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ORIGINAL RESEARCH

Clinical features and outcomes of patients with microscopic polyangiitis: experience of two centers

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Abstract

Background and Aim: Microscopic polyangiitis (MPA) is a rare necrotizing vasculitis that involves predominantly the small-caliber blood vessels. In this retrospective study, we aimed to evaluate the clinical findings, prognostic factors, and outcomes of MPA patients followed in two different centers. **Material and Method**: In this retrospective study, a total of 38 patients diagnosed and followed with MPA in two different centers between January 2005 and December 2019 were included. Medical records of the patients were reviewed retrospectively. The diagnoses were based on the definition of MPA in the Chapel Hill consensus conference (CHCC-2012). In addition to the socio-demographic characteristics, clinical features, laboratory and immunological parameters; time passed for the diagnosis, treatment, outcomes, and follow-up time were recorded for each patient. The Five Factor Scores (FFS; Revised FFS 2009) and Birmingham Vasculitis Activity Score (BVAS; Version 3) were applied in all patients. **Results**: In a total of 38 patients (10 females, 28 male) were included in the study. The mean age of the participants was 54.52 $\pm$ 8.21 (range: 32-74) years. The mean time passed for the diagnosis was 2.93 $\pm$ 2.03 (0.50-11) months and the mean follow-up period was 55.0 $\pm$ 30.51 (2-124) months. At admission, the mean BVAS was 18.28 $\pm$ 5.73 (8-35). The FFS results were as follows; 0 in 4 (10.5%) patients, 1 in 27 (71.1%) patients, 2 in 7 (18.4%) patients. The most common symptoms at admission were dyspnea, cough, and hemoptysis. Renal failure was present in 31 (81.5%) of the patients, at admission. The most common immunologic finding was the p-ANCA positivity in 26 (68.4%) patients. Among all patients, 25 (65.8 %) did not have any other attacks after the diagnosis. In follow-ups, 12 (31.5%) patients were passed away and vasculitis associated mortality rate was 18.4%. The effects of some factors on mortality including age $\geq$ 65 years, male gender, renal involvement, p-ANCA positivity, decreased oxygen saturation ($<$ 90%), having anemia at admission, having FEV1/FVC $<$ 70 in spirometry, having a FFS score of 2, and having a BVAS $>$ 18 were examined (Table 6). Only having an FFS score of 2 and BVAS $>$ 18 were determined as the factors significantly affecting mortality (P: 0.01). **Conclusion**: Pulmonary symptoms are more predominant in MPA. Though many patients did not have any other attacks after the diagnosis, the vasculitis associated mortality may reach about 20%. BVAS and FFS are still the best determinants of mortality.

Keywords

Microscopic polyangiitis; Autoimmune vasculitis; Birmingham Vasculitis Activity Score (BVAS); Five Factor Scores (FFS)

1. Introduction

Microscopic polyangiitis (MPA) is a rare necrotizing vasculitis that involves capillaries, arterioles and venules; predominantly the small-caliber blood vessels. Its annual incidence varies between 5-10 / 1 million and its prevalence between 20-50 / 1 million [1]. The incidence of the disease increases with age and reaches the highest level in the 6^{th} and 7^{th} decades. Typical clinical signs of the MPA are rapidly progressing glomerulonephritis and alveolar bleeding [2].

Microscopic polyangiitis is an autoimmune disease that belongs to the group of Anti Neutrophilic Cytoplasmic Antibody (ANCA) associated vasculitis. ANCA positivity is detected in about 80% of patients [3, 4]. The most commonly encountered type of ANCA is the perinuclear ANCA (p-ANCA), showing specificity to myeloperoxidase (MPO) antigen. In a small proportion of patients, antibody formation against proteinase 3 (PR3) can be seen. The main pathological findings are

observed in the biopsies of kidneys and lungs. On the other hand, a small proportion of MPA-patients apart from being c-ANCA positive also can be ANCA negative. Focal and segmental glomerulonephritis and crescents are detected in kidney biopsies. In lung biopsy, there is necrotizing vasculitis and pulmonary hemorrhage in microscopic examination [3].

