CASE REPORT

MESALAZINE-INDUCED EOSINOPHILIC VARIANT OF WEGENER'S GRANULOMATOSIS IN AN ULCERATIVE COLITIS PATIENT

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A 24-year-old woman presented with two weeks history of progressive shortness of breath associated with sharp chest pain. She had been on mesalazine for two years for Ulcerative Colitis. Chest X-ray showed bilateral pulmonary infiltrates with left sided pleural effusion. Blood investigations revealed, positive pANCA, negative cANCA and peripheral eosinophillia. Video assisted thoracoscopic lung biopsy specimen was consistent with eosinophillic variant of Wegener's granulomatosis. She responded to combination of withdrawal of mesalazine and high dose steroids. To our knowledge this is the first reported case of mesalazine induced eosinophilic variant of Wegener's granulomatosis.

Keywords: Mesalazine, Pulmonary, Infiltrate, Eosinophillia, Inflammatory Bowel Disease, Ulcerative Colitis

INTRODUCTION

Inflammatory bowel disease (IBD) is associated with variety of respiratory manifestations such as chronic bronchitis, chronic bronchiolitis, bronchiectasis, bronchiolitis oblitrans, tracheal obstruction, pulmonary infiltrates and serositis leading to effusion.[1–3]

Drugs used to treat IBD are also known to be associated with pulmonary injury and toxicity which could be irreversible. We report a case of mesalazine toxicity.[2]

CASE REPORT

A 24-year-old woman was admitted to hospital with two weeks history of progressive shortness of breath associated with sharp chest pain, aggravated on deep inspiration. She had eight years history of Ulcerative Colitis (UC) which was initially managed with azathioprine and for the last two years her disease has been controlled with mesalazine 800 mg twice a day. Ulcerative colitis had been controlled on above regime.

On examination, she was short of breath at rest with respiratory rate of 26 per minute. Her pulse rate was 126 per minute, saturation 97% on air, temperature 37.4 °C and blood pressure 125/67 mmHg. Chest examination showed signs of pleural effusion on left base. Routine blood investigations showed raised total white blood cell count 15.400/mm^3, peripheral eosinophilia 1.1×10^9/litre, C-reactive protein (87 mg/L) and ESR (67 mm/1^{st} hr). Liver and kidney function test were normal. Plain chest X-ray (Figure-1) confirmed left sided pleural effusion with opacity in left upper zone. The patient clinically improved as well as CRP and WBC came down.

Repeat plain chest X-ray showed new opacity in right upper lobe with persistent left upper lobe opacity but effusion on the left side completely resolved.

Lung function test revealed a forced expiratory volume in one second (FEV_1) of 2.11 litres (67% of predicted) forced vital capacity (FVC) 2.37 litres (66% of predicted). FEV_1/FVC ratio 89%. Diffusion Capacity ($D_{L_{CO}}$) 5.5 mmol/kpa.min (60% of predicted). Serum perinuclear, antinuclear cytoplasmic antibody positive (pANCA 1:80) and cANCA were negative. Repeated blood and sputum cultures were negative for bacterial growth including mycobacterium. Computerised scan of chest showed diffuse shadowing in left upper lobe and lingual lobe. There was limited disease in right upper zone (Figure-2).

The transbronchial biopsy specimen from left upper lobe showed increased number of macrophages in air spaces and some interstitial thickening but no evidence of Wegener's Granulomatosis (WG) or vasculitis. Her video assisted thoracoscopic lung biopsy showed nodules of extensive nectrotic lung tissue and multiple areas of abscess formation with significant number of eosinophilic and multinucleated giant cells. In addition there were granulomatous and necrotising vasculitis with obliterated vessels (Figure-3).

This appearance is consistent with eosinophilic variant of Wegener's granulomatosis secondary to mesalazine. Therefore mesalazine was stopped and she was started on prednisolone 40 mg/day. She was seen in out patients eight weeks later, her symptoms resolved, eosinophil count decreased, pANCA level became normal and repeat chest X-ray showed no infiltrates.

