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ORIGINAL ARTICLE

Clinical Characteristics and Outcome of ANCA-Associated Vasculitis; Experience of A Single Reference Vasculitis Center

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ABSTRACT

Objective: The aim of the study is to describe the clinical characteristics of Antineutrophil cytoplasmic antibodies-associated vasculitis and to analyze the parameters affecting the outcome.

Materials and Methods: The study is a retrospective cohort study. Totally 130 patients with Antineutrophil cytoplasmic antibodies-associated vasculitis (18 years and over) who were followed up between October 2014 and October 2019 were analyzed. Demographic data, laboratory values, clinical course, thorax computed tomography findings and treatment approaches were noted from the charts of patients. Patients were divided into two groups as those with pulmonary involvement and non-pulmonary involvement.

Results: We retrospectively reviewed the medical records of 130 patients with Antineutrophil cytoplasmic antibodies-associated vasculitis; 111 with granulomatosis with polyangiitis, 15 with microscopic polyangiitis, 1 with eosinophilic granulomatosis with polyangiitis, and 3 with other types of vasculitis. The ratio of having the abnormality in thoracic computed tomography was 72.2%. There were 84 cases with pulmonary involvement and 46 cases with non-pulmonary involvement. The frequency of microscopic polyangiitis was significantly higher (p=0.034) in non-pulmonary involvement cases.

There were 67 cases with proteinase 3 Antineutrophil cytoplasmic antibodies and 39 cases with myeloperoxidase Antineutrophil cytoplasmic antibodies positivity. Most of the cases with proteinase 3 Antineutrophil cytoplasmic antibodies positivity were classified as granulomatosis with polyangiitis, this was statistically significant. Recovery was referenced for the outcome. Any of the variables were found statistically significant effective on outcome.

Conclusions: Cases with pulmonary involvement were more than the cases without pulmonary involvement in our study. microscopic polyangiitis was significantly higher in non- pulmonary involvement cases. We studied on a large group, and these significant findings may have important implications for the investigation, pathogenesis, and treatment of Antineutrophil cytoplasmic antibodies-associated vasculitis.

Keywords: Antineutrophil cytoplasmic antibodies-associated vasculitis, pulmonary involvement, outcome, clinical characteristics, thorax computed tomography.

INRODUCTION

Antineutrophil cytoplasmic antibodies (ANCA) associated vasculitis (AAV) is a necrotizing vasculitis of small blood vessels. It can affect multiple organ systems, but mostly upper and lower respiratory tracts, eyes, skin, and kidneys [1].

Pulmonary involvement rates vary from 25 to 80 %, in AAV [2, 3]. Although, pulmonary involvement is a major characteristic feature of granulomatosis with polyangiitis (GPA), and eosinophilic granulomatosis with polyangiitis (EGPA; formerly Churg Strauss Syndrome), is rarely seen in microscopic polyangiitis (MPA) [4].

AAV can be classified based on serology, as the presence of myeloperoxidase (MPO-ANCA) and proteinase 3 (PR3-ANCA). MPO-ANCA- and PR3-ANCA-associated vasculitis is shown as genetically different patterns. MPO-ANCA is mostly seen in MPA, PR3-ANCA is commonly associated with GPA.

Most symptoms are progressive dyspnea (50-73%) and cough (21-60%), besides extrapulmonary symptoms (80%) [5]. Patterns of pulmonary involvement are interstitial pneumonia, nodules or cavities, pleural effusion, pulmonary infiltrate (parenchymal infiltration), endobronchial involvement, alveolar hemorrhage, and respiratory failure [6].

The radiological findings in AAV are poorly defined. Computed tomography (CT) shows lung parenchymal lesions, such as consolidation, ground glass opacities, interlobular septal thickening, appearance of honeycomb, reticular shadowing and interstitial pneumonia [5, 7]. There are few studies with small sample sizes, focuses on CT findings of GPA. Also, there are some cases; 18% of MPO-ANCA-positive patients are reported as having normal thoracic CT [8-11].

