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Etiology and outcome of pulmonary renal syndrome: Retrospective study from a tertiary care hospitaln

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CASE SERIES

Etiology and outcome of pulmonary renal syndrome: Retrospective study from a tertiary care hospital

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Abstract

To determine the aetiology, clinical characteristics and outcome of patients admitted with pulmonary renal syndrome (PRS). This retrospective analysis was conducted at Aga Khan University Hospital from 2011 to 2015. A total of 17 adult patients admitted with PRS were included and followed up for a period of one year for the outcome of PRS as recovery, dialysis dependency or death. Anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV) was found to be the single most frequent cause in 13 (76.4%) patients. The commonest cause of AAV was found to be Granulomatous polyangitis (GPA) in 10 (58.8%) followed by Microscopic angitis in 3 (17.6%) patients. Around 12 (70.5%) patients survived, 11 (64.7%) recovered while 1 patient remained dialysis dependent. Mortality rate was 29.4% and all these patients had severe alveolar haemorrhages. None of our patient died or relapsed during one year follow up.

Keywords: Pulmonary renal syndrome (PRS), diffuse alveolar haemorrhages (DAH), acute kidney injury (AKI), Antineutrophil cytoplasmic autoantibody (ANCA) associated vasculitis, anti-glomerular basement membrane (GBM) disease, systemic lupus erythematosus (SLE).

Introduction

The term pulmonary renal syndrome (PRS) was first described by Good pasture in 1919.[1] PRS is characterized by the occurrence of rapidly progressive glomerulonephritis (RPGN) and diffuse alveolar haemorrhages (DAH) simultaneously secondary to an underlying autoimmune cause.[1] The parallel histologic findings include focal and segmental necrotizing glomerulonephritis with crescents on renal biopsy and alveolar capillaritis on lung biopsy. Many common clinical conditions can mimic PRS, nonetheless a high index of suspicion for PRS is critical as early diagnosis and treatment remarkably improves outcome. PRS can be caused by a number of diseases but the most common causes include anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV), anti-glomerular basement membrane (anti GBM) disease and systemic lupus erythematosus (SLE).[2] These diseases account for about 70-80% causes of PRS.[3,4] The prevalence and the outcome data for the causes that lead to PRS is available, however, the exact incidence of PRS as a syndrome is limited to few studies because of rarity of condition. The causes of PRS in Pakistan might be the same as in rest of the world but due to lack of awareness and education, patients usually present late to the hospital so the outcome may differ. This analysis was done to find out the clinical presentation, aetiology and outcome of PRS in our patient population.

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Patients and Methods

This retrospective analysis was conducted at Aga Khan University Hospital (AKUH), Karachi, Pakistan from 2011 to2015. Following patients with acute kidney injury (AKI) were included;

1. AKI with simultaneous pulmonary involvement along with positive ANCA (P-ANCA or C-ANCA) or anti GBM antibodies OR
2. AKI with simultaneous pulmonary involvement along with positive antinuclear antibody (ANA), anti-double stranded (dsDNA) or both OR
3. AKI with simultaneous pulmonary involvement along with renal biopsy (if done) evidence of
   a. Focal necrotizing glomerulonephritis with linear, granular or no deposit on immunofluorescence (IF) OR
   b. Crescentic Glomerulonephritis with linear, granular or no deposit on IF OR
   c. Mesangio-capillary Glomerulonephritis with deposits of immunoglobulin in capillary wall, sub endothelium and/ or mesangium on IF

AKI was defined by Kidney Diseases Improving Global Outcome (KDIGO) criteria[5] as a rise in serum creatinine

of ≥ 0.3 mg/dl from the baseline within 48 hours or a rise in creatinine 1.5 times from the baseline within the last 7 days.[5]

Baseline serum creatinine was retrieved from the outpatient records within the last 3 months. When not available, patients were considered to have AKI when the presentation was acute with active urine sediment and normal sized kidneys on ultrasound.

Pulmonary involvement was defined by the presence of any two or more of the following:

a. Respiratory symptoms including either cough, shortness of breath or haemoptysis
b. Direct visualization of bleeding via bronchoscopy or the presence of hemosiderin laden macrophages
c. Unilateral or bilateral new alveolar infiltrates on CXR
d. Unexplained Hb of < 10g/dl or haematocrit ≤30%

The patients were followed till one year and the outcome of the patients was recorded as:

1. Recovered
2. Died
3. Dialysis dependent

Recovery was complete if serum creatinine was normalized or reached baseline, or partial when there was a reduction in serum creatinine from the admission creatinine and patient became dialysis free.

Data was collected after approval from hospital ethical review committee. All data was entered and analysed using SPSS 19 and mean, median and percentage was calculated to describe the data.

Results

A total of 17 patients with PRS were managed at our institution from 2011 to 2015. Base line characteristics of patients are shown in Table 1. The most frequent cause of PRS came was granulomatous polyangitis (GPA) as shown in Table 2. Renal biopsy was done in 7 patients. All patients were found to have crescentic glomerulonephritis (GN). Linear deposition of IgG along glomerular basement membrane was found in 2 patients while in rest of the patients immunofluorescence was negative.

