (31.7)
Macroscopic hematuria	14 (34.1)
Decreased urine output	11 (26.8)
Systolic blood pressure (mmHg)*	129±21.1
Diastolic blood pressure (mmHg)*	81.1±10.4
Mean arterial blood pressure *	97±12.9
Presence of pretibial edema	13 (31.7)
Rash	5 (12.2)
Use of RAS blockade	5 (12.2)
Use of calcium channel blockers	8 (19.5)
Other antihypertensives	7 (17.7)
Use of antiaggregants	5 (12.2)
Ejection fraction (%)	58±5.9
Valvular heart pathology	6 (14.6)
Recent history of URTI	5 (12.2)

Table 1. Demographic and clinical characteristics at admission (Cont.)

	n (%)
Systemic involvement of vasculitis	
Pulmonary involvement	24 (58.5)
Cavernosis	7 (29.2)
Infiltration	13 (54.2)
Mass	3 (12.5)
Nodüle	1 (4.2)
Upper respiratory tract involvement	15 (36)
Paranasal sinus	8 (53)
Nose	9 (60)
Hearing problems	3 (7)
Neurologic involvement	6 (14.6)
Sign of eye vasculitis	2 (4.9)
Need for dialysis at the time of diagnosis	21 (51.2)
Pauci-immune vasculitis	
Anti-MPO positive	24 (58.5)
Anti-PR3 positive	12 (29.3)
ANCA negative	5 (12.2)

BMI: Body mass index; NSAİ: Non-steroid anti-inflamatuar; RAS:Renin-anjiotensin system; URTI: Upper respiratory tract ınfectıons; ANCA: Anti-neutrophil cytoplasmic antibody; Anti-MPO: Antimyeloperoxidase; Anti-PR3: Antiproteinase 3; *: Mean±Std; **: Median(IQR).

At the end of the follow-up of the 21 patients who required dialysis at admission, 5 (23.8%) died, 7 (33.3%) continued to need dialysis, and 9 (42.8%) no longer required dialysis.

It was determined that remission was achieved in 78.9% of the patients following remission induction therapy. Only 1 patient was given rituximab as part of remission induction treatment, as this patient did not accept cyclophosphamide treatment. This patient died during treatment due to disease exacerbation and infection.

Remission was achieved in 30 of the 41 patients who received remission induction treatment. Eight patients did not achieve a renal response to the treatment provided. Two of the remaining three patients were not evaluated because they had only received the first dose of induction therapy at the time of file review. Among the three patients whose remission induction treatment success could not be evaluated, one was in the group receiving corticosteroid and plasmapheresis, and two were in the group receiving corticosteroid and cyclophosphamide.

The success rates of remission induction treatment were found to be as follows:

Table 2. Treatments and treatment responses in remission induction

	Patients who received emission induction treatment (n=41) n (%)	Patients who achieved remission with remission induction therapy (n=30) n (%)	Patients not in remission with remission induction therapy (n=8)* n (%)
Cyclophosphamide+Corticosteroid	9 (2.9)	7 (23.3)	0
Cyclophosphamide+Corticosteroid+Plasmepheresis	26 (63.4)	19 (63.3)	7 (87.5)
Corticosteroid	3 (7.3)	3 (10)	0
Corticosteroid+Plasmapheresis	2 (4.8)	1 (3.3)	0
Rituximab+Steroid+Plasmapheresis	1 (2.4)	0	1 (12.5)

*: Evaluation was not made for the 3 patients who were followed up because they only received the first dose of induction therapy. Anti-MPO: Antimyeloperoxidase; Anti-PR3: Antiproteınase 3; RRT: Renal Replacement Therapies; KDIGO: Kidney Disease: Improving Global Outcomes.

- 100% in the group given cyclophosphamide and corticosteroid,
- 73% in the group given cyclophosphamide, corticosteroid, and plasmapheresis,
- 100% in the group given corticosteroid and plasmapheresis,
- 100% in the group receiving corticosteroid alone (Table 2).

While 51% of the patients were on hemodialysis at admission, this rate decreased to 22% (9 patients) at the last patient visit. Six of the 41 patients died during the follow-up period, resulting in a survival rate of 85.4%.

When the causes of death were investigated:

- One patient died due to gastrointestinal bleeding, likely caused by steroids.
- One patient died from hypervolemia after not receiving hemodialysis treatment.
- One patient developed pulmonary tuberculosis during azathioprine use and subsequently died.
- One patient died from disease activation and infection during remission induction treatment with rituximab.
- Two patients experienced sudden cardiopulmonary arrest during dialysis while in remission and receiving renal replacement therapy (RRT).

Half of the deaths were attributed to severe side effects of the immunosuppressive drugs.

The success rates of remission maintenance treatment were as follows:

- 82% in the patient group receiving azathioprine,
- 100% in the patient group receiving rituximab,
- 33% in the patient group receiving steroids alone.