Pulmonary involvement has main effect on prognosis and relapse rate; as pulmonary disease and early lung involvement is increasingly recognized in cases with raised morbidity and mortality in AAV [7, 12-15]. Also, outcome of disease especially, relapse rate, severity and system involvements differ between ANCA specificities. Before the immunosuppressive therapy, the mortality rate was 80% at one year. Whereas usage of immunosuppressive therapy decreased the mortality rates, as the recent studies reported to a 55% survival in MPA and 75% GPA, at 10 years [16, 17].

As the pulmonary involvement is main prognostic factor, it is essential to clarify the characteristics of pulmonary involvement in AAV to be effective on the morbidity and mortality. Therefore, in our study we examined the cases with pulmonary involvement in a large cohort and searched for the role of ANCA seropositivity in AAV cases with pulmonary disease. The aim of this study is to evaluate clinical features and prognostic factors of AAV cases.

MATERIALS AND METHODS

Patients

The study was designed as a retrospective cohort study. In this study, 130 AAV patients (aged of 18 and over) who were followed up between October 2014 and October 2019 in our center were analyzed.

Our center is one of the main referral vasculitis centers in the country. Executive committee of the Vasculitis center consists of physicians from many departments, including Rheumatology, Pulmonology, Nephrology, Radiology and Pathology. Multidisciplinary approach improves management of the patients. These patients are followed in the Rheumatology Department, then consulted with Chest Diseases Department in each follow up and are considered together. ANCA-Associated Vasculitis is defined as according to the 2012 revised International Chapel Hill Consensus Conference on the Nomenclature of Systemic Vasculitis [18]. For the classification of vasculitis, American College of Rheumatology (ACR) 1990 criteria were used [19]. The patients were classified into 2 groups according to pulmonary involvement as: cases with pulmonary involvement (PI) and the cases without pulmonary involvement (non- PI). The study was approved by the Ethics Committee (2-2017- GO 17/157). Birmingham Vasculitis Activity Score version 3 was used to assess the disease activity at the time of diagnosis [20]. Patients whose data are missing and do not come to regular check-ups were excluded from the study.

Definitions

Remission was defined as the absence of clinical and laboratory evidence of vasculitis activity. Relapses were defined as recurrence of signs or new symptoms after a remission had been achieved. Uncontrolled vasculitis (worsening unresponsive to treatment) was defined as the occurrence of new manifestations or aggravation of manifestations already present despite treatment for the disease [21].

Data

The following data were collected: date/age at diagnosis; gender; comorbidities; type of AAV; initial respiratory symptoms, ANCA subtypes, organ systems involvement at disease onset and throughout the disease course; laboratory data (erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), albumin, estimated glomerular filtration rate (eGFR), at diagnosis and during follow-up; radiological findings from Thorax CT, duration of illness; relapses, remission, worsening progression, treatment approaches, knowledge of deaths recorded from the hospital database. All reports of Thorax CT imaging were evaluated by radiology specialist.

Outcome was defined according to clinical findings (additional symptoms, any change of complaints), radiological data (any progress compared to former CT), and laboratory results (inflammatory markers such as sedimentation, CRP).

Statistical Methods

SPSS Windows version 21.0 package program was used for statistical analysis. Mean ± standard deviation was used for numerical variables as descriptive statistics. Number and% values were used for categorical variables. $P<0.05$ was considered statistically significant. Student t test and Mann Whitney U test were used to compare normally distributed features in two independent groups. Relationship analysis between variables at quantitative measurement level was analyzed by Pearson Chi-square and Fisher Exact tests. The univariate logistic regression models were conducted to specify candidate variables in multivariate logistic regression. Backward elimination was performed with those variables. The results of final logistic regression models were represented with odds ratio (OR), 95% of confidence interval and p-value.

RESULTS

We retrospectively reviewed the medical records of 130 AAV patients; 111 with GPA, 15 with MPA, 1 with EGPA, and 3 with other types of vasculitis (Figure 1). We have excluded EGPA, because there was only 1 case with EGPA, and this would not have clear statistics. Also, 3 cases with other types of vasculitis were excluded. Analysis were made between 126 patients (111 cases with GPA and 15 with MPA).

Patients were divided into two groups as those with pulmonary involvement (PI) and non-pulmonary involvement (non-PI). There were 84 cases with PI and 46 cases with non- PI. Table 1 shows the demographic, clinical, and laboratory characteristics of the study groups. According to serologic classification, MPO positivity was found as 28.6% in PI, 32.6 % in non-PI. This was not statistically significant. The frequency of MPA was 7.1% in PI cases, 19.6% in non-PI cases, this was significantly difference (p=0.034).

