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Successful Treatment of New Onset Granulomatosis with Polyangiitis (GPA) With a Combination of Intravenous Immunoglobulin (IVIG) and Plasma Exchange during Sepsis: A Case Report

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ABSTRACT

Granulomatosis with polyangiitis (GPA) is a life-threatening disease with wide spread systemic involvement. Commonly glucocorticoids and immunosuppressant are used to treat this disease. We herein report the case of a 32-year-old gentleman with vasculetic skin lesions and Fournier's gangrene of perianal region with severe sepsis required extensive debridement and antibiotics, developed diffuse alveolar hemorrhage and he required ventilatory support. After a combination of steroid, plasma exchange and intravenous immunoglobulin (IVIG), had complete recovery. He was discharged on Mycophenolate and tapering doses of steroids. In conclusion, plasma exchange with glucocorticoid therapy and IVIG may be effective in treating severe ANCA-associated vasculitis with sepsis.

Keywords: ANCA associated vasculitis, Granulomatosis polyangitis, Sepsis, Diffuse alveolar haemorrhage, Intravenous immunoglobulins

INTRODUCTION

Antineutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV) is a group of diseases (granulomatosis with polyangiitis, eosinophilic granulomatosis with polyangiitis and microscopicpolyangiitis), are characterized by inflammation and destruction of small and medium-sized blood vessels with presence of circulating ANCA (1). Cytoplasmic staining pattern is characteristic of either granulomatosis with polyangiitis (GPA) or microscopic polyangiitis(MPA) (2). Multisystem involvement is common with high mortality rate. We described a case with severe AAV and sepsis that had complete recoverey with plasma exchange, steroids, IVIG in addition to antibiotic and debridement.

Case report

A 32 years old physically challenged (deaf and dumb by birth) gentleman, presented to the clinic with polyarthralgia, purpuric rashes of extremities and mouth ulcers (negative ANCA and ANA reports) responded well to short course of oral steroid . 6 weeks later attended to the emergency department with fever , relapsing of purpuric rash over limbs, scrotal swelling with foul smelling dicharge from a necrotic wound.

His routine blood test including total leucocytic count (TLC), differncial leucocytic count (DLC), Tyroid function test including (TSH, free T3 and T4), Platelet count, coagulation profile, Liver function test

(LFT), were normal. Sputum culture for acid fast bacilli (AFB) test was negative. Renal functions were mildly impaired at the time of admission. S. creatinine was 139µmol/L. Urine analysis showed albumin traces,WBC 8/µL, RBC 12/µL ,4 epithelial cells. Chest X-ray(CXR) performed on admission was normal.Swab was taken from scrotal wound and sent for culture and sensitivity which revealed K. pneumoniae , P.auerogenosa and heavy growth of E.coli. Blood culture was negative.CRP level on admission was high (378 mg/L).His vasculitis work up repeated and found to be positive for anti-Proteinase 3 (PR3) ANCA in high titers. Rest RA factor, Anti-GBM, ANA, HIV, HBS assays were negative.

CT abdomen revealed multiple air pockets in soft tissue of perianal region extending into the scrotum suggestive of Fournier's gangrene. Pelvis MRI showed perianal branching tract with internal opening at anal canal 12 o'clock position, about 2.5mm above the anal verge. Echocardiography was normal.

With above clinical findings and investigation results, patient was diagnosed as severe GPA with Fournier's gangrene of perianal region with severe sepsis.

He was treated with IV antibiotics & extensive debridement done by surgeon. His sepsis was improving and CRP levels came down. On 5th day of admission patient developed dyspnoea and cough. Repeat CXR revealed ground glass opacities in right lung base which was suggestive of Diffuse Alveolar Hemorrhage (DAH). CT imaging (image1) and Bronchoscopy (image 2) confirmed the DAH. His kidney functions detoriate further (estimated glomerular filtration rate 35.38 ml/min/1.73m2, S. creatinine increased to 177µmol/L) and hematuria increased without urinary casts. Patient required ventilatory suport and induction of remission started with Plasma Exchange , IV methyl Prednisolone and IVIG followed by maintenance which consisted Mycophenolate Mofetil and oral steroids in tapering doses. Patient had excellent recovery (estimated glomerular filtration rate > 90 ml/min/1.73m2) and complete resolution of lung pathology (image 1b) as well skin lesions.