Pulmonary capillaritis and necrotizing glomerulonephritis are known as the most common clinical pictures. However, skin, mucous membranes, brain, heart, gastrointestinal system (GIS) and muscle tissue may also be involved. The clinical picture includes symptoms of glomerulonephritis, fever, myalgia, arthralgia, and weight loss. Due to the life-threatening multiple organ failure, rapid immunosuppressive therapy may be essential to reduce mortality and long-term morbidity during flares. However, even though the immunomodulatory therapy is initiated, the disease tends to progress. Since signs, symptoms, and biomarkers overlap between several vascular diseases, the diagnosis and predicting prognosis is challenging in patients with MPA. Although the Birmingham Vasculitis Activity Score (BVAS) and Five Factor Scores (FFS) are used to evaluate the disease activity and severity and treatment response; it is difficult to estimate the prognosis [2, 3].

Various case reports have been published regarding MPA patients, but case series are very limited. In this retrospective study, we aimed to evaluate the clinical findings, prognostic factors, and outcomes of MPA patients followed in two different centers. We will discuss the symptoms, laboratory data, spirometry findings, clinical features, and outcomes of the patients. In this way, we aimed to determine the general characteristics and prognostic markers in MPA.

2. Material and method

In this retrospective study, a total of 38 patients diagnosed and followed with MPA in two different centers Istanbul Okmeydanı Trainning and Research Hospital and Izmir Metropolitan Municipality Hospital between January 2005 and December 2019 were included. Medical records of the patients were reviewed retrospectively. The study was approved by the local ethics committee; Bezmialem Vakıf University Non-interventional Research Ethics Committee (2011-KAEK-25 2019/12-04).

The diagnoses were based on the definition of MPA in the Chapel Hill consensus conference (CHCC-2012) [5]. The diagnosis of MPA depends on the clinical, radiological, and histological findings. In this study, in 26 of 38 patients, the diagnosis was confirmed histologically by renal biopsy and in 9 of them by bronchoscopic biopsy. In the remaining 5 patients, the diagnosis was confirmed with the clinical, radiological, laboratory data, and the biopsies obtained from skin lesions. Exclusion criteria were as follows; being under 18 years of age, the presence of other autoimmune diseases, and a history of malignancy. Patients with other small-vessel vasculitis such as Wegener's granulomatosis or other connective tissue disease-related vasculitides were also excluded from the study.

The diagnosis is made by appropriate clinical findings and tissue biopsy. To define MPA:

1) Presence of rapidly progressive glomerulonephritis (RPGN) and/or alveolar hemorrhage;

2) Histological display of small-sized vessel vasculitis or segmental pauci immune necrotizing glomerulonephritis (GN) and/or;

3) The presence of symptoms showing small vessel involvement (e.g. purpura) without GN and/or alveolar bleeding.

In addition to the socio-demographic characteristics, clinical features, laboratory and immunological parameters; time passed for the diagnosis, treatment, outcomes, and follow-up time were recorded for each patient. In terms of clinical features; in addition to the symptoms and findings, organ involvement at the time of admission is included. Laboratory parameters including white blood cell (WBC) and platelet count, hemoglobin, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), creatinine, liver enzymes, and the presence of hematuria and proteinuria on urine analysis at the time of diagnosis were recorded. Among the immunological parameters, antinuclear antibody (ANA), ANCA, anti-ds DNA, and anti-GBM results were recorded. Radiological findings were also evaluated.

According to the 5 Factor Scores (FFS; Revised FFS 2009) used for prognosis determination; the patients were evaluated for age $>$ 65, the presence of heart failure, gastrointestinal involvement and kidney failure. 1 point is given for each parameter to exist and the patients are categorized as 0; none, 1; only 1 parameter score and 2; Having 2 or more parameter scores. Birmingham Vasculitis Activity Score (BVAS; Version 3) was applied for the determination of disease activity [6, 7].

