Wegener's Granulomatosis with Fungal Lung Infection in a Child

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Introduction

Wegener's granulomatosis, characterized by multi-system granulomatous inflammation and necrotising vasculitis, is rarely seen in children and, to date, there are less than 100 cases reported in the world literature in children under 15 years of age. No published Indian report is available. We report a case of a 13-year old boy who presented with typical features, had a rapid course and succumbed due to massive pulmonary hemorrhage.

Case Report

A 13 year old boy, presented with a history of fever, joint pains, cough and redness of eyes of 1 week duration. History revealed repeated episodes of epistaxis for the past 8 months diagnosed by ENT specialist as chronic vestibulitis with a non-healing ulcer in the right vestibule. The child was also being managed in the dental OPD for bleeding gums for the past 1 month, which was diagnosed as gingivitis. He had an episode of blood in stool 2 weeks before admission. He had been treated for primary complex in early childhood and there was a recent history of contact with pulmonary tuberculosis in the family.

Examination revealed a moderately built child weighing 40 kg with positive findings of fever, pallor, conjunctival congestion, nasal crusting of right nostril, bleeding gums, effusion of right knee and decreased air entry with crepitations in right axilla and infra-scapular areas. He was started on cefotaxime and amikacin for pneumonia and investigated for a bleeding diathesis or connective tissue disorder.

Initial investigations revealed a Hb of 11 gm%. TLC 9500/cumm ($P_{60}L_{34}E_3M_3$), ESR 50mm fall in first hour, C-reactive protein +ve, mild proteinuria with 3-4 RBCs/hpf on urine examination, platelet count 2.4 lacs/cumm, coagulation profile (BT, CT, PT, PTT) normal, peripheral blood smear normal, Rheumatoid Factor +ve, ANA -ve, ASO titre normal, Widal -

ve, Mantox-ve, ultrasound of abdomen normal, blood and urine cultures sterile. Chest radiograph showed bilateral streaky opacities both upper zones and right lower zone with right hilar prominence.

Over the next 3-4 days he deteriorated with increasing epistaxis, breathlessness and streaky hemoptysis. Petechial hemorrhages appeared on the hard palate and he had swelling and tenderness of both ankle joints, though knee joint swelling had subsided. He also developed a macular-papular rash over both feet, which later turned into a blotchy, hemorrhagic rash suggestive of a vasculitis (Fig 1). Investigations at this stage showed a Hb of 9.8gm%, TLC 8000/cumm ($P_{60}L_{24}E_{10}M_2$), platelet count 5.3 lacs/cumm, sputum for AFB -ve, moderate proteinuria with 10-15 RBCs/hpf and RBC casts in urine. Blood urea was 27 mg% and serum creatinine 0.8 mg%. Chest X-ray showed progress of lesions to involve all areas of the lung bilaterally with areas of breakdown in right lower zone. CT scan chest showed patchy consolidation with multiple cavitations and pulmonary hemorrhage both lungs, more in the right base (Fig. 2). Ultrasound abdomen showed a loss of cortico-medullary differentiation both kidneys. Sputum culture grew *Candida albicans*. PCR for tuberculosis (sputum) and tubercular IgM were negative. In view of the involvement of upper and lower respiratory tracts and kidneys with features suggestive of a vasculitis, Wegener's granulomatosis was suspected and anti neutrophil cytoplasmic antibodies (ANCA) studies and skin biopsy were sent. Nasal biopsy was not attempted because of poor general condition and persistent bleeding from the nose. He was also started on Liposomal Amphotericin B. Meanwhile, he developed progressive respiratory distress and required oxygen and blood transfusion. ANCA report showed normal p-ANCA but c-ANCA levels of 1:100 (strongly positive) on immunofluorescence. A diagnosis of Wegener's granulomatosis was made and he was immediately put on high dose prednisolone along with cyclophosphamide. However, within 48 hours he had an episode of massive

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Fig. 1 : Vasculitic rash seen on lower limbs

hemoptysis and went into acute respiratory failure. He required positive pressure ventilation with very high settings on IMV (MAP 20) to maintain adequate oxygenation and succumbed to a pneumo-mediastinum after 48 hours of ventilation. Duration of hospitalization was 2 weeks. Skin biopsy report received post-mortem showed a lymphocytic vasculitis. Post-mortem was refused by the relatives.

