EDITORIAL

Pulmonary Renal Syndrome

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Pulmonary renal syndrome (PRS) is a rare, severe and life-threatening condition characterized by presence of diffuse alveolar haemorrhage (DAH) and glomerulonephritis. Common causes of PRS include autoimmune diseases like ANCA associated vasculitis (AAV) including microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA) and eosinophilic granulomatosis with polyangiitis (EGPA) and anti-glomerular basement membrane antibodies (anti-GBM) disease.[1] Rarely, PRS can be seen associated with other autoimmune diseases like systemic lupus erythematosus (SLE), IgA vasculitis, mixed cryoglobulinemia and antiphospholipid syndrome (APS). Infections like leptospirosis, dengue and drugs like hydralazine, propylthiouracil and d-penicillamine have also been associated with the development of PRS.[1,2] It is essential to quickly diagnose and initiate therapy in patients with PRS as it is associated with high mortality.

Even though AAV are the most common causes of PRS, exact disease specific incidence of PRS is not known. DAH has been reported to occur in 8-36% of patients with AAV and among them, 25% to 57% of patients require renal replacement therapy.[3] We previously reported PRS in 10 out of 92 patients with AAV, 5 among GPA and 5 among MPA patients.[4] Anti-GBM disease is a rare disease with an incidence rate of around 1 per million.[3] Among patients with anti-GBM disease, 60-80% of them have lung and kidney involvement suggestive of PRS.[3] Lung involvement in the form of DAH is very rare in SLE patients, however, 40-100% of these patients have coexisting lupus nephritis.[5] In IgA vasculitis, renal involvement is common and manifested as IgA nephropathy but DAH is a rare manifestation.[6] DAH and renal involvement in APS are seen as a part of catastrophic APS and is characterized by thrombotic microangiopathy and rarely capillaritis on histology.[7] Up to 90% of patients with mixed cryoglobulinemia have glomerulonephritis while DAH is present in 3.2% of patients.[8]

Data exclusively on clinical features, etiology, management and outcomes of PRS is scarce. In a study reported in this issue of the journal, Gokhale et al. have described the etiology and short-term outcomes of 25 patients with PRS from a tertiary care centre in Mumbai, India. Out of 25 patients, 18 patients had underlying autoimmune diseases while 7 patients had PRS secondary to infections. Among the autoimmune diseases, AAV was the most common etiology, noted in 12 patients (7 with GPA, 4 with MPA and 1 with EGPA). PRS was secondary to SLE in 5 patients and anti-GBM disease was the cause in one patient. Leptospirosis and dengue fever were the infections noted among the other 7 patients.

Clinical features of DAH include breathlessness, haemoptysis, fall in haemoglobin level and respiratory failure. It is important to note that in about a third of the patients with DAH, haemoptysis may be absent hence, a high index of suspicion is required to diagnose DAH.[9] Gokhale et al. have also reported that haemoptysis was present in only 68% of patients in their cohort of 25 patients. Chest radiology shows infiltrates in perihilar areas with peripheral sparing but in 25% of patients, chest radiography may be normal.[1] Gokhale et al. reported that 14.3% of chest radiographs were normal in their study. Renal involvement is characterized by presence of active urinary sediments and proteinuria with or with out deranged renal functions. Serological tests for ANCA, anti-GBM antibodies, ANA and cryoglobulins help in differentiating various causes of PRS. Most common finding on histopathology is the presence of small vessel vasculitis. Pattern of immune complex deposition also helps in differentiating the etiology of PRS. AAV are characterized by minimal or no immune deposits while the immune deposits are in a liner fashion in anti-GBM disease.[3]

PRS is associated with high mortality if not treated early and aggressively. In the study by Gokhale et al., 32% of the patients died despite aggressive immunosuppressive therapy and other supportive measures. Early initiation of immunosuppression is essential in patients of PRS with underlying autoimmune disease. High dose intravenous methylprednisolone and cyclophosphamide or rituximab help in achieving remission among these patients. Steroids were used in all patients by Gokhale et al. while cyclophosphamide was given in 72% of patients and rituximab in 8% of patients. Plasma exchange has been proven to be effective in reducing progression to end stage renal failure among patients with severe renal involvement in AAV and anti-GBM disease.[10,11] The results of PEXIVAS trial are awaited and the trail may help in providing more definitive evidence on role of plasma exchange in severe manifestations of vasculitis.[12] Antimicrobial should be initiated if the underlying etiology is infection. Other supportive measures like mechanical ventilation, renal replacement therapy and blood transfusions may be required in these patients. In the report by Gokhale et al., all 8 patients who received invasive ventilation died, indicating poor prognosis in patients who present with severe manifestations like respiratory failure.

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