Case Report

A case report of a successfully treated patient of granulomatosis with polyangitis and diabetes mellitus

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ABSTRACT

Granulomatosis with polyangitis (previously known as Wegener's granulomatosis) is an antineutrophilcytoplasmic antibody (ANCA) associated vasculitis (AAV). Its main characteristics are necrotizing granulomatous inflammation and paucimmune vasculitis in small and medium sized vessels. Here, we present a case history of a 42-year-old diabetic patient, who presented with cough, epistaxis, deafness and acute kidney injury. Though ANCAs were negative, imaging and histopathological features were consistent with the diagnosis of granulomatosis with polyangitis. With supportive management of diabetes and renal failure, the patient was given immunosuppressive therapy with 4 cycles of intravenous methylprednisolone and cyclophosphamide resulting in improvement of renal function and respiratory symptoms.A high degree of suspicion is needed for diagnosis of granulomatosis with polyangitis as it is relatively rare and timely treatment may result in favourable outcome.

Key words: *ANCA-associated vasculitis, granulomatosis with polyangitis, glomerulonephritis,*

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INTRODUCTION

Granulomatosis with polyangitis (GPA) is a multisystem disease, commonly involves the respiratory tract and kidneys[1]. The annual incidence of the disease was 1.3 per 100,000 people in USA according to a study conducted in 2015.[2] The German pathologist Friedrich Wegener described it in 1936 leading to the eponymous name " Wegener's granulomatosis"[3].Around 10% with patients GPA may be ANCA negative[4]. GPA is a very aggressive disease and even with treatment 50% patient may become dialysis dependant[5,6] and a good number of them usually require long term immunosuppression. Here, we report a case of ANCA negative GPA which was successfully treated with immunosuppression and ultimately had a good recovery.

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CASE REPORT

A 42-year-old, diabetic man presented with the complaints of cough with scanty amount mucoid sputum, epistaxis, deafness and reduced amount of urine production for 15 days followed by anuria for 3 days. It was associated with leg edema, breathlessness and drowsiness for 1 day.There was no history of fever, chest pain, earache or discharge from ear, bone pain, skin lesion, gum bleeding, joint pain, burning micturition, trauma, weight loss or night sweats. There was no history of tuberculosis or exposure to any known tuberculosis patient. He did not have any history of taking nephrotoxic drugs or anticoagulants. He has no history of renal disease, hypertension, bronchial asthma or any bleeding disorder. He is diabetic for 2 years and was on oral anti-diabetic drugs. He took tablet azithromycin 500 mg once daily for 5 days previously but his symptoms persisted.

Table I Initial investigations of the patient

CBC	8.8 gm/dl , WBC- 15,700/cmm (N-77%, L-7%), PLT-294,000/cmm
Renal function test	Creatinine-12.3 mg/dl , urea-146mg/dl, Na-143 mmol/L, K-7.6 mmol/L, Cl-112mmol/L, HCO3-25 mmol/L
Urine analysis	WBC- 10-15/hpf,RBC- plenty (8% dysmorphic on phase contrast),Protein- ++ ,No cast, urine C/S - Growth of *E. coli* (1×10^5 CFU/ml) sensitive to imipenem, amikacin, netilmicin, nitrofurantoin)
P-ANCA ,C-ANCA, C3, C4	Negative
UTP	0.84 gm/24hrs (after establishing adequate urine output)
Hb A1C	10.4%
Audiogram	Shows conductive type of deafness bilaterally

On examination, the patient looked puffy, had peri-orbital swelling, anemia and leg edema. His blood pressure was 140/90 mm Hg. He had crusting over nasal septum, bilateral basal crepitation on lung auscultation and Glasgow Coma Scale (GCS) was 13/15. His plantar reflex was extensor bilaterally and he had non-proliferative diabetic retinopathy. There was no lymphadenopathy, bony tenderness or organomegaly or features of meningeal irritation. Bed side urine albumin was 1+.

Biochemical tests revealed anemia with leucocytosis, features of renal failure and uncontrolled diabetes mellitus. Urine analysis showed haematuria and proteinuria and growth of E.coli, Markers of glumerulonephritis were negative (Table-I).

X-ray PNS showed feature of sinusitis and chest X-ray showed nodular opacity as seen in (Figure 1 and 2).