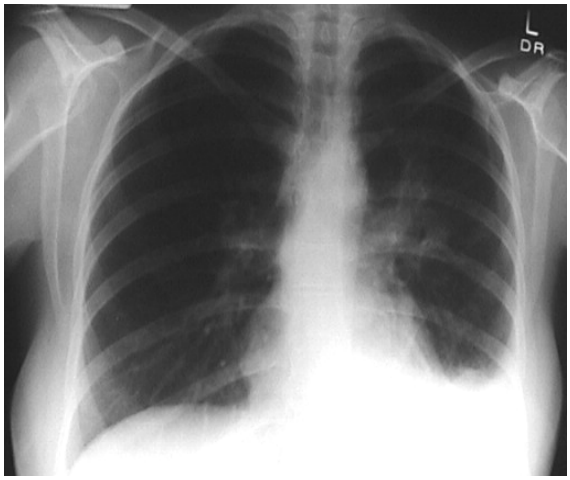

Figure-1: Plain Chest X-ray

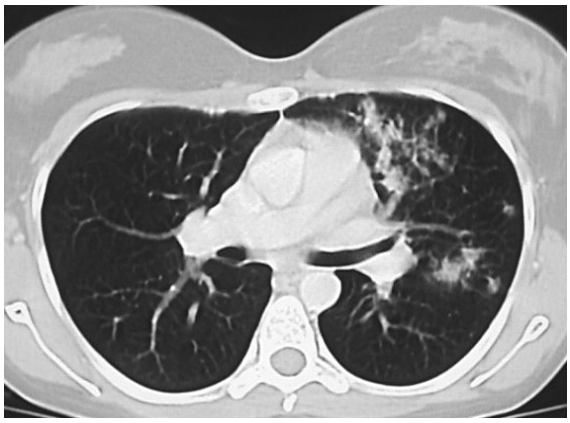

Figure-2: Computerised Scan of Chest

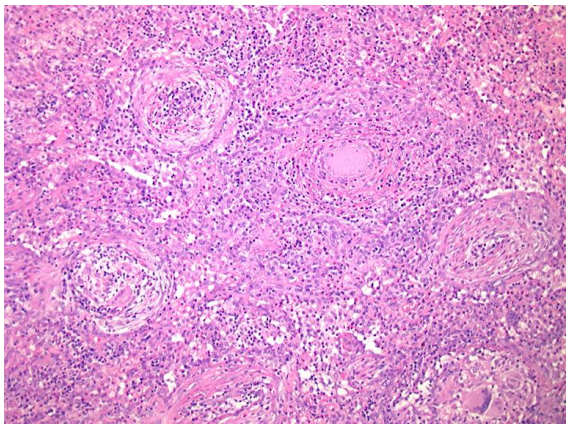

Figure-3: Eosinophilic infiltration and multinucleated giant cells with necrotising vasculitis seen on biopsy

DISCUSSION

Respiratory involvement in inflammatory bowel disease has been well described in literature.[1] The pulmonary involvement includes chronic bronchitis, bronchiectasis, chronic bronchiolitis, bronchiolitis obliterans with organizing pneumonia, tracheal obstruction, pulmonary infiltrates, necrotic parenchymal nodules and serositis leading to effusion.[2,3] Drug related pulmonary involvement can be difficult to differentiate from pulmonary involvement due to IBD itself.[2]

Mesalazine is associated with variety of pulmonary injury/toxicity, although they are rare (0.01%) but can cause irreversible lung damage. In literature pulmonary infiltrates and eosinophilic pneumonia are most commonly reported side effect due to mesalazine.[5,6] The pathogenesis of mesalazine induced lung injury is not clearly known, although an immunologic mechanism is most likely. Direct drug toxicity is other possibility. Time to onset of symptoms after start of mesalazine therapy varies widely from a few days to years. Lung toxicity seems to be independent of mesalazine dose. Patients often present with progressive dyspnoea associated with non productive cough and fever. Chest X-ray abnormalities and peripheral blood eosinophilia are common finding on investigations.[7]

Our patient had history of Ulcerative Colitis for more than seven years and she had been taking mesalazine for two year. Her UC had been inactive for long time. She presented with signs and symptoms of pneumonia which failed to respond to antibiotics. Her p-ANC was positive and c-ANC was negative. Myeloperoxidase and proteinase antibody were both negative. In Wegener's granulomatosis 85–95% cases have positive cANCA with positive myeloperoxidase antibody. pANCA is positive only in 5–15% cases of WG. Video assisted thoracoscopic lung biopsy showed significant eosinophilia and nodular granulomatosis necrotising vasculitis. This appearance is compatible with diagnosis of eosinophilic variant of Wegner's granulomatosis. Mesalazine has been reported to cause pulmonary eosinophilia, eosinophilic pneumonia and BOOP.[8,10] We could not find any case report of mesalazine induced eosinophilic variant of Wagner's granulomatosis on literature search. Our case showed an excellent response to withdrawal of mesalazine and introduction of steroid therapy. Radiological appearance returned to normal. Clinically she is not breathless and systemically she is feeling well in herself which can be explained as a positive response to our treatment.

In view of widespread eosinophilc infilterate and necrotising vasculitis, her serology and excellent response to withdrawl of mesalazine with steroid therapy, it is highly likely that aetiological factor was mesalazine. We believe that this is the first report of mesalazine induced eosinophilc variant of Wagner's granulomatosis.

We are planning to gradually reduce the steroids. Absence of recurrence of disease after stopping steroids will be another evidence to prove our diagnosis.

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