GRANULOMATOSIS WITH POLYANGIITIS: A RARE DIFFERENTIAL OF NON-RESOLVING CONSOLIDATION

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PRESENTATION OF CASE

Granulomatosis with polyangiitis (GPA), formerly known as Wegener's granulomatosis, is a rare form of vasculitis. It targets small-sized blood vessels and causes inflammation and damage to blood vessels most commonly in the nose, sinuses, ears, lungs and kidneys. It is an autoimmune disorder with unknown cause. It may present with upper and lower respiratory lesions, renal failure, cranial neuropathies, ocular inflammation, and cutaneous vasculitis. Patients with pulmonary affection present with respiratory signs and symptoms, including cough, haemoptysis, and dyspnoea. Haemorrhage, cavitary lesions in the lungs, and pulmonary fibrosis are the customary lung manifestations. We hereby narrate a rare case of a patient presenting to us with respiratory symptoms and a chest radiograph suggestive of non-resolving consolidation.

A 59 years old man was referred to our department for symptoms of cough with mucoid expectoration associated with streaky haemoptysis, intermittent fever and exertional dyspnoea of Modified Medical Research Council (MMRC) grade 1 since 6 months. He was a non-smoker with no past history of Pulmonary Tuberculosis (PTB). He had comorbidity in form of Diabetes mellitus (DM). Before visiting our hospital, he was evaluated with a chest radiograph (CXR) suggestive of left lower zone cavity with consolidation. He was diagnosed as community acquired pneumonia (CAP) and was treated with oral and injectable antibiotics with no relief of symptoms and hence had followed up to our side. His general examination was normal, on Respiratory System examination breath sounds were reduced on right lower chest.

The diagnosis was clinched on transbronchial lung biopsy histopathological examination showing a necrotising granulomatous inflammation with vasculitis.

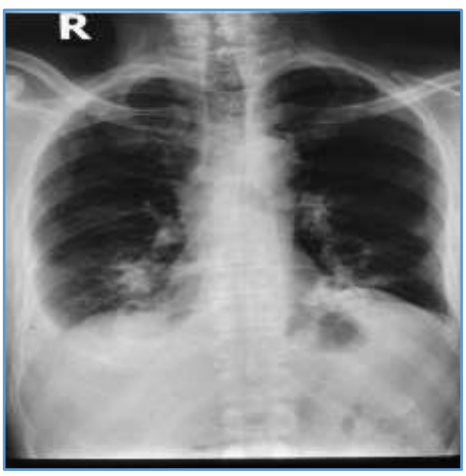

Figure 1. CXR Suggestive of Left Lower Zone Cavity with Consolidation with Right Sided Pleural Effusion

Figure 2. High Resolution Computed Tomography (HRCT) of Thorax showing Multiple Nodules with Cavitation in Lung Parenchyma with, Mediastinal and Left Hilar Lymphadenopathy and Mild Right Sided Pleural Effusion

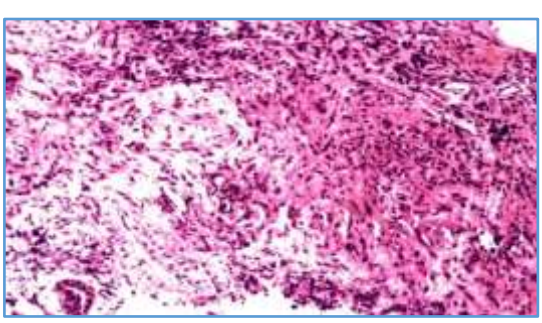

Figure 3. Photomicrographs of histopathological examination of TBLB tissue demonstrating necrotising granulomatous inflammation with Polyangiitis.

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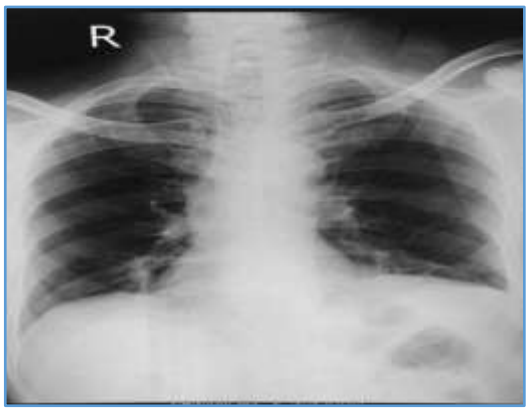

Figure 4. CXR Suggestive of Resolution in Consolidation and Pleural Effusion after 2 Months of Therapy

CLINICAL DIAGNOSIS

Granulomatosis with Polyangiitis (GPA)

DIFFERENTIAL DIAGNOSIS

- Tuberculosis
- Malignancy

PATHOLOGICAL DISCUSSION

Haematological and biochemical investigations were within normal limits. His repeat CXR was suggestive of right lower zone consolidation with right sided pleural effusion (figure 1). A diagnostic thoracocentesis was done. Pleural fluid cytobiochemical analysis showed an exudative effusion with neutrophilic predominance with red blood cells and a normal adenosine deaminase (ADA) level. Pleural fluid and Sputum cartridge based nucleic acid amplification test (CBNAAT) did not detect mycobacterium tuberculosis (MTB). Pleural fluid and sputum were also negative for acid fast bacilli (AFB) culture. Electrocardiogram (ECG) was within normal limits. Patient was evaluated with a Contrast Enhanced Computed Tomography (CECT) and a High-Resolution Computed Tomography (HRCT) of thorax showing multiple nodules with cavitation in lung parenchyma with largest nodule approximately 2.7 cms. in diameter, mediastinal and left hilar lymphadenopathy and mild right sided pleural effusion (Figure 2).