All patients were treated with systemic steroids. For induction therapy, intravenous (IV) pulse methylprednisolone was given to 15 (88.23%) patients, whereas oral deltacortil at 1mg/kg was given to 2 patients, cyclophosphamide was given to 12 patients (8 patients received oral and 4 patients received IV), IV rituximab was given to 2 patients while in 3 patients immunosuppressive other than methylprednisolone could not be given because they died early within 2-3 days of hospital stay due to severe alveolar haemorrhages. Plasmapheresis and haemodialysis sessions are shown in Table 1. During the study period, IV methylprednisolone was followed by oral prednisolone at 1 mg/kg which was tapered over 3 months. During maintenance phase 7 patients received azathioprine whereas 4 received Mycophenolate Mofetil. Outcome of patients according to the aetiology of PRS is shown in Table 2. We found 100% mortality in patients with SLE. In patients who recovered, 4(36.3%) patients

Table-1: Base line characteristics of patients with pulmonary renal syndrome.

Variables	n (%)
Age (mean)	45.5 ± 15.3 years
Sex	
Female	13(76.5)
Co morbid	
Asthma	4(23.5)
Ischemic heart disease	3 (17.6)
SLE*	2(11.7)
Diabetes mellitus	1 (5.9)
Hypertension	1 (5.9)
Symptoms at presentation	
Weakness	17 (100)
Shortness of breath	13 (76.5)
Fever	10 (58.8)
Hemoptysis	9 (52.9)
Nausea/ vomiting	7 (41.2)
Cough	6 (35.3)
Oliguria	5 (29.4)
Edema	2 (11.8)
CXR findings	
Bi-alveolar infiltrates	13 (76.5)
Un-alveolar infiltrates	1 (5.9)
Nodular infiltrates	2 (11.8)
Consolidation	2 (11.8)
Cavitary lesions	1 (5.9)
Creatinine on admission mg/dl[medianIQR]	3.5 (1.1- 12)
Haematocrit on admission g/dl[medianIQR]	24.5 (16- 34.7)
Hospital course	
Patients requiring dialysis	5 (29.4)
< 2 weeks	3 (17.6)
2-6 weeks	1 (5.9)
>6 weeks	1 (5.9)
Plasmaphresis	10 (58.8)
< 5 sessions	3 (17.6)
5-10 sessions	7 (41.2)
Non- invasive mechanical ventilation	7 (41.2)
Intensive care unit/ Mechanical ventilation	9 (52.9)
Vasopressors/ septic shock	7 (41.1)

SLE* systemic lupus erythematosus.

Table-2: Causes and Outcome of patients admitted with PRS at 6 weeks.

Outcome (n=17)	GPA(n=10) 58.8%	MPA(n=3) 17.6%	SLE(n=2) 11.7%	Anti-GBM (n=2) 11.7%
Recovered 11 (64.7%)	9 (90%)	1 (33.3%)	0	1 (50%)
Died 5 (29.4%)	1 (10%)	2 (66.6%)	2 (100%)	0
Dialysis dependent 1(5.9%)	0	0	0	1 (50%)

GPA= Granulomatous angitis, MPA= Microscopic polyangitis, SLE= Systemic erythematosus, APLA= Antiphospholipid antibody syndrome, GBM= Glomerular basement membrane.

required haemodialysis and 4(36.3%) patients required ventilator support. None of the patients relapsed during one year follow up.

At one year follow up, serum creatinine reached < 1.2 mg/dl in 5 (45.4%) patients with GPA and 1 patient with anti GBM disease. In the remaining 5 patients (1 with MPA and 4 with GPA) the reduction in serum creatinine was > 50% from the admission creatinine but did not reach baseline.

Discussion

PRS is a fulminating condition that should be promptly diagnosed and treated to prevent mortality and to preserve renal functions. We performed this retrospective case analysis and found AAV (76%) as the most frequent cause of PRS. Most of the patients who present with RPGN have renal limited disease. Pulmonary involvement along with RPGN is a rare entity and data on the aetiology and outcome is limited. AAV and GPS are rare disorders with an incidence of 10 cases/million and 1 case/million respectively.[6] In our study, GPA (58.8%) was found to be the leading cause of AAV followed by MPA. This is in comparison with another study by Hugh et al who found AAV as the leading cause (71%) with equal number of GPA and MPA.[4] Another study by Saxena et al found AAV in 70% patients with PRS.[7] In contrast to our results, Srinivas et al from India found SLE (53.8%) as the leading cause of PRS in critically ill patients[8] whereas, we could find only 2 (11.7%) patients of SLE presenting with PRS and both came with catastrophic APLA. Anti GBM disease is a very rare disorder and was found in only 2 patients and this is comparable to other studies.[4,7,8]

Our study revealed a mortality rate of 29.4% which is in contrast to another study by Saxena et al which reported an early mortality of 12%.[7] In another survey by Hugh et al, mortality at one month was found to be 35% which is close to our mortality rate. Other studies have reported a very high mortality rate of 50-60% in PRS patients requiring ventilator support.[8,9] In this study the most common cause of death was severe respiratory distress followed by nosocomial infection.[10] In another study from India, mortality was 71.4% in SLE patients with PRS and majority of the patients died within a week of admission secondary to severe respiratory distress and infection.[8] GPS is also a rare condition with poor outcome. In one case series of 67 patients, dialysis dependency or death occurred in about 90% of patients with GPS.[11] In our study, 12 (70%) patients survived the acute phase though one patient remained dialysis dependent. The patients who recovered had a reasonable outcome at one year with regard to both longevity of life and preservation of renal functions as none of our patients relapsed during one year follow up.

Conclusion

We found GPA the commonest form of PRS with relatively better outcome. Mortality is significantly higher in patients with PRS who develop respiratory failure and require ventilator support. Further large prospective studies are needed to outline the aetiology and outcome of PRS from Pakistan.

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