Discussion

Wegener's granulomatosis is a rare form of autoimmune vasculitis of the small and medium-sized blood vessels. It is characterized by localized granulomatous inflammation of the nasal mucosa and lung tissue, and usually progresses into generalized necrotizing granulomatous inflammation of the blood vessels of other systems specially kidney, eyes and skin. In 1931, Heinz Klinger reported the first two patients and five years later Friederick Wegener described the syndrome in three more patients. Since then, there have been a consistent number of reports in the Western literature, though less than 15% of cases are seen in children below 18 years of age [1]. It usually affects young and middle-aged individuals though it can occur at any age, the youngest age of onset reported being 2 months [2]. An increasing number of cases are being reported from India, the youngest reported so far being 16 years of age. Here the disease may initially be misdiagnosed as tuberculosis [3].

Symptoms of Wegener's granulomatosis include fatigue, weight loss, fever, shortness of breath, cough with hemoptysis, joint pains, para-nasal sinus inflammation, nasal ulcerations or bloody nasal discharge, eye involvement, neuropathy, skin nodules or ulcers, pleuritis and frank pulmonary hemorrhage [4].

Definite criteria for the diagnosis have been laid down by the American College of Rheumatology in 1990 [5]. Abnormal urinary sediment (red cell casts or greater than 5 red blood cells per high power field), abnormal findings on chest radiograph (nodules, cavities or fixed

Fig. 2 : CT scan of chest showing nodular lesions with breakdown and hemorrhage

infiltrates), oral ulcers or nasal discharge, and granulomatous inflammation on biopsy are taken as the diagnostic criteria. The presence of 2 or more of these 4 criteria is recommended for the purpose of classification and is associated with a sensitivity of 88.2% and a specificity of 92.0%. Our case fulfilled 3 of these criteria. In addition, c-ANCA was strongly positive. ANCA is positive in the majority of cases of Wegener's granulomatosis, especially against proteinase 3. It may also be positive against myeloperoxidase, cathepsin G, lactoferrin, and elastase [2]. This, and the classical clinical picture of upper and lower respiratory tract disease along with kidney involvement, differentiates Wegener's from other pulmonary renal syndromes like microscopic polyangitis, Goodpasture disease, systemic lupus erythematosus, Henoch-

Schönlein purpura and hemolytic-uremic syndrome [6]. The current diagnosis of Wegener's granulomatosis depends on one or more of the following criteria: a positive c-ANCA test, the presence of granulomatous, necrotizing vasculitis, and a clinical course typical of the disease [2]. A negative biopsy does not exclude the diagnosis [7,9]. In our case, only a skin biopsy was possible due to the critical condition of the child, which showed definitive evidence of vasculitis.

Childhood-onset is complicated five times more often by subglottic stenosis and twice as often by nasal deformity [4]. We had a secondary fungal infection as a complication. ANCA antibodies have been used in adults to determine activity and progress of the disease [2]. A disease-specific activity index has recently been suggested to determine progress and response to treatment [8]. The prognosis has dramatically improved from the 18%, 5-month survival rate before the era of immunosuppressive therapy to the current remission rate

of over 75% with a regimen of cyclophosphamide and glucocorticoids [1]. A period of 3-12 months usually passes from the time of the first symptom to the diagnosis in the majority of patients and a significant rate of relapse and disease or treatment-related morbidity still occur [9]. In conclusion, a high index of suspicion and careful investigation of all children with persistent nasal lesions is recommended to arrive at an early diagnosis so that treatment can be started promptly and effectively.

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