Recurrent haemoptysis with anaemia in a 16 year old man

Q1: What is the probable diagnosis?
Diffuse alveolar haemorrhage (DAH)—secondary to idiopathic pulmonary haemosiderosis (IPH)

Q2: What are the differential diagnoses of recurrent haemoptysis?
Haemoptysis is usually caused by focal disorders of the airways or lung parenchyma. The most common causes are bronchiectasis, pneumonia, lung malignancies, and tuberculosis.1 On rare occasions, the haemoptysis may be caused by diffuse alveolar haemorrhage.1 In this patient, recurrent haemoptysis, iron deficiency anaemia, bilateral parenchymal opacities, and haemosiderin laden macrophages in bronchoalveolar lavage point towards diffuse alveolar haemorrhage.

Q3: What are the differential diagnoses of diffuse alveolar haemorrhage?
DAH is a rare syndrome that occurs mostly in association with systemic autoimmune diseases. It is commonly associated with ANCA associated vasculitides, connective tissue disorders, or asbestosis membrane antibody syndromes.1 DAH may be caused by microscopic polyangiitis or Wegener’s granulomatosis (pauci-immune pulmonary-renal vasculitis).1 These disorders have few or no immune deposits and as mentioned above are associated with ANCA (perinuclear or cytoplasmic respectively) and also have multi-system involvement. Isolated pauci-immune pulmonary capillaritis is a small vessel vasculitis of unknown aetiology with or without positive serology for P-ANCA. Upper respiratory tract involvement such as rhinitis, sinusitis, and otitis media are typical. Lung biopsy shows pulmonary capillaritis without immune complex deposits, necrotising granuloma, or asbestosis membrane antibody.2 However, in our case there was no evidence of upper respiratory tract involvement and ANCA (both P and C) was also negative. Furthermore, transbronchial lung biopsy was normal. Therefore, the above possibilities can be excluded. Alveolar haemorrhage may also be the presenting feature of systemic lupus erythematosus (SLE) in 12% of cases.3 It is more commonly seen in patients with established disease. There was no clinical or laboratory (ANF negative) evidence of SLE. Patients of Goodpasture’s syndrome may initially present with haemoptysis.4 However, they have concomitant renal involvement. There was no renal involvement and anti-GBM antibodies were negative thereby ruling out Goodpasture’s syndrome. Idiopathic pulmonary haemosiderosis is a rare cause of alveolar haemorrhage and is a diagnosis by exclusion.

Discussion

IPH is a disease of uncertain cause characterised by recurrent episodes of alveolar haemorrhage, haemosiderosis, and secondary iron deficiency anaemia. Virchow first described IPH in 1865 as “brown induction”. It is most common in childhood and rarely seen in adults. It is often fatal although some patients may recover completely. The sex distribution is equal in childhood but the disease is twice as common in adult males than females. The aetiology is largely unknown, but may be related to some toxic insecticides and infections.7-9 The cause may be immunological (supported by eosinophilia, increased plasma cells in the reticuloendothelial system, aggregation of mast cells in the lungs, and the presence of cold agglutinins): Some cases of IPH are secondary to gluten enteropathy.10 Haemosiderin containing macrophages are plentiful in the alveolar spaces and interstitium. The intensity and duration of the pulmonary haemorrhage varies individually ranging from continuous mild intrapulmonary to acute fatal haemoptysis. Accordingly iron deficiency anaemia varies.

Functionally there is restrictive pattern of lung volumes. Transfer factor for carbon monoxide (T1CO) is a useful investigation in alveolar haemorrhage. It is actually the product of alveolar volume (VA) and carbon monoxide transfer coefficient (KCO). VA is mild reduced because of alveolar filling with blood, and KCO is considerably increased because the inhaled CO reacts with extravascular haemoglobin.10-11 A increased T1CO with considerably increased KCO and mildly reduced VA are characteristic of alveolar haemorrhage.10 But it is essential to adjust KCO and T1CO to a normal haemoglobin concentration because of the fluctuating anaemia in these patients.10 A minority of patients have generalised lymphadenopathy and hepatospleno-megaly.12-14 A chest radiograph in the acute phase shows blotchy shadows in bilateral middle and lower zones or reticulonodular infiltrates/ground glass appearance. Ground glass appearance, thickening of interlobular septa, and honeycombing may be seen on the computed tomogram. Iron deficiency is prominent and may be profound.15 Siderophages may be found in sputum, BAL fluid, tracheal or gastric aspirates. Capillaritis has been described but microscopic vasculitis is not found.

Optimal treatment is not clear. Corticosteroids are the mainstay of treatment. The role of azathioprine, cyclophosphamide, and plasmapheresis in the event of corticosteroid failure is anecdotal. The course of the disease is variable. Prognosis varies with the intensity of disease.16-18 Our patient was treated with corticosteroids (prednisolone in a dose of 1 mg/kg body weight) and iron and folic acid supplementation. He has done well and on follow up for the past three years with no evidence of relapse. Prednisolone was gradually tapered off. Presently, no corticosteroids are being given. On the last follow up he had haemoglobin count of 120 g/l with a normal chest radiograph.

Final diagnosis
DAH secondary to idiopathic pulmonary haemosiderosis.

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SELF ASSESSMENT ANSWERS

Learning points

- All cases of haemoptysis are not because of tuberculosis in South Asia.
- DAH should be suspected in patients of recurrent haemoptysis with anaemia, with or without radiological features and with increased transfer factor for carbon monoxide (with mildly decreased VA and considerably increased KCO).
- IPH is a diagnosis of exclusion, when other secondary causes of DAH have been ruled out.
- Immunosuppressive treatment should be tried in all cases.

Differential diagnosis of diffuse alveolar haemorrhage

1 Systemic vasculitis syndrome
   - Wegener’s granulomatosis
   - Microscopic polyangiitis
   - Henoch-Schönlein purpura
   - Behçet’s syndrome
   - Mixed cryoglobulinaemia
   - Churg-Strauss syndrome

2 Connective tissue disorders
   - Systemic lupus erythematosus
   - Rheumatoid arthritis
   - Scleroderma
   - Mixed connective tissue disorder
   - Polymyositis or dermatomyositis

3 Antibasement membrane disease
   - Glomerulonephritis associated alveolar haemorrhage

4 Infections
   - Drugs or toxic agents
   - Pulmonary metastasis
   - Organ transplantation

5 Acute respiratory distress syndrome
   - Cardiac disorders
     - Mitral stenosis
     - Congestive heart failure
     - Pericarditis

6 Bleeding disorders
   - Disseminated intravascular coagulation
   - Thrombotic thrombocytopenic purpura
   - Oral anticoagulants

7 Pulmonary vascular disorders
   - Pulmonary-capillary haemangiomatosis
   - Arteriovenous malformations
   - Idiopathic pulmonary haemosiderosis

8 Other disorders
   - Antiphospholipid syndrome
   - Heiner’s syndrome (antibodies to cows’ milk protein)
   - Isolated pauci-immune pulmonary capillaritis

References

References
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