The most common organ involvement was renal, in whole and in each group (Table 1). Eye involvement was seen in 11 patients in whole with the statistically higher rates in non-PI ones (p=0.011). Hearing loss

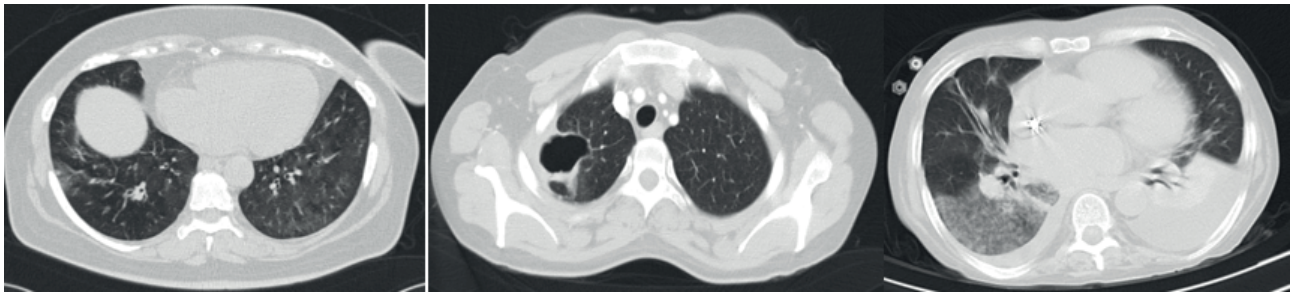

Figure 1. Images of Thorax CT from both ANCA associated vasculitis subtypes, MPAN, GPA (wegener), and EGPA (Churg Strauss), respectively

Table 1. Demographic, clinical, and laboratory characteristics of the study groups

	PI (pulmonary involvement) (n=84)	Non-PI (n=46)	All patients (n=130)	P value
Age (year)	55.5 ±15.4	47.5 ±17.3	52.7 ±16.3	**0.008**
Gender (male/female)	35/49	26/20	61/69	0.088
Birmingham Vasculitis Activity Score (BVAS)	16.45±7.40	15.20±5.55	15.89±6.64	0.218
Number of cases with comorbidity	53 (63.1%)	25 (54.3%)	78 (60%)	0.33
Hypertension	33 (39.3%)	19 (41.3%)	52 (40%)	0.822
Congestive heart failure (CHF)	8 (9.5%)	1 (2.2%)	9 (6.9%)	0.114
Coronary arterial disease	16(19%)	5 (10.9%)	21 (16.2%)	0.226
Atrial fibrillation	2 (2.4%)	0 (0%)	2 (1.5%)	0.292
Diabetes Mellitus	15 (17.9%)	5 (10.9%)	20 (15.4%)	0.291
Chronic obstructive pulmonary disease (COPD)	6 (7.1%)	2 (4.3%)	8 (6.2%)	0.526
Asthma	5 (6%)	2 (4.3%)	7 (5.4 %)	0.698
Malignancy	6 (7.1%)	2 (4.3%)	8 (6.2%)	0.526
ANA positivity	16 (19.8%)	14 (33.3%)	30 (24.4%)	0.096
Rheumatoid factor(RF) positivity	14 (19.4%)	16(43.2%)	30 (27.5%)	**0.008**
PR3 ANCA positivity	44 (52.4%)	23 (50%)	67 (51.5%)	0.795
MPO ANCA positivity	24 (28.6%)	15 (32.6%)	39 (30%)	0.631
GPA cases	75 (89.3%)	36 (78.3%)	111 (85.4%)	0.089
MPA cases	6 (7.1%)	9 (19.6%)	15 (11.5%)	**0.034**
EGPA cases	1(1.2%)	0 (0%)	1 (0.8%)	0.458
Neurologic involvement	2 (2.4%)	3 (6.5 %)	5 (3.8%)	0.240
Renal involvement	41 (49.4%)	21 (45.7%)	62 (48.1%)	0.667
Arthrosis involvement	9(10.7%)	13 (28.3%)	22 (16.9%)	0.683
Eye involvement	3 (3.6%)	8 (17.4%)	11 (8.5%)	**0.011**
Hearing loss	8 (9.5%)	14 (30.4%)	22 (16.9%)	**0.002**
Gastrointestinal system (GIS) involvement	0 (0%)	2 (4.3%)	2 (1.5%)	0.054
Dermal involvement	6 (7.1%)	5 (10.9%)	11 (8.5 %)	0.465
Presence of initial symptoms (cough, dyspnea, chest pain)	78 (94%)	12 (26.1%)	90 (69.8%)	**0.001**
Cough	70 (84.3%)	8 (17.4%)	78 (60.5%)	**0.001**
Dyspnea	68 (81.9%)	7 (15.2%)	75 (58.1%)	**0.001**
Chest pain	24 (28.9%)	0 (0%)	24 (18.6%)	**0.001**
Hemoptysis	48 (57.8%)	6 (13%)	54 (41.9%)	**0.001**
Immune suppressive treatment	81 (97.6%)	46 (100%)	127 (98.4%)	0.298
Corticosteroid	81 (97.6 %)	42 (91.3%)	123 (95.3%)	0.104
Cyclophosphamide	52 (62.7%)	46 (55.4%)	103 (56.6%)	0.842
Azathioprine	21 (25.6%)	29 (34.9%)	57 (31.3%)	0.398
Methotrexate	7 (8.4%)	8 (9.6%)	23 (12.6%)	0.405
Mycophenolate mofetil	11 (13.4%)	12 (14.5%)	22 (12.1%)	0.544
Rituximab	30 (36.6%)	18(39.1%)	48 (37.5%)	0.081
Plasma exchange	9 (11%)	5 (10.9%)	14 (10.9%)	**0.001**
Outcome	48(59.3%)	26 (56.5%)	74 (58.3%)	0.764