Response to the treatment was defined as stabilization or reduction of clinical symptoms and laboratory abnormalities. Relapses were defined as new systemic vasculitis symptoms or worsening of one or more of the first symptoms of the disease. The causes of death were divided into 3 subgroups: vasculitis related, not associated with vasculitis, and other/unknown. The long-term survival of the patients was determined by having contact with the patients or their first-degree relatives.

2.1 Statistical analyses

All statistical analyses were performed using IBM SPSS for Windows version 21.0 (SPSS, Chicago, IL, USA). Descriptive statistics were performed. Kolmogorov-Smirnov test was used to assess the assumption of normality. Continuous variables were expressed as mean $\pm$ standard deviation. Categorical variables were summarized as counts (percentages). Crosstabs were performed to determine the effects of various factors on mortality. A two-tailed P-value < 0.05 was considered as statistically significant.

TABLE 1. The frequencies of symptoms at admission.

Symptoms	Number of patients (%)
Dyspnea	38
Cough	36 (94.7)
Sputum	22 (57.9)
Hemoptysis	31 (81.6)
Chest pain	20 (52.6)
Fever	26 (68.4)

Descriptive statistics are performed.

3. Results

A total of 38 patients (10 females, 28 male) were included in the study. The mean age of the participants was 54.52 ± 8.21 (range: 32-74) years. The mean time passed for the diagnosis from the onset of the first symptom was 2.93 ± 2.03 (0.50-11) months and the mean follow-up period was 55.0 ± 30.51 (2 -124) months.

At admission, the mean Birmingham Vasculitis Activity Score was 18.28 ± 5.73 (8-35). The Five-factor score results were as follows; 0 in 4 (10.5%) patients, 1 in 27 (71.1%) patients, 2 in 7 (18.4%) patients.

The frequencies of symptoms at admission are summarized in Table 1. The most common symptoms at admission were dyspnea, cough, and hemoptysis.

Laboratory data of the participants at admission are summarized in Table 2. Inflammation markers including white blood cell count, ESR and CRP levels were higher than normal. The mean creatinine level was also higher than normal, with the presence of anemia in most of the patients.

TABLE 2. Laboratory data of the participants at admission.

Laboratory data	Mean ± SD	Range
ESR (mm/h)	40.78 ± 5.91	28.00-55.00
WBC (µ/mm^3)	14831.57 ± 2206.39	9600.00-18000.00
HCT (%)	30.14 ± 4.49	18.50-37.10
HB (g/dL)	9.83 ± 1.52	5.50-12.80
CRP (mg/dL)	67.57 ± 56.03	24.00-204.00
BUN (mg/dL)	35.91 ± 12.76	18.90-54.00
Creatine (mg/dL)	2.53 ± 1.06	1.00-4.80
Uric acid (mg/dL)	6.58 ± 0.69	5.00-7.40
Total protein (g/dL)	6.45 ± 0.34	5.80-6.90
Albumin (g/dL)	3.33 ± 0.43	2.60-3.80
Globulin (g/dL)	3.37 ± 0.80	2.30-5.40
Alb/glob ratio	1.04 ± 0.32	0.48-1.60

ESR: Erythrocyte sedimentation rate, WBC: White blood cell count, HCT: Hematocrite, HB: Hemoglobin, CRP: C-reactive protein, BUN: Blood urea nitrogen. Descriptive statistics are performed.

TABLE 3. Spirometry findings of MPA patients at admission.

Spirometry findings	Mean ± SD	Range
FEV1	69.00 ± 11.94	54.00-88.00
FVC	78.21 ± 5.61	68.00-91.00
FEV1/ FVC	87.73 ± 14.04	68.00-110.00

Descriptive statistics are performed.

