C-ANCA positive GPA with pulmonary involvement: a case report

Abdukarim S, Sokwala A, Ali SK, Otieno FO

Faculty, Internal Medicine, Aga Khan University, Nairobi, Kenya

Corresponding author:
Dr. Fredrick O Otieno.
Email: fred.otieno@aku.edu

Abstract

Granulomatosis with polyangitis (GPA) represents a rare cause of systemic vasculitis with relatively even fewer cases reported from Africa. The possible explanations for the relatively low incidence are thought to be because of possibly actual low prevalence in this population, low index of suspicion for the condition and under-diagnosis due to lack of diagnostic services. In this case report we present a 75 year old female with cytoplasmic anti-neutrophil cytoplasmic antibody (c-ANCA) positive granulomatosis with polyangitis with predominantly pulmonary involvement admitted with pneumonia and Acute Respiratory Distress Syndrome (ARDS) who transiently improved with immunosuppressive therapy, plasma exchange and rituximab but eventually succumbed due to septic shock.

Key words: C-ANCA, Pulmonary, Granulomatosis, Vasculitis.

Introduction

The incidence of vasculitis including GPA in Africa and Kenya is unknown, though thought to be relatively rare as it is globally. It is however on the rise with improving diagnostic services and standardization of diagnosis criteria. Cases remain largely unreported or undiagnosed due to lack of diagnostic services and financial constraints[1]. In addition, guidelines for diagnostics and treatment are largely derived from studies from Western sources.

GPA represents a small-medium vessel vasculitis as per the Chapel-Hill classification of vasculitides[2]. It is one of the Antinuclear Cytoplasmic Antibodies (ANCA) Associated Vasculitis (AAV). It is characterized by necrotizing granulomatous inflammation involving the upper and lower respiratory tracts and a necrotizing vasculitis affecting small to medium vessels. GPA may present with symptoms of upper and lower respiratory tract involvement with or without renal involvement with glomerulonephritis.

The American College of Rheumatology (ACR) criteria for the diagnosis of GPA require two of the following[3]:

(i) Features of nasal or oral inflammation
(ii) Abnormalities on chest radiography showing nodules, infiltrates or cavities
(iii) Abnormally on urinalysis – microscopic haematuria/proteinuria
(iv) Biopsy evidence of granulomatous inflammation

GPA is associated with PR3-ANCA antibodies which are positive in 82-94% of cases[4]. Up to 10% may however have antibody negative GPA[5].

Establishing a diagnosis early is key as it causes early initiation of treatment that can be life and organ saving. Treatment involves immunosuppressive therapy.

When untreated, GPA poses a high mortality with a mortality rate of up to 90% at two years. Treatment studies have reported mortality rates ranging from 12 to 28% at 7 to 8 years' 6-8 to 24 to 44% at 4 to 10 years 9-13. Causes of mortality include infections related to use of immunosuppressive therapy, organ effect (lung or renal) and cardiovascular disease[6, 7].

Case presentation

A 75 year old female presented to our facility with a history of dyspnea for 5 days associated with fevers and a productive cough. She denied any chest pain, rashes or a travel history.

She had been on prednisolone and azathioprine for c-ANCA positive GPA as an outpatient with no recorded flares or prior hospitalizations. The diagnosis was made 4 years prior on the basis of long standing cough and dyspnea with CT chest revealing nodular lesions with biopsy findings of non caseating granulomas. Her c-ANCA test was positive. She had been treated for pulmonary tuberculosis prior to the diagnosis of GPA with no positive microbiological studies and

persistence of her symptoms. She was also reported to have deterioration in her vision and managed for scleritis. She was not known to have any other medical comorbids. She was lost to follow up however, last seen 7 months prior to her admission.

On initial assessment her vitals were: BP 110/70 mmHg pulse rate 96/minute temperature: 38.5 degrees celsius respiratory rate: 20/minute SPO2: 90% on non rebreather mask at 15 liters/minute. She had no peripheral edema. Her examination was remarkable for bilateral coarse crepitation on respiratory auscultation.

Her initial diagnostic evaluation was as follows – haemoglobin 11.9 g/dl, WBC count 8.58, neutrophils 88%, platelet count 265. Sodium 132 mmol/L, creatinine 88 mmol/L BUN 8.1 mg/dL. Procalcitonin was elevated at 6.51 ng/ml and C-Reactive Protein was 291 mg/L. Arterial blood gas analysis revealed respiratory alkalosis with hypoxemia. C-ANCA was tested positive and p-ANCA negative. A urinalysis at the time revealed haematuria and mild proteinuria. CT of the chest revealed bilateral perihilar and lower lobe consolidations and patchy upper lobe opacities bilaterally. Sputum studies including ZN stain and geneXpert for tuberculosis were negative. PCR for PCP was also negative. Tests for HIV/ hepatitis B/hepatitis C were negative.