Third columns are the data of whole cases. They did not used for comparison. Only first and second columns were compared.

was seen in 22 cases with the statistically higher rates in non-PI ones (p=0.002). In PI cases, there was no case with gastrointestinal system involvement, arthrosis involvement (10.7%) was the second most common involvement after renal involvement (49.4%).

Presence of initial symptoms, such as cough, dyspnea, chest pain were found statistically higher

Table 2. Comparison of laboratory values between PI and non-PI cases

	PI cases	Non-PI cases	Total cases	P value
	Mean ±SD	Mean ±SD	Mean ±SD	
Urea (mg/dL)	45.85± 31.39	35.65±27.73	42.52±30.49	0.096
Creatinine (mg/dL)	2.48±6.33	1.57±1.77	2.07±4.83	0.201
eGFR	33.8±19.56	39.0±32.16	35.75±24.11	0.691
AST (IU/mL)	24.70±21.59	20.86±12.21	22.95±17.99	0.134
ALT (IU/mL)	30.17±27.10	19.82±14.08	25.45±22.68	**0.001**
Albumin (g/dL)	3.66±0.70	3.69±0.69	3.67±0.70	0.772
ESR (mm/h)	46.74±30.65	35.73±26.79	41.72±29.39	**0.011**
CRP (mg/dL)	8.12±12.48	4.75±7.05	6.58±10.47	**0.023**

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in PI cases (p=0.001) (Table 1). There is a significant difference between the groups in terms of ALT, ESR, CRP values and those with PI had higher values (Table 2).

The demographic, clinical, and laboratory characteristics according to ANCA sensitivity (PR3 ANCA positivity and MPO ANCA positivity) were given in Table 3a. There were 67 cases with PR3 ANCA positivity, 39 cases with MPO ANCA positivity. Comorbidity was found in 53.7% of cases with PR3 ANCA positivity, in 79.5% of cases with MPO ANCA positivity, this was statistically significant (p= 0.008). Most of the cases with PR3 ANCA positivity were classified as GPA (95.5%), among the cases with MPO ANCA positivity frequency of GPA was found 28.2%, this was statistically significant (p=0.001). The only difference for the other system involvements was the renal and nasal involvement. Renal involvement was found as 42.4% and 66.7% in cases with PR3 ANCA positivity and MPO ANCA positivity; respectively, by the statistically significant difference (p=0.016). Nasal involvement was found as 35.8% and 15.4% in cases with PR3 ANCA positivity and MPO ANCA positivity; respectively, by the statistically significant difference (p=0.024). Skin involvement was only seen in 11 cases with PR3 ANCA positivity.