Among participants, six of them reported that they never smoked, while 12 quitted smoking and 20 were still smoking. The mean Spirometry findings at admission are summarized in Table 3.

TABLE 4. Urinary findings of MPA patients at admission.

Urinary findings	Number of patients (%)
Proteinuria	26 (68.4)
Urinary Leukocyte (+)	24 (63.2)
Microalbuminuria	32 (84.2)
Oliguria	22 (57.9)
Hematuria	36 (94.7)
Glucosuria	10 (26.3)

Descriptive statistics are performed.

At admission, the mean oxygen saturation was 90.52 ± 4.37 (84.00-96.00). DLCO was decreased in 32 (84.2%) patients. The endobronchial lesion was present in 20 of the patients. Thorax computed tomography (CT) findings were as follows; bronchiectasis in 32 (84.2%) patients, infiltration in 28 (73.7%) patients, fibrosis in 12 (31.6%) patients, and pleural effusion in 6 (15.8%) patients.

Renal failure was present in 31 (81.5%) of the patients, at admission. Dialysis was required at the first admission in 11 (28.9%) patients and in 3 more patients in follow-ups. Urinary findings at admission are summarized in Table 4. Hematuria and microalbuminuria were the most common urinary findings at admission.

TABLE 5. Clinical findings and comorbidities of the study participants.

Clinical findings	Number of patients (%)
Arthralgia	15 (39.4)
Myalgia	11 (28.6)
Ocular involvement	1 (2.6)
Skin Rashes or purpura	36 (94.7)
Mononeuritis multiplex	15 (39.4)
CNS involvement	2 (5.2)
Chronic rhinosinusitis	12 (31.6)
Epistaxis	12 (31.6)
Liver function test elevations	3 (7.9)
Severe GIS involvement	3 (7.9)
Renal involvement	36 (94.7)
Heart failure	3 (7.9)
Diabetes Mellitus	6 (15.8)
Hypertension	12 (31.6)
Coronary Artery disease	10 (26.3)
COPD	8 (21.1)
Asthma	8 (21.1)

CNS: Central nervous system, GIS: Gastrointestinal system, COPD: Chronic obstructive pulmonary disease. Descriptive statistics are performed.

Immunologic findings of the patients at admission were also recorded. The most common finding was the p-ANCA

TABLE 6. The effects of some clinical characteristics on mortality.

Criteria	Mortality in patients with the criteria	Mortality in patients without the criteria	*P*
Age ≥ 65 years	**3/7**	**4/31**	**0.11**
Male gender	**6/28**	**1/10**	**0.65**
Renal involvement	**5/31**	**2/7**	**0.39**
p-ANCA positivity	**5/26**	**2/12**	**0.92**
Decreased oxygen saturation (< 90%)	**4/16**	**3/22**	**0.42**
Anemia at admission	**5/28**	**2/10**	**0.92**
FEV1/FVC < 70	**2/8**	**5/30**	**0.63**
FFS: 2	**4/7**	**3/31**	**0.013**
BVAS > 18	**6/15**	**1/23**	**0.01**

Crosstabs were performed to determine the effects of various factors on mortality.

positivity in 26 (68.4%) patients, RF positivity in 22 (57.9%) patients and c-ANCA positivity in 14 (36.8%) patients.

Clinical findings and comorbidities of the study participants at admission are summarized in Table 5. Skin rashes were present in more than 90% of the patients.

In follow-ups, 26 of the participants were under corticosteroid + cyclophosphamide treatment, while 12 were treated with both immunosuppressive treatment and plasma exchange. All attacks were recorded during follow-ups. Among all patients, 25 (65.8 %) did not have any other attacks after the diagnosis, 8 (21.1 %) patients had one more attack during follow-ups, 3 (7.9%) patients had 2 attacks, 1 (2.6%) patient had 3 attacks and 1 (2.6%) patient had 4 attacks.

