ORIGINAL ARTICLE

Determine the Clinical Pattern of Anti-Neutrophil Cytoplasmic Antibody Associated Vasculitis and Examine the Long Term Prognostic Factors of Patients and Renal Survival and Relapse

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ABSTRACT

Aim: To examine the prognostic factors of renal survival and relapse in anti-neutrophil cytoplasm antibody associated vasculitis with long term follow-up.
Study Design: Retrospective cohort study.
Place & Duration of Study: Department of Nephrology, Shaikh Zayed Hospital Lahore from 1st January 2018 to 30th June 2018.
Methods: In this study total 35 patients of both sex with renal biopsy-proven anti neutrophil cytoplasm antibody associated vasculitis were included. Patients ages were >35 years. Complete follow-up of more than 15 years was taken to examine the renal survival and relapse.
Results: There were 22 (62.86%) males and 13 (37.14%) patients were females. Ten (28.57%) patients were of ages between 35 to 50 years and 25 (71.43%) patients had ages more than 50 years. Nineteen patients (54.29%) had microscopic polyangitis and 45.71% patients had diagnosis with granulomatosis with polyangiitis. Histopathological examination was recorded as focal, crescentic, mixed and sclerotic glomerulonephritis in 11 (31.43%). 10 (28.57%), 8 (22.86%) and 6 (17.14%) patients. According to treatment, cyclophosphamide with corticosteroids were given to 80% and azithoprine with corticosteroids in 74.29%. The fifteen year patients survival was 15 (42.86%). We observed patients with ages more than 55 years and myeloperoxidase anti-neutrophil cytoplasm antibody were associated with shorter patient's survival time. Renal survival was noted in 23 (65.71%). At 15 years follow-up relapse free survival was 11.43%.
Conclusion: The patients and renal survival in anti-neutrophil cytoplasm antibody associated vasculitis with glomerulonephritis had better results as compared to relapse
Keywords: Pattern, Vasculitis, Prognostic, Survival, Relapse

INTRODUCTION

Granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA) are the primary types of vasculitis that are associated with anti-neutrophil cytoplasm antibody (ANCA). Renal vasculitis is the most common severe manifestation of ANCA-associated vasculitis (AAV) typically presented with rapidly progressive glomerulonephritis (GN). Dialysis is often needed during the AAV diagnostic phase, although renal recovery and withdrawal from dialysis after treatment may occur. However, treatment per se may cause significant morbidity, and patients with impaired renal function may be particularly prone to treatment-emergent adverse events.[1] Renal impairment at diagnosis also predicts poor renal[2–5] and patient survival[6,7].

Medication based on cyclophosphamide (CYC) and corticosteroids (CS), which have been used since the 1970s[8], changed AAV prognosis from lethal to a chronic relapsing disease. Approximately one-half of the patients experience a relapse within five years after diagnosis[9,10].

Biopsy-proven pauci-immune necrotizing GN is a gold standard for the diagnosis of renal AAV. In 2010, a histopathologic classification with focal, crescentic, mixed, and sclerotic categories of GN in AAV (AAGN) was introduced[2].

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The purpose of this study was to describe the clinical profile at diagnosis and the long-term outcome of newly diagnosed, biopsy-proven renal AAV patients during a follow-up of 15 years at a tertiary clinic. We also assessed prognostic factors, including histological classification, which influence patient and renal survival and relapse.

MATERIALS AND METHODS

The retrospective study was conducted at Department of Nephrology, Shaikh Zayed Hospital from 1st January 2018 to 30th June 2018. A total 35 patients of both sex with renal biopsy-proven anti neutrophil cytoplasm antibody associated vasculitis were included. Patients ages were >40 years. Patient's medical record was collected from the hospital administration. All the patients were divided into two groups MPA and GPA. Renal limited vasculitis was considered as a form of MPA. Patient's medical history was examined from the record until 31st December 2017. Time of diagnosis was defined as a time of admission to the nephrology department. For ANCA-testing, ANCA specificity against myeloperoxidase (MPO-ANCA) and proteinase 3 (PR3-ANCA) obtained from the enzyme-linked immunosorbent assays (ELISA) were used. A kidney biopsy was performed in all patients within 1 week after admission. Kidney function was measured using the estimated glomerular filtration rate (GFR) determined by the CKD-EPI formula.[13] Glomerular filtration rate was

recorded at the time of diagnosis and at 1, 3, 5, 10, and 15 years. End-stage renal disease (ESRD) was defined as the need for permanent dialysis or transplantation. Patient survival, renal survival, and relapses were recorded until the end of follow-up. Renal histology was re-evaluated by a single pathologist (TT) and categorized into four classes of AAGN: (A) focal (at least 50% of glomeruli were normal), (B) sclerotic (at least 50% of glomeruli were sclerotic), (C) crescentic (at least 50% of glomeruli presented with cellular crescents), and (D) mixed. All the statistical data was analyzed by SPSS 19.

