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Case Study

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RELAPSING GRANULOMATOSIS WITH POLYANGITIS COMPLICATED BY CHRONIC KIDNEY DISEASE AND OPPORTUNISTIC INFECTIONS

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ABSTRACT

Granulomatosis with polyangitis is an uncommon, multisystem autoimmune disorder with an as yet undetermined incidence. Renal manifestations are a characteristic feature of this necrotizing vasculitis and largely determine the prognosis of the disease. Frequent relapses necessitate the need for maintenance treatment using immunosuppressants and corticosteroids, the cumulative doses which can in turn precipitate opportunistic infections. We herein report a relapse case of granulomatosis with polyangitis in a 57 year old male patient who presented with fever, cough, blood tinged sputum and polyarthralgia. Clinical,radiological and histo-pathological assessments revealed granulomatosis with polyangitis complicated by significant renal impairment and opportunistic infections, namely pneumonia and candidiasis. Rapid remission was attained using a combination of prednisone and rituximab.With intensified antibiosis and symptomatic therapy, the patient recovered and was discharged on the 14th day post admission. This report illustrates the importance of early diagnosis and a multi-modal approach in attaining remission and preventing the late complications of this rare disorder.

KEYWORDS: Granulomatosis with polyangitis, Wegener's granulomatosis, crescentic glomerulonephritis, opportunistic infections.

INTRODUCTION

Granulomatosis with polyangitis (GPA),formerly known as Wegener's granulomatosis is a rare,relapsing autoimmune disorder with multisystem involvement.It is characterised by necrotizing vasculitis of small and medium-sized blood vessels as well as granulomatous inflammation of the respiratory and renal system.[1] Kidney involvement is evident in about 45-90% of patients with GPA,usually within two years of onset and is manifested as pauci-immune and crescentic glomerulonephritis with a very rapid decline of renal function.[2] The etio-pathogenesis of the disorder has been attributed to anti-neutrophilic cytoplasmic antibodies(ANCA),along with several complex interactions involving genetics and environmental factors.[3] A complete clinical, radiological and histo-pathological assessment aids in the diagnosis of the disease. Clinical evaluation is crucial in evaluating the site and extent of involvement. Laboratory tests include a complete blood count, renal function tests,tests for inflammatory markers, electrolytes and titers of ANCA. Radiological assessment of lungs,trachea and sinuses are vital in delineating the pulmonary involvement. Furthermore, the presence of vasculitis and immune deposits can be confirmed by histo-pathological evaluations.[4]

Treatment for GPA involves an induction and maintenance phase with the use of immune-suppressants and corticosteroids in a variety of combinations. Plasmapheresis is indicated in case of rapidly declining kidney function, presence of antibodies or other complications.[5]

Here,we present a case of granulomatosis with polyangitis complicated by chronic kidney disease and opportunistic infections.Since GPA is associated with significant morbidity and mortality, this report emphasizes the importance of early recognition and prompt treatment in improving the clinical outcomes.

CASE REPORT

A 56 year old male patient presented with a one week history of fever, productive cough and blood tinged sputum.He also had complaints of polyarthralgia since the past 12 days.The first diagnosis of ANCA associated vasculitis was in 2016 and the patient received five doses of cyclophosphamide and four doses of rituximab since then. Past histopathological findings revealed pauci-

immune crescentic glomerulonephritis,for which he underwent five sessions of plasmapheresis.

Physical examination showed the presence of multiple joint tenderness and swelling with bilateral chest crepitations. The vitals were normal at the time of admission. Initial laboratory investigations revealed significant renal impairment with BUN 267.8 mg/dL and serum creatinine 9.2 mg/dL. The haemoglobin level was 10.1 g/dL at time of admission and showed further decrease on subsequent days. PCV was 21.4 % and peripheral smear indicated dimorphic anaemia with neutrophilia. Urine analysis was positive for albumin (+++), WBC (10-12 cells), RBC (40-45 cells), epithelial cells (1-2) with a P/C ratio of 4.8.The electrolyte panel was also abnormal with low sodium (119 mEq/L) and bicarbonate (5.6 mEq/L) levels. Ultrasonography reports demonstrated a hyper-echoic renal parenchyma with altered corticomedullary differentiation, suggestive of chronic kidney disease. Moderate pus cells and gram negative bacilli (Klebsiella) was seen in the sputum sample. The patient also had a WBC count of 12,890 cells,neutrophil band of 94%, ESR of 100 mm/hr and CRP of 18.1 mg/L, all of which were indicative of an acute infection. A chest radiograph reportedly showed evidence of right lower lobe pneumonia. GPA relapse was suspected based on the serology report,which was positive for PR3-ANCA(c-ANCA).