In follow-ups, 12 (31.5%) patients were passed away. In those 12 patients, the causes of mortality were as follows: alveolar hemorrhage in 6 patients, GIS bleeding in one patient, sepsis in one patient, pneumonia in one patient, pulmonary emboli in one patient, and heart failure in two patients. Alveolar hemorrhage and GIS bleeding were the vasculitis associated causes of mortality and for that reason vasculitis associated mortality rate was 18.4%.

The effects of some factors on mortality including age ≥ 65 years, male gender, renal involvement, *P*-ANCA positivity, decreased oxygen saturation (< 90%), having anemia at admission, having FEV1/FVC < 70 in spirometry, having an FFS score of 2, and having a BVAS > 18 were examined (Table 6). Only having an FFS score of 2 and BVAS > 18 were determined as the factors significantly affecting mortality (*P*: 0.01).

4. Discussion

In this study we analyzed the clinical findings and outcomes of 38 MPA patients and we determined that: 1) The most common symptoms at admission were dyspnea, cough and hemoptysis; 2) Inflammatory markers and serum creatinine levels were higher with the presence of anemia in most of the patients at admission; 3) The main findings of thorax CT were the bronchiectasis and the infiltration; 4) At admission, renal failure was present in more than 80% of the patients and hematuria and microalbuminuria were the most common urinary findings; 5) p-ANCA and/or RF positivity were the most common immunological findings, and determined in more than 60% of the patients; 6) Skin rashes and purpura were the most common systemic clinical findings; 7) More than 60% of the patients did not have any other attacks after the diagnosis; 8) In follow-ups, 12 (31.5%) patients were passed away and vasculitis associated mortality rate was 18.4%; 9) Age ≥ 65 years, male gender, renal involvement, p-ANCA positivity, decreased oxygen saturation (< 90%), having anemia at admission, having FEV1/FVC < 70 in spirometry were not associated with the mortality; but having a FFS score of 2 and BVAS > 18 were determined as the factors significantly affecting mortality (*P*: 0.01).

MPA is a rare form of necrotizing vasculitis having a slight male predominance (male: female ratio of 1.8 : 1), with an average age of onset between 50-60 years [8]. In this study the male: female ratio was 2.8 and the mean age of the participants was 54.52 ± 8.21 years.

Renal involvement is the major clinical feature of MPA and reported in 80-100% of the patients which can range from asymptomatic proteinuria or hematuria to end-stage renal disease requiring dialysis. The characteristic finding on renal biopsy is glomerular crescents and the focal segmental necrotizing glomerulonephritis [9]. In this study, renal failure was present in 81.5% of the patients at admission, and hematuria and microalbuminuria were the most common urinary findings, in accordance with the previous literature.

Pulmonary involvement is reported in more than 50% of patients, in general. The main manifestations are hemoptysis and alveolar hemorrhage, pleural effusion, infiltrates, and pleuritis. The characteristic pulmonary manifestation of MPA is diffuse alveolar hemorrhage [10]. In this study, the most common symptoms at admission were dyspnea, cough, and hemoptysis. This may be associated with the asymptomatic characteristics of renal involvement. At admission, the mean oxygen saturation was 90.52 ± 4.37 and DLCO was decreased in more than 80% of the patients. The main thorax CT findings were the bronchiectasis and the infiltration, which were also in accordance with the previous literature.

Skin lesions are found in 30-60% of patients and palpable purpura is the most common manifestation [11]. In this study,

skin lesions were also the most common systemic manifestations of MPA patients. Constitutional symptoms such as arthralgia, myalgia, and weight loss were also present in more than 30% of the patients.

Though the most frequent gastrointestinal symptom in MPA is abdominal pain, gastrointestinal bleeding may occur in approximately 25% of the patients, which may be life-threatening [12]. In this study, severe GIS involvement was determined in 3 patients and one of these patients was passed away due to GIS bleeding.