Ninety-one cases (72.2%) had an abnormal thoracic CT study. 84 patients have pulmonary involvement and thoracic CT findings. The rest of seven of 91 patients have abnormal thoracic CT, but unrelated to primary disease. The most common abnormalities were nodular opacity (n= 53) and ground glass opacities (n=49). Radiologic findings

Table 3a. Demographic, clinical, and laboratory characteristics according to ANCA sensitivity

	PR 3 ANCA (n=67)		MPO ANCA (n=39)		All (n=106)		P
	n	%	n	%	n	%	
Female	25	37.3	26	66.7	51	48.1	0.004
Male	42	62.7	13	33.3	54	50.9	
Active smoker	9	15.5	4	11.1	13	13.8	0.547
Comorbidity	36	53.7	31	79.5	67	63.2	0.008
HT	22	32.8	22	56.4	44	41.5	0.018
CHF	3	4.5	4	10.3	7	6.6	0.248
CAD	7	10.4	10	25.6	17	16.0	0.040
AF	2	3.0	0	.0	2	1.9	0.276
DM	5	7.5	14	35.9	19	17.9	0.001
COPD	4	6.0	2	5.1	6	5.7	0.856
Asthma	1	1.5	4	10.3	5	4.7	0.040
Malignity	5	7.5	2	5.1	7	6.6	0.641
ANA	13	21.0	11	28.9	24	24.0	0.364
RF	16	28.1	8	26.7	24	27.6	0.889
ANCA	59	88.1	36	92.3	95	89.6	0.489

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were given in Table 3b. Reticular opacity was seen in cases with PR3 ANCA positivity with a ratio of 14.9% and 2.6% of the cases with MPO ANCA positivity, this was statistically significant (p=0.048). Also, cavitary lesion was seen in 20.9% of cases with PR3 ANCA positivity, whereas in 5.3% of the cases with MPO ANCA positivity, by the statistically significant difference (p=0.032).

According to the results of the study, there is a significant difference between cases with PR3 ANCA positivity and MPO ANCA positivity in terms of urea, creatinine, ALT, AST values. ALT and AST was higher in cases with PR3 ANCA positivity, whereas urea and creatinine were higher in cases with MPO ANCA positivity (Table 4).

There were 111 patients with GPA, 15 with MPA, 1 with EGPA. The rest of 3 cases were diagnosed as other vasculitis types. Between GPA and MPA cases presence of comorbidity, asthma, HT, DM, congestive heart failure was statistically different. In Table 5a, demographic and laboratory characteristics and in Table 5b radiologic findings and treatment modalities according to ANCA associated vasculitis subtypes were given.

Table 6 shows the factors related to outcome. Before the analysis, the relationships between the variables in the study and the outcome variables were examined, and the variables that were found to be significant were included in the logistic regression model. Recovery was referenced for