Observed side effects related to the immunosuppressive treatments are summarized in Table 3. Serious side effects of immunosuppressive drugs developed in 34.1% of the patients. No serious side effects occurred during plasmapheresis procedures.

Renal survival was observed in 65.8% of the patients, while patient survival was 85.4%. Patients without renal and patient survival were included in the group reaching the cumulative endpoint. It was observed that 34.1% of the patients reached the cumulative endpoint. The mean tGFR of 27 patients who were followed up was 47.2±27.4 ml/min/1.73 m², and 28% of them remained antibody-positive.

Table 3. Observed side effects and frequency of side effects related to the treatments given

Side Effect	n (%)
Cyclophosphamide+Steroid regimen-related serious side effects (n=35)	
1. Infection	6 (17)
2. Cytopenia	2 (5)
3. GI bleeding	1 (2)
Azathioprine+Steroid regimen-related serious adverse events (n=17)	
1. Infection	3 (17)
2. Cytopenia	1 (5)
Rituximab+steroid-related serious adverse events (n=5)	
1. Infection	1 (20)

GI: Gastrointestinal system.

Discussion

While the annual incidence of ANCA-associated vasculitis in Europe is 19 per million population, its prevalence ranges between 100–250 per million population.[5] Although many studies have been conducted abroad on this patient group, there is no data yet regarding the situation in our country. Our study, in which we retrospectively evaluated the data of 41 adult pauci-immune necrotizing glomerulonephritis patients who were followed up and treated in the nephrology unit of our hospital (a reference center for glomerular diseases), is valuable as it provides insight into the data from our country.

Although ANCA-associated vasculitides are seen across all age groups, they are more frequently observed in older individuals.[6] In our study, which included only adult patients, the age of disease onset ranged widely from 19 to 78 years, with a mean age of 54.1±16.7 years. While similar rates are observed in both sexes, studies have shown that ANCA-associated vasculitides are more common in the white race.[1] In our study, there was no significant gender difference in disease prevalence (53.7% female). All of the patients in our study were Caucasian; however, approximately 2% were immigrants, and 10% were refugees.

Patients most commonly present with constitutional symptoms such as fever, weight loss, and loss of appetite. These symptoms may sometimes begin months before the onset of organ involvement.[1,5,7] In our study, constitutional symptoms were the most frequent reason for admission, observed in 75.6% of the patients.

Although pauci-immune vasculitis can present as a disease limited to the kidney, systemic involvement is prominent in most patients.[1] Ear, nose, and throat involvement in pauci-immune vasculitis is primarily seen in patients with granulomatous polyangiitis but can also occur in microscopic polyangiitis.[1,6,8] In our study, 36.6% of the patients had upper respiratory tract involvement. Additionally, these patients may have trachea and pulmonary parenchyma involvement, with hilar lymphadenopathies, nodular opacities, and pulmonary infiltrates visible on PA chest X-rays.[9] In our study, lung involvement was observed in 59% of the patients, with radiological findings comprising 54.2% infiltration, 29.2% cavitation, 12.5% mass, and 4.2% nodule. Furthermore, 31.7% of the patients experienced hemoptysis at admission.

Although less common, skin, eye, neurological, cardiac, and gastrointestinal systems may also be involved. Neurological involvement related to vasculitis was detected in 6 patients (14.6%), and eye involvement was observed in 5% of the patients. Patients diagnosed with ANCA-associated vasculitis should be approached multidisciplinary, and all these systems should be screened. It is essential to remember that while vasculitis cases limited to the kidney may manifest as isolated renal involvement, some patients may relapse years later with involvement of other systems.[6,10]

Anti-neutrophil cytoplasmic antibody-associated vasculitides, although classified as granulomatous polyangiitis, microscopic polyangiitis, vasculitis limited to the kidney, and eosinophilic granulomatous polyangiitis, exhibit similar kidney biopsy findings (e.g., focal necrotizing, crescentic, pauci-immune glomerulonephritis). In clinical practice, granulomatous polyangiitis is considered when granulomas are found in any organ along with destruction in the upper respiratory tract and/or nodular or cavitary lesions in the lower respiratory tract. If there is nasal disease and necrotizing vasculitis in the biopsy without granulomas, the diagnosis is accepted as microscopic polyangiitis. However, this classification does not reliably distinguish all patients.

New classifications based on ANCA serology may be more practical, as granulomatous changes might be overlooked in biopsies, and some patients initially presenting with findings suggestive of microscopic polyangiitis may later develop findings more compatible with granulomatous polyangiitis during follow-up. According to a study, anti-PR3 or anti-MPO positivity may be more useful than the granulomatous polyangiitis or microscopic polyangiitis classifications in predicting recurrence and long-term outcomes.[4]

Patients with granulomatous polyangiitis, microscopic polyangiitis, or renal-limited vasculitis receive the same immunosuppressive therapy. However, a study by Sanders et al.[11] demonstrated that patients with persistent PR3-ANCA positivity after induction therapy have a higher rate of recurrence within five years of diagnosis. Persistent PR3-ANCA positivity should be considered when choosing maintenance therapy, particularly regarding its duration and the choice of immunosuppressive drugs.