Biopsy from nasal septum showed feature of necrotizing vasculitis (Figure-III) and renal biopsy showed feature of pauci-immune glomerulonephritis suggestive of ANCA- associated vasculitis (Figure IV).

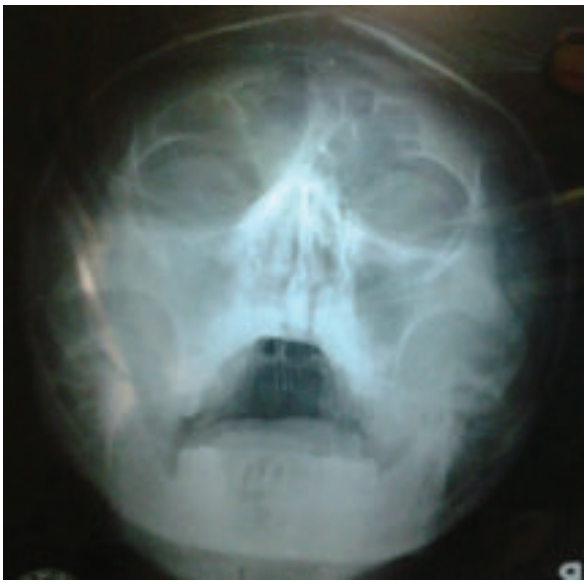

Figure 1 X-ray paranasal sinuses showed bilateral maxillary sinusitis

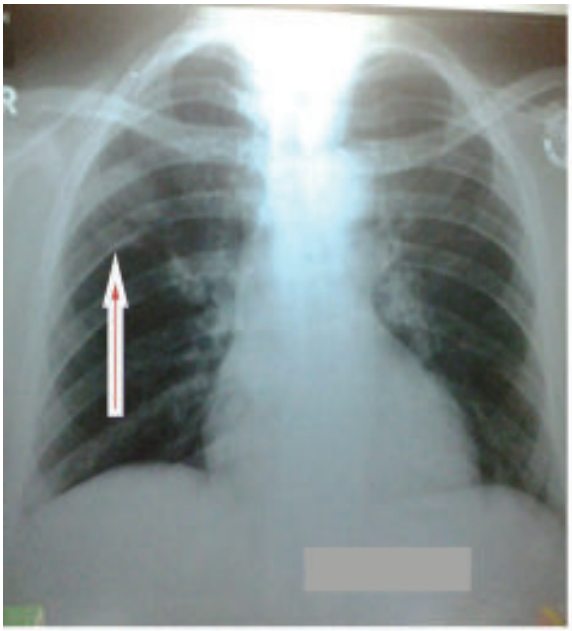

Figure 2 Chest X-ray (P-A view) showed nodular opacity covering upper and mid zone of right lung field

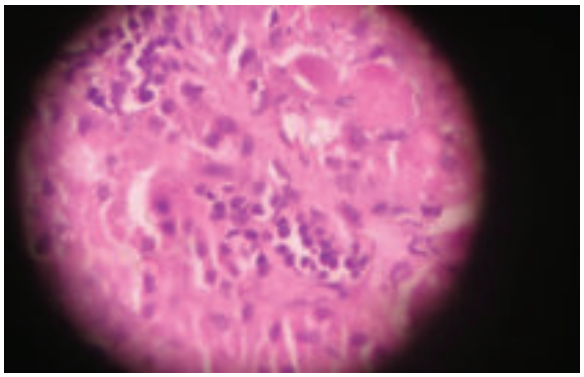

Figure 3 Biopsy from nasal septum showed focal inflammatory destruction of the lining epithelium with infiltration of acute and chronic inflammatory cells and few epitheloid cells, evidence of vasculitis and tiny foci of necrosis