Table 3b. Clinical and radiologic characteristics according to ANCA sensitivity

	PR 3 ANCA (n=67)		MPO ANCA (n=39)		All cases		P
GPA	64	95.5	25	64.1	89	84.0	**0.001**
MPA	2	3.0	11	28.2	13	12.3	**0.001**
EGPA	1	1.5	0	.0	1	.9	0.443
DAH	12	17.9	8	21.1	20	19.0	0.694
Pulmonary involvement	44	65.7	24	61.5	68	64.2	0.669
Neurological involvement	3	4.5	1	2.6	4	3.8	0.618
Nasal involvement	24	35.8	6	15.4	30	28.3	**0.024**
Renal involvement	28	42.4	26	66.7	54	51.4	**0.016**
Arthrosis involvement	10	14.9	7	17.9	17	16.0	0.682
Eye involvement	4	6.1	5	12.8	9	8.6	0.232
Hearing loss	15	22.4	3	7.7	18	17.0	0.052
GIS involvement	1	1.5	1	2.6	2	1.9	0.696
Dermal involvement	11	16.4	0	.0	11	10.4	**0.008**
Symptom (initial)	45	68.2	28	71.8	73	69.5	0.698
Cough	38	57.6	24	61.5	62	59.0	0.690
Dyspnea	37	56.1	22	56.4	59	56.2	0.972
Chest pain	12	17.9	4	10.5	16	15.2	0.312
Hemoptysis	32	48.5	11	28.2	43	41.0	**0.041**
Chest radiological sign (CT)	51	76.1	27	73.0	78	75.0	0.312
Interlobular septal thickening	13	19.4	10	26.3	23	21.9	**0.041**
Ground glass opacities	24	36.4	17	44.7	41	39.4	0.723
Reticular opacity	10	14.9	1	2.6	11	10.5	**0.048**
Nodular opacity	33	50.0	14	36.8	47	45.2	0.194
Cavitary lesion	14	20.9	2	5.3	16	15.2	**0.032**
Infiltrate	9	13.4	7	18.4	16	15.2	0.494
Bronchiectasis	5	7.5	3	7.9	8	7.6	0.936
Cysts	1	1.5	2	5.3	3	2.9	0.265
Pleural effusion	19	28.4	6	15.8	25	23.8	0.146
Fibrosis	10	15.2	6	15.8	16	15.4	0.931
Honeycomb	0	.0	2	5.3	2	1.9	0.058

Third columns are the data of whole cases. They did not used for comparison. Only first and second columns were compared.

Table 4. Comparison of laboratory values between cases with PR3 ANCA positivity and MPO ANCA positivity

Variables	PR3 ANCA (n=67)	MPO ANCA (n=39)	p
Urea (mg/dL)	41.93 ± 29.97	58.58 ±36.13	0.064
Creatinine (mg/dL)	1.73±1.78	2.55±2.29	0.057
GFR	15.20±7.79	28.25±15.84	0.147
AST (IU/mL)	24.67±20.61	16.05±5.87	**0.002**
ALT (IU/mL)	30.87±28.26	14.87±4.82	**0.001**
Albumin (g/dL)	3.65±0.74	3.65±0.61	0.979
ESR (mm/h)	43.67±28.97	36.74±27.84	0.231
CRP (mg/dL))	6.74±9.17	6.27±14.90	0.839

Table 5a. Demographic and laboratory characteristics according to ANCA associated vasculitis subtypes

	GPA (n=111)		MPA (n=15)		All patients (n=126)		P
	n	%	n	%	n	%	
Female	50	45.0	10	66.7	60	47.6	0.282
Male	60	54.1	5	33.3	65	51.6	
Active smoker	12	12.4	2	15.4	14	12.7	0.759
Comorbidity	61	55.0	13	86.7	74	58.7	**0.019**
HT	37	33.3	12	80.0	49	38.9	**0.001**
CHF	6	5.4	3	20.0	9	7.1	**0.039**
CAD	18	16.2	3	20.0	21	16.7	0.712
AF	2	1.8	0	.0	2	1.6	0.600
DM	15	13.5	5	33.3	20	15.9	**0.049**
COPD	7	6.3	1	6.7	8	6.3	0.957
Asthma	3	2.7	3	20.0	6	4.8	**0.003**
Malignity	5	4.5	2	13.3	7	5.6	0.161
ANA	24	23.1	6	40.0	30	25.2	0.158
RF	24	25.8	6	46.2	30	28.3	0.127
PR3 ANCA	64	57.7	2	13.3	66	52.4	**0.001**
MPO ANCA	25	22.5	11	73.3	36	28.6	**0.001**

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the outcome. None of the laboratory values, any comorbid diseases, nor radiologic findings, either treatment modalities have statistically significant effects on outcome (p>0.05).

DISCUSSION

In the present study, we evaluated demographic, clinic, laboratory findings, thoracic CT abnormalities and treatment modalities of 130 AAV cases. We classified them according to clinical sub-types, ANCA serology, and presence of pulmonary involvement or not.

The most common symptoms at presentation were nonspecific. The initial symptoms followed by cough, dyspnea, chest pain and hemoptysis in PI cases. Most cases had multisystem involvement; among them renal involvement was the most common one. Renal involvement was present in almost half of patients (48%). Gastrointestinal and neurologic involvements were the least ones. In comparison of the cases with PR3 ANCA positivity and MPO ANCA positivity; only difference for the other system involvements was the renal and nasal involvement. The Renal involvement was statistically higher in cases with MPO ANCA positivity. On the other hand, nasal involvement was more in cases with PR3 ANCA positivity.

