Diffuse alveolar hemorrhage in a patient of rheumatoid arthritis

Sir,

Rheumatoid arthritis (RA) is a systemic disease with frequent lung involvement ranging from an asymptomatic involvement to being a major cause of mortality. Its myriad presentations range from benign pleural effusions to the more distressing interstitial lung diseases.[1] Diffuse alveolar hemorrhage (DAH) associated with RA is a rare entity and poses a diagnostic dilemma to the clinician.

A 45-year-old female presented with progressive complaints of productive cough and dyspnea over 4-5 months. There was no associated fever, significant weight loss or chest pain. She also had recurrent frank episodes of hemoptysis. There was a preceding history of arthralgias involving ankles, wrist and hands over past 1-2 years along with significant morning stiffness for which patient was not on any long-standing treatment.

Clinically the patient had pallor and no other significant finding on general examination. Joint examination revealed a tender joint score of 14 with no joint deformity. Respiratory examination revealed a grade 4 dyspnea (modified medical research council scale), respiratory rate of 30/minute along with use of accessory respiratory muscles and saturation of 78% on room air. On chest auscultation there were inspiratory crepitations along with normal vesicular breath sounds.

Investigations revealed anemia (hemoglobin = 6 gm/dl) a mildly elevated total leukocyte count (TLC = 11000/mm^3) and elevated erythrocyte sedimentation rate (60 mm/hr). Liver and renal function tests were within normal limits as was the urinary routine/microscopy. Coagulation profile and platelet counts were within normal limits. Chest X-ray (CXR) showed bilateral infiltrates especially in middle and lower zones [Figure 1]. 2-D Echo showed a normal cardiac status. Computed tomography of thorax done revealed bilateral alveolar shadows predominantly in perihilar distribution [Figure 2]. Bronchoscopy was done and revealed a progressively bloody lavage and bronchoalveolar lavage (BAL) for AFB smear, fungal smear and bacterial culture was negative. Patient was screened for RA factor in view of significant history of arthralgias with morning stiffness and the titer was markedly elevated (70 IU). Anti nuclear and antineutrophil cytoplasmic antibodies were within normal limits. Radiographs of hands along with wrists demonstrated synovial thickening with no bony erosions.

On the basis of triad of hypoxemia, hemoptysis and bilateral infiltrates on CXR and progressively hemorrhagic

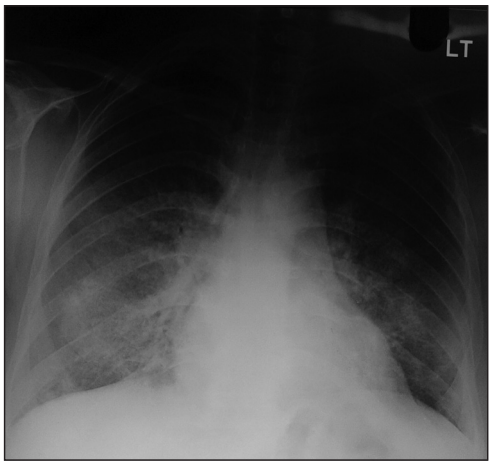

Figure 1: CXR showing middle and lower zone infiltrates

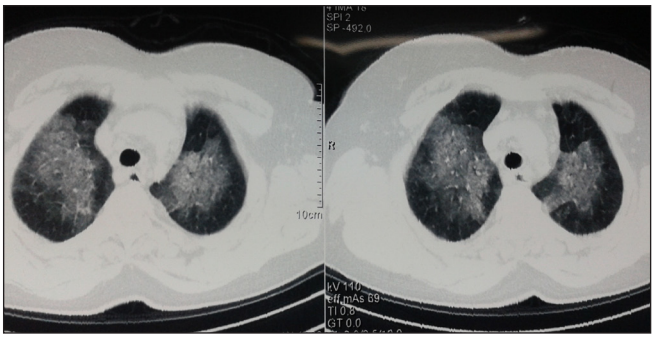

Figure 2: Computed tomography of chest showing bilateral infiltrates predominantly perihilar distribution

BAL she was diagnosed as a case of alveolar hemorrhage syndrome. In view of symmetrical joint involvement, significant morning stiffness, markedly positive RA factor and prolonged duration (EULAR classification score of >6) she was diagnosed as a case of RA-associated DAH.