Mononeuritis multiplex and distal symmetrical polyneuropathy are the predominant peripheral nervous system manifestations of MPA [13]. In this study, we determined mononeuritis multiplex in approximately 40% of the patients.

The mainstay of the treatment in MPA is immunosuppression including glucocorticoids and cyclophosphamide. In this study, all patients were under cyclophosphamide treatment and plasma exchange was required in about 30% of the patients [14].

In this study, vasculitis associated mortality rate was 18.4% and interestingly we did not determine any association of age $\geq$ 65 years, male gender, renal involvement, p-ANCA positivity, decreased oxygen saturation ($<$ 90%), having anemia at admission, having FEV1/FVC $<$ 70 in spirometry with the mortality; but having an FFS score of 2 and BVAS $>$ 18 were determined as the factors significantly affecting mortality. Five-year survival was defined as around 75% in ANCA associated vasculitis. Both the active disease and the treatment modalities may have a role in mortality and morbidity [15]. Abe *et al.* [16] reported that in elderly Japanese patients with severe microscopic polyangiitis, age, disease severity, the 1996 FFS, and the 2009 FFS at diagnosis were the prognostic factors for both mortality and relapse-free survival. However, the mean age of the patients at onset was more than 70 in that study and in our study; the number of patients having an age $\geq$ 65 years was only 7. The low number of elderly patients may be the reason that we did not determine age as a significant factor in mortality. Recently, Park *et al.* [17] investigated the factors associated with all-cause mortality in patients with MPA and with granulomatosis polyangiitis (GPA) and reported that old age ($\geq$ 65 years), male gender, diabetes mellitus and hypertension at diagnosis, ANCA positivity, BVAS and FFS (2009) were not associated with all-cause mortality. They determined that only the fibrosis-4 index was associated with all-cause mortality during the follow-up in patients with MPA and GPA. BVAS and FFS are known to be useful to predict survival in antineutrophil cytoplasmic antibody-associated vasculitis and our results also support this finding [18, 19].

Retrospective design is the main limitation of the study. Though this is a rare disease, larger studies with more patients are warranted to determine the prognostic factors.

In conclusion, pulmonary symptoms may be more predominant in MPA patients. Though many patients did not have any other attacks after the diagnosis, the vasculitis associated mortality may reach about 20%. BVAS and FFS (2009) are still the best determinants of mortality. Future studies are warranted to define new prognostic markers in MPA.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study has been reviewed and approved by an Ethical Committee of Bezmialem University (2011- KAEK-42 2020/04-01).

AUTHOR CONTRIBUTIONS

Dasdemir Ilkhan Gulay: Processing, preparation and writing of the collected information; Critically and intellectually evaluating the content of the article; Analysis of the content of the article; Regulation of the presentation of the information and data in the article; Evaluating the accuracy of the data; Methodology; Statistical evaluation of the article data and the arrangement and interpretation of these data. Celikhisar Hakan: Literature search and analysis; Design and concept of the article; Project administration; Case collection, data gathering and work flow planning; Forming the general lines and framework of the study.

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CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

DATA AVAILABILITY

The data used to support the findings of this study are available from the corresponding author upon request.

REFERENCES

[1] Berti A, Cornec D, Crowson CS, Specks U, Matteson EL. The epidemiology of antineutrophil cytoplasmic autoantibody-associated vasculitis in olmsted county, minnesota: A twenty-year US population-based study. Arthritis & Rheumatology. 2017; 69: 2338-2350.

[2] Greco A, De Virgilio A, Rizzo MI, Gallo A, Magliulo G, Fusconi M, *et al*. Microscopic polyangiitis: Advances in diagnostic and therapeutic approaches. Autoimmunity Reviews. 2015; 14: 837-844.

[3] Karras A. Microscopic polyangiitis: New insights into pathogenesis, clinical features and therapy. Seminars in Respiratory and Critical Care Medicine. 2018; 39: 459-464.