RESULTS

There were 22 (62.86%) males and 37.14% patients were females. Ten patients had ages between 40 to 50 years in which 4/16 (25%) in GPA Group and 6 (31.58%) in MPA, 25 patients had ages more than 50 years in which 12/16 (75%) in GPA and 13/19 in MPA Group. From all the patients 19 (54.29%) patients had microscopic polyangitis and 45.71% patients had diagnosis with granulomatosis with polyangiitis (Table 1). Histopathological examination was recorded as focal, crescentic, mixed and sclerotic glomerulonephritis in 11 (31.43%). 10 (28.57%), 8 (22.86%) and 6 (17.14%) patients (Table 2). According to treatment, cyclophosphamide with corticosteroids was given to 80% and azithoprine with corticosteroids in 74.29%. We observed mortality at 1 years, 5 year, 10 year and 15 years as 2 (5.71%), 6 (17.4%), 15 (42.86%) and 20 (57.14%). The fifteen year patient's survival was 15 (42.86%). We observed patients with ages more than 55 years and myeloperoxidase ANCA were associated with shorter patients survival time. Renal survival at 1 year was (30 (85.71%), at 5 years 28 (80%), at 10 years 25 (71.42%) and at 15 years 23 (65.71%). At 15 years follow-up relapse free survival was 11.43% (Table 3).

Table 1: Demographical details and diagnosis of patients (n=35)

Variable	GPA Group n=16	MPA Group n=19
Gender		
Male	10 (62.5%)	12 (63.16%)
Females	6 (37.5%)	7 (36.85%)
Age-Wise (years)		
40 to 50	4 (25%)	6 (31.58%)
> 50	12 (75%)	13 (68.42%)
Cardiovascular Disease	2 (12.5%)	3 (15.79%)
Creatinine	162 (55-1650)	253 (63-2350)
Glomerular GFR	15 (1-90)	7 (4-120)
ANCA		
Protienase3	13 (81.25%)	2 (10.53%)
Myeloperoxidase	2 (12.5%)	18 (94.74%)
BVA Score protienuria g/day		
less than 0.5	2 (12.5%)	3 (15.79%)
0.5 to 3.0	11 (68.75%)	11 (57.89%)
Above 3.0	2 (12.5%)	6 (31.58%)
Organ Involvement		
Renal	16	19
General symptoms	14	13
Lungs	10	3
Skin	4	2
Eyes	1	4
Abdominal	1	3
Cardiac	0	1

Table 2: Histopathological examination according to classes

Classes	No.	%
Focal	11	31.43
Crescentic	10	28.57
Mixed	8	22.86
Sclerotic	6	17.14

Table 3: After treatment complete follow-up record

Characteristics	Patients survival	Mortality
1 Year	33 (94.29%)	2 (5.71%)
5 Year	29 (82.6%)	6 (17.4%)
10 Year	20 (57.14%)	15 (42.86%)
15 Year	15 (42.86%)	20 (57.14)
1 Year	30	85.71
5 Year	28	80
10 Year	25	71.42
15 Year	23	65.71
Relapse Free		
At 15 Years	4	11.43

DISCUSSION

The present study was conducted to examine the clinical examination and outcome of a 15 years follow up in patients with renal anti-neutrophil cytoplasm antibody associated vasculitis ANCA-AV confirmed with kidney biopsy. In our study we found maximum patients 54.29% were in MPA group. In this study 94.74% patients was in ANCA-MPO and 81.25% patients of GPA was in ANCA-PR3. We cannot observed that GPA or PR3 ANCA vasculitis would have a higher incidence in this area. These results showed similarity to other study[11]. In the present study similar findings to other study regarding MPA and GPA. In which MPA cases were high as compared to GPA[12]. The diagnostic delay of 4 months was equivalent in MPA and GPA. This is consistent with recent studies reporting a shortening of the gap between the start of symptoms and diagnosis[13-16].

In this study, we found that renal involvement was 100% in all MPA and GPA cases. These results was similar to other study in which renal involvement was 100%[17]. We examine histopathology findings according to classes and found focal in 31.43%, Crescentic in 28.57%, mixed in 22.86% and sclerotic in 17.14%. We observed that from all these classes most of the patients were MPA. These results shows similarity to some other studies in which mostly patients were in MPA according to the histopathology classes[17,18].

According to treatment, cyclophosphamide with corticosteroids was given to 80% and azithoprine with corticosteroids in 74.29% in the present study. We observed mortality at 1 years, 5 year, 10 year and 15 years as 2(5.71%), 6(17.4%), 15(42.86%) and 20(57.14%), The Overall patients survival was 42.86%. Many of other studies conducted regarding AAV reported that patients survival rate was 40 to 50%.[19-21] We also observed from this study that overall renal survival at 15 years follow-up was 65.71% and relapse free survival was 11.43%. These results show similarity to some other studies in which renal survival was 50 to 70% and renal relapse free survival was reported 10 to 18%[22-25].

CONCLUSION

In our cohort of renal AAV, a younger age was related to a favorable patient survival, and better GFR at diagnosis was related to improved renal survival, as may be anticipated. MPO-ANCA was a negative predictor of both patient and renal survival. Patients with GPA were more prone to relapse than MPA patients. In addition, we observed that AAGN classification was predictive, as the risk of progressing to ESRD increased with the ascending category of focal, crescentic, mixed and sclerotic AAGN. We concluded that the patients and renal survival in anti-neutrophil cytoplasm antibody associated vasculitis with glomerulonephritis had better results as compared to relapse.

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