The clinical pathogenesis of PR3-ANCA and MPO-ANCA is different, as it is associated more likely to involve granulomatous inflammation after an exposure to respiratory bacteria in PR3-ANCA whereas silial occupation occurs in MPO-ANCA

Table 5b. Radiologic findings and treatment modalities according to ANCA associated vasculitis subtypes

	GPA (n=111)		MPA (n=15)		All patients (n=126)		P
	n	%	n	%	n	%	
Immunosuppressive therapy	108	98.2	15	100.0	123	98.4	0.599
Corticosteroid	105	95.5	15	100.0	120	96.0	0.399
Cyclophosphamide	69	62.7	8	53.3	77	61.6	0.483
Azathioprine	30	27.5	5	33.3	35	28.2	0.639
Methotrexate	12	10.9	0	0	12	9.6	0.178
Mycophenolate Mofetil	16	14.7	3	20.0	19	15.3	0.592
Rituximab	44	40.4	3	20.0	47	37.9	0.127
Plasma exchange	14	87.2	0	0.0	14	11.3	0.141
Outcome	64	59.3	7	46.7	71	57.7	0.355
Symptom(initial)	80	72.1	8	53.3	88	69.8	0.138
Cough	69	62.7	6	40.0	75	60.0	0.092
Dyspnea	21	19.1	2	13.3	23	18.4	0.134
Chest pain	45	40.9	7	46.7	52	41.6	0.589
Hemoptysis	83	74.8	8	53.3	91	72.2	0.671
Chest radiological sign (CT)	83	74.8	8	53.3	91	72.2	0.082
Interlobular septal thickening	22	19.8	4	26.7	26	20.6	0.539
Ground glass opacities	41	37.3	8	53.3	49	39.2	0.232
Reticular opacity	13	11.7	0	0.0	13	10.3	0.162
Nodular opacity	48	43.6	5	33.3	53	42.4	0.449
Cavitary lesion	21	18.9	1	6.7	22	17.5	0.241
Infiltrate	19	17.1	2	13.3	21	16.7	0.712
Bronchiectasis	8	7.2	1	6.7	9	7.1	0.939
Cysts	1	.9	1	6.7	2	1.6	0.094
Pleural effusion	26	23.4	2	13.3	28	22.2	0.378
Fibrosis	16	14.5	2	13.3	18	14.4	0.900
Honeycomb	0	0	1	6.7	1	.8	**0.006**

Third columns are the data of whole cases. They did not used for comparison. Only first and second columns were compared.

[22-24]. That's why, bronchiectasis as an indicator of chronic injury and alveolar obstruction, seen more in MPO-ANCA. Mohammad et al. reported 44% of bronchiectasis, another study as 20%, we had less than all with a rate of 7.6% [25, 26]. Former studies found bronchiectasis more in patients with positive MPO-ANCA, we found similar rates of bronchiectasis in both cases; MPO and PR3 ANCA positivity [26, 27]. Parallel to the reported data that nodular disease with cavitation was more common in cases with positive PR3-ANCA, our prevalence of cavitary lesion was more (almost 4 times) in cases with PR3 ANCA (20.9%) (5.3% in cases with MPO ANCA) [28].

Mohammad et al. reported 80% of pulmonary abnormalities on thoracic CT [25]. The frequency of abnormal thoracic CT findings was 72.2% in our study. This was similar with previous studies reported the abnormal CT findings in 69%-82% [11]. As in the general literature reported that, there were no major differences in CT findings between ANCA serotype, our findings were like that [25]. The most common abnormalities were nodular opacity (45.2%) and ground glass opacities (39.4%), without difference among the PR3-ANCA and MPO-ANCA positive cases. Researchers found the most common pulmonary finding as nodules with or without cavitation, with a ratio of 50%, like supported in our data [28].