Discussion

We have presented a case of a patient who's presented initially with musculoskeletal features and negative anti-PR3. He had good response with short course of oral steroids. Again after 4 months, he presented with features of sepsis due to scrotal gangrene and oral ulcers as a initial presentation (which again was non specific to diagnose GPA), which resulted in a delay in diagnosis and due to sepsis it was difficult to treat him with imunosupressants. Later after admission patient developed acute kidney injury and DAH. His anti-PR3 ANCA came out to be high this time which helped us to reach the correct diagnosis and treat successfully.

Diagnosis of systemic vasculitides has been challenging as diagnostic criteria are constantly evolving and pathogenesis is not well understood. Factors including patient age, gender, ethnicity, affected vessel size, and the presence of granulomatous inflammation and the presence of specific antibodies must be considered as many disease processes may overlap (3). In 1990 the American College of Rheumatology formulated a definition of GPA for nomenclature purposes to include necrotizing granulomatous inflammation within the upper or lower respiratory tract, vasculitis within small to medium sized blood vessels, and commonly associated simultaneous glomerulonephritis (Image 3) (4). In 2012 the Chapel Hill Consensus Conference expanded on this definition to include ANCA antibodies (5). To date, no diagnostic criteria for GPA exists (6). The development of clinical guidelines is important as our patient's anti-PR3 was initially negative and universal clinical guidelines may prevent missed opportunities for diagnosis in the future.

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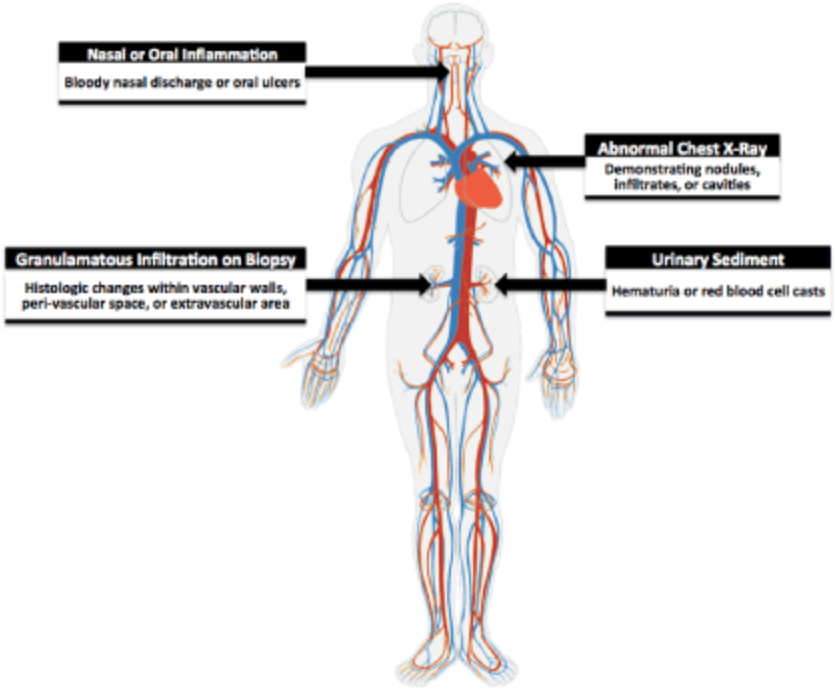

Image 3: Criteria for GPA. The American College of Rheumatology classifies a patient to have GPA if they present with at least 2 of these 4 symptoms (sensitivity is 88.2% and specificity 92.0

The specificity and sensitivity of serologic testing in GPA is directly related to the extent and activity of the disease (7). In the generalized form involving several organ systems, the specificity of the c-ANCA test is over 90% (8,9). Amongst these patients, over 90% will be positive for anti-PR3 ANCA. In limited disease with only pulmonary or renal involvement, up to 40% of ANCA may be negative (10).