She was admitted to the High Dependency Unit (HDU) and started on antibiotics empirically. Was also initiated on high dose steroids and continued on the azathioprine. She had worsening respiratory distress and type 1 respiratory failure requiring intubation and mechanical ventilation by her fifth day of admission. Her course was complicated by a right sided pneumothorax detected after 2 days of ventilation for which she had a chest tube inserted with resolution of the pneumothorax. She was commenced on plasmapheresis on the 8th day of admission and received four sessions of the same (days 8, 10, 15 and 18 of admission). She developed oliguric acute kidney injury on her 13th day of admission requiring 2 sessions of dialysis. Her renal function recovered progressively with normalization of her creatinine and good urine output. She received induction with rituximab at 3 weeks given her first organ-threatening relapse and she demonstrated clinical improvement with improving ventilator requirements as well as neurological status. She however later developed septic shock with positive blood culture for Acinetobacter baumanii and succumbed despite adequate treatment.

Figure 1: Chest radiograph on admission

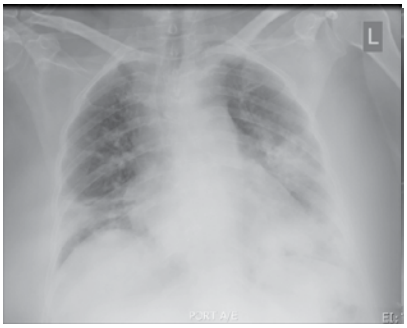


Figure 2: After immunosuppressive treatment/antibiotics

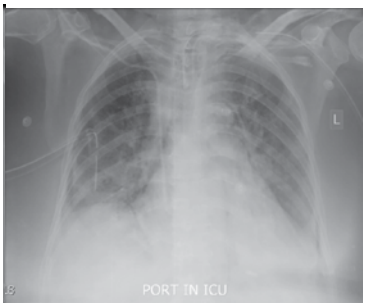
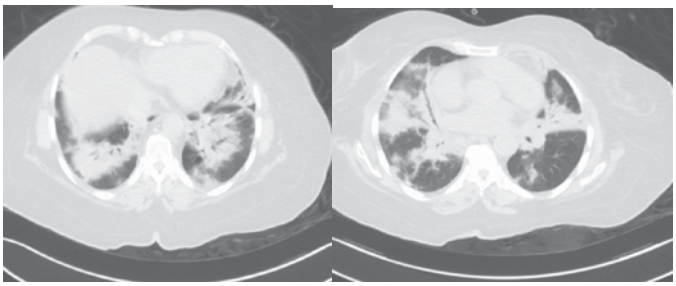


Figure 3: CT scan of the chest at admission



Discussion

GPA categorized as a small-medium vessel, ANCA associated vasculitis is thought to be relatively rare with overall incident rates of AAV in Europe reported to be between 13-20/million. There are no local studies on prevalence or incidence in Africa. A literature review revealed no locally reported cases in Kenya. Some of the reasons behind relatively fewer cases being reported locally include: A truly lower prevalence, lack of suspicion for the condition among physicians and lack of diagnostic services. In addition, the clinical features such as constitutional symptoms with respiratory symptoms may mimic more prevalent infectious conditions such as tuberculosis, as was the case in the patient. The incidence of GPA is known to increase with age[8]. Our patient had the diagnosis first made at 71 years of age.

GPA may present with nonspecific constitutional symptoms, symptoms of upper/lower respiratory tract involvement or renal involvement with glomerulonephritis. In two studies in Tunisia on patterns in GPA, the most common symptoms at presentation were ear, nose and throat symptoms followed by pulmonary symptoms[9]. Our patient initially presented with chronic cough and dyspnea. She also developed ocular symptoms which are known to occur[10].

The diagnosis of GPA is based on clinical, imaging and laboratory criteria. Early diagnosis is vital as it enables institution of early treatment that can be life and organ sparing. In addition to clinical symptoms/signs, a biopsy of affected organ demonstrating characteristic histological features plays a key role in diagnostic work up. Where suspicion is high however, diagnostic evaluation shouldn't delay treatment. ANCA testing should be done in any patient suspected of having vasculitis. Positivity rates for c-ANCA in GPA are reported to be between 82-94%[4]. Locally, a Tunisian study by Ben Ghorbel *et al*[9] determined c-ANCA to be positive in 90% of the 30 patients in the case series.

Treatment of GPA largely involves immunosuppressive therapy. Initial immunosuppressive therapy in patients with a life or organ threatening presentation involves glucocorticoids in combination with either rituximab or cyclophosphamide[11]. In addition, plasma exchange may be used in patients with rapidly worsening renal function or severe renal dysfunction[12], anti-glomerular basement antibody positivity[13,14] or pulmonary haemorrhage[15,16]. On admission and during her hospital course she received glucocorticoid therapy, rituximab and plasmapheresis with demonstrated clinical improvement and radiologic improvement in the lung infiltrates. Despite the improvement she later developed septic shock with Acinetobacter baumanii cultured from blood.

Conclusion

While c-ANCA granulomatosis with polyangitis is relatively rare in our local setting, it is prudent to have a high index of suspicion for the condition for appropriate and timely management. In this case report we present a 75 year old female on follow up for c-ANCA positive GPA admitted with a relapse with predominantly pulmonary involvement and concurrent community acquired pneumonia with severe ARDS who improved on treatment with immunosuppressive therapy, rituximab and plasmapheresis and antibiotics but eventually succumbed due to septic shock

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