The patient also underwent a fiberoptic bronchoscopy (FOB) along with a transbronchial lung biopsy (TBLB). FOB revealed an inflamed bronchial mucosa without any evident ulceration or endobronchial lesion. The histopathological examination of TBLB tissue revealed a necrotising granulomatous inflammation with polyangiitis which gave the diagnosis of a vasculitis (Figure 3). Hence, he was investigated for presence of Rheumatoid Arthritis (RA) Factor which was negative, Antinuclear Antibodies (ANA) test was also Negative. However cytoplasmic antineutrophil cytoplasmic antibodies (C-ANCA) was positive. This clinched our diagnosis of GPA. He was also screened for renal involvement. Urine examination showed pus cells. Ultrasonography of kidney ureter and bladder was within normal limits. Patient was started on oral corticosteroids tablet prednisolone 1 mg/kg weight in tapering doses and Cyclophosphamide 2 mg/kg weight. The patient was followed up after 2 months of therapy. He showed marked clinical improvement with radiological resolution (Figure 4).

Granulomatosis with Polyangiitis (GPA) earlier known as Wegener's Granulomatosis is an autoimmune inflammatory disease involving the small and medium sized blood vessels of the body. The incidence of the disease is noted to be rising and the prevalence previously evaluated as 3 cases per 100,000 has now been noted to be as high as 15.7 cases/100,000 patients.[1] Autoimmune vasculitis syndrome is an umbrella term which includes entities related with the antineutrophilic cytoplasmic antibody (ANCA)[2] namely Eosinophilia Granulomatosis with Polyangiitis (EGPA), polyarteritis nodosa, and microscopic polyangiitis. The American College of Rheumatology (ACR) classification criteria for diagnosis of GPA include the following: (1) abnormal urinary sediment (red cell casts or greater than 5 red blood cells per high power field), (2) abnormal findings on chest radiograph (CXR) (nodules, cavities, or fixed infiltrates), (3) oral ulcers or nasal discharge, and (4) granulomatous inflammation on biopsy. The presence of 2 or more of these 4 criteria was associated with a sensitivity of 88.2% and a specificity of 92.0%[3] in various studies. The disease commonly affects the pulmonary system with a predominant lung parenchymal involvement seen in around 85-92% patients. Pleural involvement in the Wegener's granulomatosis patients is relatively rare and occurs in 10% of patients. We herein report an atypical presentation of this disease in form of non-resolving consolidation with pleural effusion.

GPA is a peculiar clinicopathological entity characterised by granulomatous vasculitis of multiple organ systems.[4] It tends to be largely underdiagnosed and underreported owing to its rare occurrence and a significant amount of overlap with other commonly encountered pulmonary conditions like infections and malignancies. This holds true particularly in a developing country like India where tuberculosis is endemic.[5] It exhibits ubiquity as far as organ involvement is concerned however the pulmonary system and the renal system are its most common soft targets. Renal affliction occurs in form of glomerulonephritis associated haematuria and proteinuria and may lead to renal failure eventually. Pulmonary involvement typically involves all the three components namely the lung parenchyma, airways, and pleura. However, the airways and pleura are less commonly involved as compared to the lung parenchyma. Lung parenchymal involvement customarily occurs in form of cavitary nodules or masses.

Our patient showed dual involvement in form of lung consolidation and pleural effusion. The mean age of presentation is fifth to sixth decade with no sex predilection.[6] Our patient also belonged to the same age group. Radiology has a pivotal role in the diagnosis. HRCT is more sensitive than a plain CXR and can demonstrate a constellation of findings in form of nodules, ground glass opacities, interstitial septal thickening, cavitation or peri bronchial cuffing.[7] Nodules are usually multiple, bilateral and of varying sizes, most commonly measuring between 2 and 4

cm.[7] They may occur in a centrilobular distribution, mimicking tuberculosis, hypersensitivity pneumonitis, or an acute viral, bacterial, or fungal pneumonia. Approximately 25% of nodules more than 2 cm are cavitary.[8,9] Haemorrhage may occur around nodules and manifests on HRCT as ground-glass opacity surrounding the consolidated nodule, referred to as the halo sign. The CT findings may be mistaken for metastases, lung abscesses, or septic infarcts however in appropriate clinical context may serve as valuable markers for the disease.

Bronchoscopy plays a role in assessment of the airway involvement in the disease which occurs in approximately 15 to 55% of patients.[10] The bronchoscopy findings may be evident in form of bronchial stenosis, ulceration, pseudotumor, inflammatory lesions, erythema, haemorrhage or purulent secretions. Our patient manifested erythema of the bronchial tree. In our patient we could attain a final diagnosis on histological examination of our TBLB tissue which was very noteworthy. This is a rare occurrence in this entity and usually more invasive forms of biopsy like a CT guided, thoracoscopic or lung open lung biopsy is needed. Aggressive immunosuppressive therapy for Wegener's granulomatosis is mandatory for achieving remission of the disease. Combination therapy containing glucocorticoids and cyclophosphamide is the first line regimen and exhibits remission within 6 months in up to 90% of cases.[11] Single drug therapy with glucocorticoids is associated with a lower rate of remission (56% vs. 85%) and higher rate of relapse compared with combination therapy.[12] Therapy is usually given in form of prednisone initiated at 1 mg/kg daily for 1 to 2 months followed by tapering doses along with Cyclophosphamide 2 mg/kg daily for at least 6 months. Our patient was also treated similarly. After achieving remission, maintenance immunosuppression with less toxic drugs (i.e. azathioprine or methotrexate) is recommended to prevent relapse. Our patient was an example of a limited form of the disease since clinical and radiological manifestations revealed no affected organs other than the respiratory system.

FINAL DIAGNOSIS

Lung Nodules with Cavitation and Pleural Effusion due to Granulomatosis with Polyangiitis (Wegener's Granulomatosis).

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