Pleural effusion is a nonspecific finding that may be related to systemic inflammation, heart failure, or renal dysfunction [25]. Previous studies reported the frequency of pleural effusions as 19% in whole and 26% in cases with MPO-ANCA. In our study, pleural effusion was seen in 28.4% of cases with PR3 ANCA positivity, in 15.8% of the cases with

Table 6. Factors related to outcome

	B	S.E.	Wald	p	Odds Ratio (95% CI)	
AST (IU/mL)	0.014	0.025	0.335	0.563	1.014	(0.967 1.064)
Albumin (g/dL)	-1.299	0.745	3.039	0.081	0.273	(0.063 1.175)
ESR (mm/h)	-0.028	0.019	2.18	0.14	0.973	(0.938 1.009)
CRP (mg/dL))	-0.017	0.079	0.047	0.828	0.983	(0.842 1.147)
Urea (mg/dL)	-0.012	0.013	0.869	0.351	0.988	(0.962 1.014)
Congestive heart failure	-1.177	1.567	0.564	0.453	0.308	(0.014 6.652)
Coronary artery disease	-1.428	0.869	2.703	0.1	0.24	(0.044 1.316)
Rheumatoid factor	0.839	0.942	0.794	0.373	2.315	(0.365 14.671)
GIS involvement.	2.209	1.444	2.342	0.126	9.109	(0.452 21.241)
Pleural effusion	-1.27	1.089	1.36	0.243	0.281	(0.033 2.373)
Cyclophosphamide	-0.408	0.786	0.27	0.603	0.665	(0.142 3.102)
Mycophenolate Mofetil	-0.722	1.101	0.43	0.512	0.486	(0.056 4.206)
Rituximab	-0.603	0.786	0.589	0.443	0.547	(0.117 2.554)
Plasma exchange	-21.746	14436.46	0	0.999	0	
MPO ANCA	1.095	1.156	0.898	0.343	2.989	(0.310 28.789)
PR3ANCA	-0.471	0.846	0.31	0.578	0.624	(0.119 3.279)
GPA	22.706	40192.79	0	0.999	0.001	
MPA	21.15	40192.79	0	0.999	0.001	
EGPA	42.339	56841.31	0	0.999	0.001	

Third columns are the data of whole cases. They did not used for comparison. Only first and second columns were compared.

MPO ANCA positivity. The difference may arise from the comorbidities found in previous studies.

On the contrary to literature, fibrosis was seen in almost 15-16% of our cases both with PR3 and MPO ANCA positivity. Whereas, in a multicenter report of 49 patients; fibrosis was found in an extremely high rate as 88%, in MPO-ANCA cases [29]. This marked difference can be explained by the follow up period, as it was known that pulmonary fibrosis usually was seen in late phase of disease.

As a result of basis classification of AAV, nodular opacity was related to GPA [30]. In our data 48 of nodular disease (48/53) was seen in GPA. Pleural effusion was found as 22.2 % among our all cases, 92.8% of them (26/28) were the cases with GPA and 7.1% of them (2/28) were MPA. Similarly, Guillevin et al studied on 85 cases and reported only 6% rate of pleural effusion in cases with MPA [2].

Hosoda et al. published better survival rates with the use of immunosuppressive in treatment [31]. We found none of the immunosuppressive having statistically significant effects on outcome. Current studies report any difference between AAV serotypes. Mohammad et al. found better survival in cases with positive PR3-ANCA [25]. In our study, we found any survival difference between AAV serotypes.

Pulmonary involvement is one of the most frequently reported involvement as our finding [32]. We found the most common organ involvement as renal like previous reports revealed after pulmonary involvement [5, 33]. In PI cases, there was no case with gastrointestinal system involvement. Ear-nose -throat involvement rate was reported less than 20% in recent studies [34]. Our results were similar.

Limitations

As the study retrospectively designed, we didn't have the chance of correlating results with invasive diagnostic methodologies such as lung biopsy or bronchoalveolar lavage.

CONCLUSION

Our study has many cases evaluated for demographic, clinical and outcome features in separated groups according to clinical and serologic classification. Cases with pulmonary involvement were more than the cases without pulmonary involvement in our study. MPA was significantly

higher in non-PI cases. We studied on a large group, and these significant findings may have important implications for the investigation, pathogenesis, and treatment of AAV.

CONFLICT OF INTEREST STATEMENT

All authors declare that they have no competing or financial interests.

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