Clinical features of GPA categorized by a combination of upper airway disease, lower airway disease, and glomerulonephritis (11) Patients typically present in the 4th or 5th decade of life with various nonspecific symptoms including hemoptysis, stridor, and hoarseness and wheezing. Systemic symptoms such as fever, weight loss, myalgias and headache can also be present, usually for several weeks to months (12)

Generalized or severe GPA if untreated typically carries a poor prognosis, with up to 90% of patients dying within 2 years, usually due to respiratory or renal failure. Non-renal GPA having a mortality rate of up to 40%. (13) Plasma exchange has been considered in patients with rapidly progressive renal disease (serum creatinine level >5.65mg/dL) in order to preserve renal function. (14) The European League Against Rheumatism (EULAR) 2015 recommendations that Plasma exchange should be considered for patients with AAV and a serum creatine level of ≥500 mmol/L (5.7 mg/dL). (15) Additionally, plasma exchange, along with aggressive immunotherapy, may be helpful in DAH. (16) We added Intravenous immunoglobulin (IVIG) to plasma exchange as our patient was having severe sepsis and large wound after debridement which creats difficulty in using immunosupressants. Though it was reported previously that immunosupressants gave good response as adjuvant therapy.(17)

Conclusion

Our case highlights the difficulties in diagnosing due to vague presentation of symptoms, negative anti-PR3 ANCA initially and treating this disease as our patient was having severe sepsis. It is therefore important for clinicians to be aware of these variants in order to prevent delay in accurate diagnosis and poor patient outcomes. When the diagnosis of GPA and sepsis was made, patient started with plasma exchange and IVIG in addition to steroids and antibiotics. Identifying the disease early and intensive management is life saving in AAV. IVIG can be used in treating severe vascultitis with sepsis.

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Images:

CT Scan- image 1a.

CT scan report showing right lower lung consolidation with ground glass opacity sparing the periphery of lung

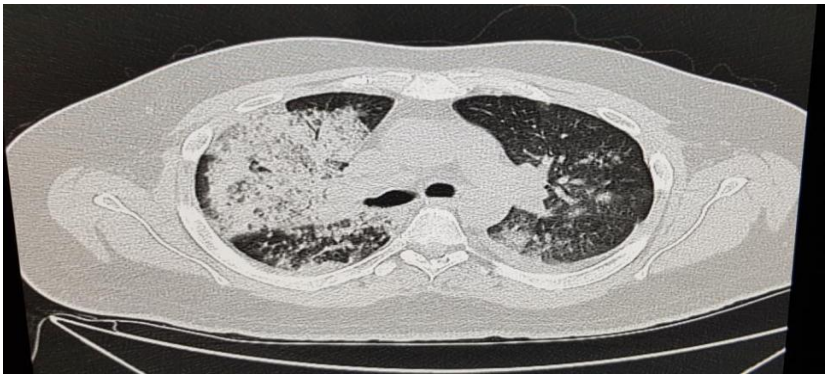


Image 1b:

CT scan report showing complete resolution of opacities in right lung (Normal report)

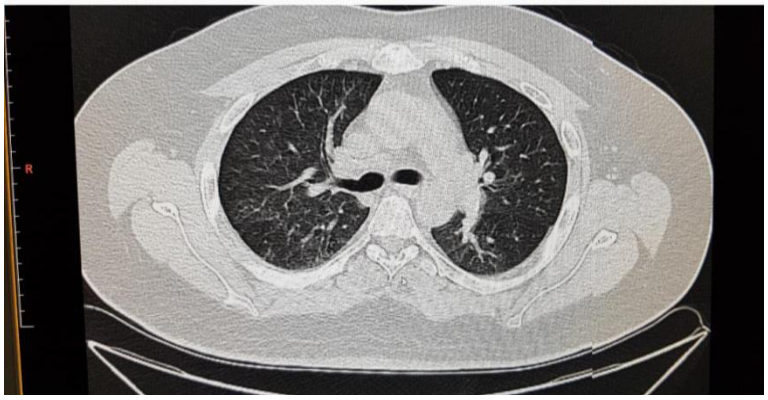
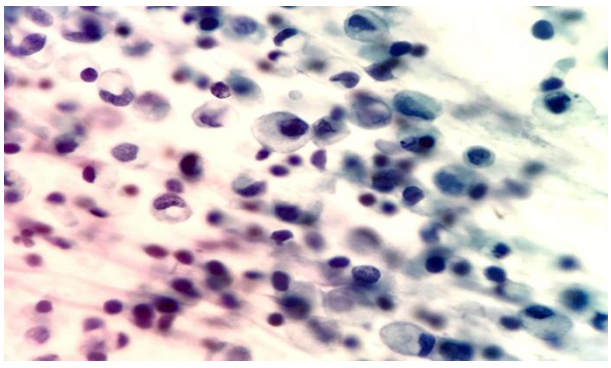


Image 2:

Broncho alveolar levage (BAL) showing haemosiderrin laden macrophages.



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