Patient was started on intravenous corticosteroids (i.v. methylprednisolone 125 mg 6 hourly) along with broad spectrum antibiotics and responded dramatically. By day 2 her oxygen requirement began to decrease and was weaned off oxygen by day 7. She experienced no further episodes of hemoptysis after third day. She remained well controlled on maintenance dose of corticosteroids at end of 3 months.

Diffuse alveolar hemorrhage is one of the rarer presentations of RA and as a presenting feature can pose a diagnostic challenge for the clinician. DAH can complicate a large number of clinical conditions. It can occur in association with vasculitis or capillaritis as in Wegener's granulomatosis, Goodpasture syndrome,

collagen vascular disease, microscopic polyangiitis and isolated pauci-immune pulmonary capillaritis, bland hemorrhages as in patients with mitral valve disease, excessive anticoagulation, due to drugs and toxins or with other patterns as in diffuse alveolar damage.[2] Overall vasculitis (Wegener's or microscopic polyangitis) is believed to be the most common cause of DAH. Among connective tissue disorders DAH has been reported in systemic lupus erythematosis,[3] Sjogren[4] and RA.[5] DAH has also been rarely reported with drugs used for RA treatment like etanercept[6] and also due to strongyloides hyperinfection in RA patient on corticosteroids. Other infective causes of DAH include mycoplasma infection, Legionnaire's disease, varicella zoster pneumonitis and invasive aspergillosis. Capillaritis limited to the alveolar wall is observed in majority of patients with RA who have acute AH.[7]

A classic triad of hemoptysis, acute fall in hemoglobin and new infiltrates on CXR is usually present in DAH though hemoptysis may not be present in 1/3 cases. Chest radiographs may show nonspecific patchy or diffuse, bilateral alveolar infiltrates. Bilateral pulmonary alveolar infiltrates that are usually perihilar or basilar with sparing of apices is classically seen in DAH especially in acute cases. It often mimics severe pneumonia or ARDS. Recurrent episodes of hemorrhage may also cause reticular interstitial opacities and pulmonary fibrosis, usually with minimal (if any) honeycombing.

Diagnosing DAH first requires confirmation of alveolar hemorrhage and then a search for an underlying etiology. Bronchoscopy with progressively bloody BAL and presence of siderophages (> 20%) is considered diagnostic in such patients and also helps in ruling out infective causes. An elevated DLco is also diagnostic in such cases. If the diagnosis is not clearly made by history, physical examination and serological markers video-assisted thoracoscopic biopsy or open-lung biopsy is the procedure of choice. The yield of transbronchial lung biopsy is limited due to small sample size.

Corticosteroids and immunosuppressive agents remain the gold standard of treatment.[2] Most experts recommend intravenous methylprednisolone in high doses although lower doses seem to have similar efficacy for 4 or 5 days, followed by a gradual taper to maintenance doses of oral steroids. Immunosuppressive drugs may be used in diffuse alveolar hemorrhage, especially when the condition is severe, when first-line therapy with corticosteroids has proven ineffective or when specific underlying causes are present. Recombinant activated human factor VII and plasmapheresis have also been used in selected cases. Rituximab has also been reported to be effective when standard therapy failed in a patient with SLE.[8] Other possible management measures include supplemental oxygen, bronchodilators, reversal of any coagulopathy, intubation and mechanical ventilation.

Our case emphasizes the consideration of DAH in a patient of RA who presents with hemoptysis and/or has radiographic appearances of pulmonary edema.

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