High dose corticosteroid pulse therapy was initiated with prednisone 60 mg for remission induction of vasculitis. In view of the decreasing haemoglobin levels, the patient was administered folic acid 5 mg/day and a transfusion of 1 pint packed RBC was made thrice.Hyponatremia was corrected with hypertonic saline (3%).Sulfomethoxazole(400 mg)/trimethoprim(80 mg) combination was started empirically to curb the infection, and was later changed to piperacillin/tazobactum 2.25 g IV TID and tablet levofloxacin 250 mg/day after receiving the culture and sensitivity report. Under intensified antibiosis,the infection gradually subsided. After completion of the antibiotic course,rituximab 1g infusion was given and the patient underwent seven sessions of hemodialysis,in view of severe non-oliguric renal failure. The nephrologist also proposed for plasmapherseis if kidney failure progressed despite hemodialysis. A gastroentereolgy consultation was made in view of poor oral intake due to vomiting, dysphagia and abdominal tenderness. The patient was found to have developed mild oropharyngeal candidiasis for which tablet fluconazole150 mg OD and clotrimazole mouth paint (1% w/v) for local application was prescribed. Vomiting was managed with metoclopramide 10 mg IV SOS and the patient was also advised to undergo an OGD if symptoms are persisting. Later on,the patient developed steroid associated behavioural abnormalities like apprehension,fear,agitation and insomnia. After psychiatry consultation, the steroid dose was reduced and haloperidol 2.5 mg IV was administered for symptom management. On the day before discharge,the patient developed tonic-clonic movement of limbs post transfusion.Phenytoin 100 mg S/C and 10% calcium gluconate was administered upon neurology review.

The patient was stable by two weeks and was discharged on the 14th day post admission,with an advise to follow up after twelve days for the second dose of rituximab.

DISCUSSION

Along with other available case reports,this report also emphasises the need for prompt diagnosis and management of GPA. Early identification is crucial as ANCA activation of neutrophils can cause oxidative damage to endothelial cells and kidney damage can be destructive.[6]

Our patients' initial presentation reflects the typical multi-system involvement associated with GPA.He manifested many typical GPA signs and symptoms including hemptysis,polyarthralgia,cough and renal failure. The clinical course of the patient and his strongly positive c-ANCA(PR3-ANCA) with negative RF and p-ANCA(MPO-ANCA) were considered diagnostic of this condition since the presence of c-ANCA directed against PR3 is most specific for GPA.[7] Usually renal involvement is considered to be severe and is the leading cause of mortality in these patients.[8] Here,the renal function of the patient showed progressive deterioration and the biopsy reports were indicative of crescentic glomerulonephritis.

The complete management of GPA consists of several modalities that are unique to this disease and are stratified based on severity. Methotrexate and glucocorticoids can induce and maintain remission in active but non-severe form of GPA. On the other hand,glucocorticoids in combination with either cyclophosphamide or rituximab are recommended options for patients with severe disease. For patients with relapsing disease who have had prior cyclophosphamide exposure,as in our case,rituximab is an excellent option.[9] The EULAR/ERA-EDTA recommendations also support the use of rituximab for major relapse of organ or life-threatening GPA.[10]

Pulmonary involvement has been found in 70-100% of GPA cases and may not only be due to the underlying vasculitis.[1] Though immunosupressants improve the prognosis,their prolonged or inappropriate use can be the reason for infectious complications. Hence,opportunistic infections are a cause of concern that requires timely management.[11]

The response to initial treatment in this case was eventful,which induced remission rapidly within a matter of weeks. The rapid and dramatic response to rituximab and prednisone supports the fact that this therapy worked best for our patient along with antimicrobial therapy for the opportunistic infections.

CONCLUSION

The main therapeutic challenge in this condition is the prevention of relapses and the occurrence of late complications. Repeated induction and long-term maintenance treatment using glucocorticoids and immunosuppressants can result in cumulative doses of these agents that can precipitate adverse drug reactions. Hence,the development of newer strategies that can maintain long term remission by reducing the glucocorticoid and immunosuppressive exposure is warranted.

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