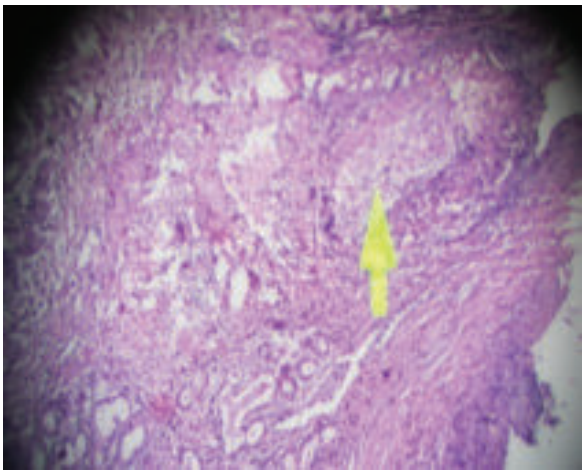

Figure 4 Renal biopsy: (Light microscopy, hematoxylin and eosin stain): all gromeruli were enlarged and hyper cellular and showed moderate to marked increase in the mesangeal cells and matrix with diffuse interstitial and periglomerular lymphocyte infiltration. Segmental necrosis was present in three glomeruli. Some blood vessels showed features of vasculitis. Direct immunofluorescence- few mesangial deposits of IgG and IgM (pauci-immune).

Patient was treated for induction remission with intravenous Methylprednisolone 1gm daily for consecutive 3 days along with intravenous cyclophosphamide 500mg/m^2 body surface area with intravenous mesna to prevent haemorrhagic cystitis. Methylprednisolone was followed by oral prednisolone of 1mg/kg bodyweight/day and continued as a tapering schedule. He also required hemodialysis for his renal failure, insulin therapy for controlling diabetes, antibiotic for urinary tract infection and packed cell transfusion. During discharge patients renal function was significantly improved (serum creatinine-1.8mg/dl).Subsequently he received monthly intravenous cyclophosphamide. After 4 months of treatment, his symptoms completely subsided with resolution of chest nodules on chest radiograph and recovery of renal function, but he had persistent proteinuria which was related to diabetic nephropathy.

DISCUSSION

GPA may present with wide spectrum of clinical manifestation. Constitutional symptoms include fever, night sweats, fatigue, lethargy, weight loss. Usual upper respiratory symptoms include rhinitis, epistaxis, and saddle nose deformity. Pulmonary infiltrates, cough, haemoptysis, chest discomfort, breathlessness, pulmonary haemorrhages are the main lung manifestations. Approximately 50% patient may have kidney involvement at presentation characterized by reduced renal function, haematuria and proteinuria [7]. In our case patient had epistaxis, pulmonary nodule, renal failure, haematuria and proteinuria.

Routine laboratory tests are non-specific in GPA which may show mild normochromic normocytic anaemia, elevated inflammatory markers, abnormal renal function tests and urine analysis (as seen in our case). Cytoplasmic antineutrophil cytoplasmic antibody (c-ANCA) is most specific for GPA (sensitivity 82-94%); but approximately 10 % cases may be ANCA negative[4] as in our case which makes it diagnostically difficult. Eilis McCarty et al reports a case of ANCA negative GPA where patient was finally diagnosed after death during autopsy[8]. Walken et al reported a case of ANCA negative GPA where diagnosis was made on clinical findings despite being ANCA negative and no supportive biopsy findings where patient symptomatically improved after treatment[9].Chest radiography and CT scan may show single or multiple nodules, among which approximately 50% may be cavitated, consolidation, patchy or diffuse ground glass opacities. In our case patient had a single pulmonary nodule.

Diagnosis usually confirmed by tissue biopsy from site of active disease, kidneys and lung biopsies are more

specific. According to Weiss et al. renal biopsy may show feature of segmental necrotizing glomerulonephritis with little or no complement deposition in 60% cases[10]. Nasal biopsy may show feature of vasculitis with foci of necrosis in 53% patients in a study by Delbuono and colleagues[11]. Both the features of segmental necrotizing pauci-immune glomerulonephritis in renal biopsy and feature of vasculitis in the nasal biopsy were similar findings in our case.

For induction of remission, cyclophophamide or rituximab with glucocorticoids may be given in life or organ threatening GPA. The remission rate in GPA ranges from 30-93%[12]. Our patient responded well with cyclophosphamide and pulse methyl prednisolone therapy. Plasma exchange may be considered in patients with rapidly progressing renal failure or in patients who are unresponsive to remission induction therapies.

Without treatment survival in GPA is 10% in 2 years[1]. So, it is important to consider this diagnosis in patients for early management to minimize mortality and morbidity.

Authors' contribution: TM managed the can and drafted manuscript. TS, MAR was involved in management of the WMMH was supervisor.

Conflicts of interest: Nothing to declare.

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