[4] Weiner M, Segelmark M. The clinical presentation and therapy of diseases related to anti-neutrophil cytoplasmic antibodies (ANCA). Autoimmunity Reviews. 2016; 15: 978-982.

[5] Jeannette, JC. Overview of the 2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides; Clinical and Experimental Nephrology, 2013; 17: 603-606.

[6] Guillevin L, Pagnoux C, Seror R, Mahr A, Mouthon L, Le Toumelin P, *et al*. The Five-Factor Score revisited: assessment of prognoses of

systemic necrotizing vasculitides based on the French Vasculitis Study Group (FVSG) cohort. Medicine (Baltimore). 2011; 90: 19-27.
[7] Mukhtyar C, Lee R, Brown D, Carruthers D, Dasgupta B, Dubey S, *et al*. Modification and validation of the Birmingham Vasculitis Activity Score (version 3). Annals of the Rheumatic Diseases. 2009; 68: 1827-1832.
[8] Chung SA, Seo P. Microscopic polyangiitis. Rheumatic Disease Clinics of North America. 2010; 36: 545-558.
[9] Savage CO, Winearls CG, Evans DJ, Rees AJ, Lockwood CM. Microscopic polyarteritis: presentation, pathology and prognosis. Quarterly Journal of Medicine. 1985; 56: 467-483.
[10] Franks TJ, Koss MN. Pulmonary capillaritis. Current Opinion in Pulmonary Medicine. 2000; 6: 430-435.
[11] Kluger N, Pagnoux C, Guillevin L, Francès C, French Vasculitis Study Group. Comparison of cutaneous manifestations in systemic polyarteritis nodosa and microscopic polyangiitis. British Journal of Dermatology. 2008; 159: 615-620.
[12] Ueda S, Matsumoto M, Ahn T, Adachi S, Oku K, Takagi M, *et al*. Microscopic polyangiitis complicated with massive intestinal bleeding. Journal of Gastroenterology. 2001; 36: 264-270.
[13] Zhang W, Zhou G, Shi Q, Zhang X, Zeng XF, Zhang FC. Clinical analysis of nervous system involvement in ANCA-associated systemic vasculitides. Clinical and Experimental Rheumatology. 2009; 27: S65-S69.
[14] Harigai M, Tsutsumino M, Takada H, Nagasaka K. Molecular targeted therapies for microscopic polyangiitis and granulomatosis with polyangiitis. Korean Journal of Internal Medicine. 2019; 34: 492-503.
[15] Yates M, Watts R. ANCA-associated vasculitis. Clinical Medicine (London). 2017; 17: 60-64.
[16] Abe Y, Tamura N, Yang KS, Matsuoka J, Kon T, Yamaji K, *et al*. Predictive factors for mortality in elderly Japanese patients with severe microscopic polyangiitis: A retrospective single-center study. Modern Rheumatology. 2017; 27: 315-319.
[17] Park HJ, Park JY, Jung SM, Song JJ, Park YB, Lee SW. Fibrosis-4 index at diagnosis is associated with all-cause mortality in patients with microscopic polyangiitis and granulomatosis with polyangiitis. BMC Gastroenterology. 2019; 19: 90.
[18] Solans-Laqué R, Rodriguez-Carballeira M, Rios-Blanco JJ, Fraile G, Sáez-Comet L, Martinez-Zapico A, *et al*. Comparison of the Birmingham vasculitis activity score and the five-factor score to assess survival in antineutrophil cytoplasmic antibody-associated vasculitis: a study of 550 patients from spain (REVAS Registry). Arthritis Care & Research (Hoboken). 2020; 72: 1001-1010.
[19] Gayraud M, Guillevin L, le Toumelin P, Cohen P, Lhote F, Casassus P, *et al*. Long-term followup of polyarteritis nodosa, microscopic polyangiitis, and Churg-Strauss syndrome: analysis of four prospective trials including 278 patients. Arthritis & Rheumatology. 2001; 44: 666-675.

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