Based on these findings, classifying patients as PR3-ANCA or MPO-ANCA positive rather than granulomatous polyangiitis or microscopic polyangiitis may be better for prognostic evaluation in this group of diseases. When patients in our study were grouped according to this classification, 58.5% were MPO-ANCA positive, 29.3% were PR3-ANCA positive, and 12.2% were ANCA negative.

Back then, the mortality rate in patients who did not receive induction therapy was approximately 80% in the first year. Nowadays, with the use of dual immunosuppressive therapy, the five-year mortality rates have decreased to around 25%, while remission rates have increased to 80–90%.[2,12,13] Dual immunosuppressive therapy (cyclophosphamide or rituximab in addition to corticosteroids) and plasmapheresis in certain special cases have been used quite successfully for induction therapy. However, the results of the randomized PEXIVAS study, which included the largest cohort of patients to date, are noteworthy.

The PEXIVAS study included 704 patients with an estimated glomerular filtration rate (tGFR) of less than 50 ml/min/1.73 m² or with alveolar hemorrhage. The study demonstrated that plasma exchange therapy does not provide additional benefits in reducing all-cause mortality or end-stage renal disease and that low-dose corticosteroid therapy is as effective as the standard dose in controlling the disease.[14]

When we evaluate the renal functions of the patients included in our study at the time of admission, the findings suggest a highly aggressive onset of renal involvement. The median tGFR was 16 ml/min/1.73 m², the median percentage of crescentic glomeruli in biopsies was 52% (IQR: 14–69), and more than half of the patients required dialysis at the time of diagnosis. All these patients with aggressive onset received induction therapy, resulting in remission in 78.9% of them.

In addition, plasmapheresis was applied to 70.7% of the patients during induction treatment in our study. When evaluating the treatment success of regimens containing plasmapheresis, remission was achieved in 73% of the patients who received cyclophosphamide, corticosteroid, and plasmapheresis, and in 100% of those who received corticosteroid and plasmapheresis. No serious side effects related to plasmapheresis were observed.

Since we are a reference center for glomerular diseases, treatment is planned under the guidance of KDIGO guidelines for many patients in our nephrology clinic. Although the results of the PEXIVAS study did not recommend plasmapheresis, the results of the MEPEX study[2] and the meta-analysis by Walsh et al.,[15] which included nine studies, supported the use of plasmapheresis. Additionally, in our study, plasmapheresis was performed in nearly all patients who required dialysis at the time of admission, and 42.8% of these patients no longer needed dialysis after treatment.

Although these findings clearly show the success of immunosuppressive drugs in achieving remission in such a severe systemic disease, more studies are needed to better understand the role and benefits of plasmapheresis treatment.

In cases of pauci-immune necrotizing glomerulonephritis that are in remission with induction therapy, maintenance therapy is recommended to reduce the frequency and severity of vasculitis recurrences. Although azathioprine remains the most commonly used agent in maintenance therapy, the use of rituximab has become more prominent following recent studies. Azathioprine has been used in many centers for years as maintenance therapy because it has been shown to provide similar remission maintenance to cyclophosphamide and better outcomes than mycophenolate mofetil in randomized controlled trials.[16,17] Since disease relapses often occur in the early stages, azathioprine maintenance therapy is typically planned for 18 months, based on the results of the CYCAZAREM study.[16]

However, the recent MAINRITSAN trial demonstrated that rituximab is superior to azathioprine in maintaining remission.[18] In our study, recurrence was observed in 17.6% of patients who used azathioprine for remission maintenance, while no recurrences were noted in patients who received rituximab.

In patients with pauci-immune vasculitis, only 29% of deaths in the first year after diagnosis are attributed to vasculitis, whereas 50% are secondary to infections caused by immunosuppressive therapy. In our study, serious side effects due to immunosuppressive drugs occurred in 34.1% of the patients, and during the follow-up of the 41 patients included in the study, 6 patients died due to severe drug-related side effects.

Conclusion

In conclusion, although most of the patients who presented to our center had severe pauci-immune necrotizing glomerulonephritis, induction and maintenance treatments were highly successful. Immunosuppressive treatments should be prioritized because of the high mortality rate among patients requiring dialysis at the time of admission. Since serious side effects develop in approximately one out of every three patients, further studies are necessary to prevent these adverse effects (e.g., prophylactic antibiotics, proton pump inhibitor use) in this patient group.

Disclosures

Ethics Committee Approval: The study was approved by Health Sciences University Istanbul Training and Research Hospital Clinical Research Ethics Committee (No: 1359, Date: 2018).

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