Rare disease

Diffuse alveolar haemorrhage in granulomatosis with polyangitis (Wegener's) with coexistent rheumatoid arthritis

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Summary

Diffuse alveolar haemorrhage is a serious manifestation of granulomatosis with polyangitis (Wegener's) with high morbidity and mortality. It is defined by the clinical triad of haemoptysis, anaemia and progressive hypoxaemia.

The diagnosis of granulomatosis with polyangitis is confirmed in an appropriate clinical setting by bronchoalveolar lavage, lung biopsy or detection of C-antineutrophil cytoplasmic antibodies.

In this report, the patient was a known case of rheumatoid arthritis and presented with diffuse alveolar haemorrhage on CT scan; the underlying cause was found to be granulomatosis with polyangitis (Wegener's) with positive C-antineutrophil cytoplasmic antibodies. Despite aggressive treatment with immunosuppressants and steroids the patient died within a few days.

BACKGROUND

The case reported is that of a patient with diagnosed rheumatoid arthritis who presented with limited form of granulomatosis with polyangitis (Wegener's) in the form of diffuse alveolar haemorrhage in both lung fields. The classical form of Wegener's granulomatosis is a multisystem disease, but sometimes the disease may present with limited organ involvement in which there is no renal involvement and no evidence of systemic vasculitis.^{1 2}

We present this case, as apart from the rarity of this clinical setting, we would like to emphasise on the importance of early diagnosis and aggressive treatment for this patient owing to significantly high death rates.

CASE PRESENTATION

A 37-year-old woman presented with complains of acute breathlessness, fever, cough and haemoptysis for 2 days. There was no complain of pedal oedema or palpitations or a history of similar complains. The patient was a known case of rheumatoid arthritis undergoing treatment for 7 months (diagnosed on the basis of clinical complaints and rheumatoid arthritis factor positivity). There was no other significant medical or operative history.

On examination, the patient was pale with tachypnoea, tachycardia and hypotension. On auscultation, bilateral diffuse coarse crepitations were noted.

INVESTIGATIONS

Blood investigations revealed a haemoglobin level of 7.3 g/dl (low), red cell count of 2.9 million/cu mm (low), white cell count of 21 600 (raised) and a significantly raised erythrocyte sedimentation rate -150 mm/h (raised).

Special investigations revealed:

- C-reactive protein positivity (>4.8 mg/dl)
- Rheumatoid arthritis factor positivity

- C-antineutrophil cytoplasmic antibody (C-ANCA) positivity
- Raised fibrinogen and fibrinogen degradation products
- Plasma D-dimer positivity in 1:4 dilution
- Normal levels of cyclic citrullinated peptide antibody to cyclic citrullinated peptide.

Urine examination was normal (ie, no evidence of macroscopic or microscopic haematuria).

Radiological investigations were also carried out. A chest x-ray revealed diffuse soft-tissue opacities with air bronchogram in the mid and lower zones of both lung fields suggestive of diffuse alveolar opacities (figure 1). There was no evidence of pleural effusion on either side. Heart size was within normal limits. Differential diagnosis of pulmonary oedema or infection was suggested and a CT scan of the thorax was advised.

Ultrasound of the abdomen was normal (renal involvement of the disease was ruled out).

On a contrast-enhanced CT scan, diffuse alveolar opacities with variable densities (10–90 HU) were noted involving both lung fields, and hence findings were suggestive of diffuse alveolar haemorrhage involving both lung fields. There were no nodular opacities or mediastinal lymphadenopathy (figure 2).

In view of the pathological and radiological findings, diagnosis of limited form of Wegener's granulomatosis with coexistent rheumatoid arthritis was confirmed (figures 3 and 4).

DIFFERENTIAL DIAGNOSIS

Goodpasture's syndrome may have pulmonary manifestations like alveolar haemorrhage presenting as haemoptysis.

However, the absence of any renal abnormality (no red blood cells in the urine and normal kidneys on ultrasound) and C-ANCA positivity made us narrow down the diagnosis to Wegener's granulomatosis.

Figure 1 Chest x-ray (anteroposterior view) showing diffuse soft-tissue opacities with air bronchogram in the mid and lower zones of both lung fields, suggestive of diffuse alveolar opacities.

The patient in this report is a known case of rheumatoid arthritis. Pulmonary manifestations of this disease are varied, the commonest being pleural effusion followed by rheumatoid nodules and diffuse interstitial fibrosis. But it may rarely present as pulmonary vasculitis or alveolar haemorrhage. However, the positivity of C-ANCA made us rule out the possibility of this rare presentation of rheumatoid arthritis.³

TREATMENT

The patient was put on ventilator support and treatment with steroids and other immunosuppressants was started. Glucocorticoids (ie, prednisolone in doses of 1 mg/kg)

Figure 2 Coronal CT scan section mediastinal window: diffuse alveolar haemorrhage.

Figure 3 Coronal CT scan section lung window: diffuse alveolar haemorrhage.

were administered daily. A single dose of cyclophosphamide (500 mg/m² of body surface area) was also given.

Serial chest x-rays showed no significant improvement over the next 4 days.

OUTCOME AND FOLLOW-UP

The patient died after 5 days of treatment owing to respiratory failure.

DISCUSSION

Diffuse alveolar haemorrhage refers to a clinical syndrome due to injury to the alveolar capillaries, arterioles and venules leading to the accumulation of red blood cells in

Figure 4 Axial CT scan section lung window: diffuse alveolar haemorrhage.

the distal air spaces. It is defined by a clinical triad of haemoptysis, anaemia and progressive hypoxaemia. Acute attacks have high morbidity and mortality and repeated episodes can lead to organising pneumonia with collagen deposition in the distal airways and fibrosis.⁴

Diffuse alveolar haemorrhage can be caused by a wide variety of conditions such as autoimmune disorders (eg, Wegener's granulomatosis, Goodpasture's syndrome, antiphospholipid antibody syndrome), pulmonary infections (eg, invasive aspergillosis, hantavirus infection), toxic exposures (eg, isocyanates, pesticides), drug reactions (eg, propylthiouracil, diphenylhydantoin, amiodarone, infliximab), cardiac disorders (eg, mitral stenosis), coagulation disorders and bone marrow or solid organ transplantation.⁵

In our patient, diffuse alveolar haemorrhage was caused by Wegener's granulomatosis.

Wegener's granulomatosis is a multisystem necrotising vasculitis and an uncommon disease that affects about 1 in 20 000 to 1 in 30 000 people. It is characterised by necrotising granulomatous vasculitis of the upper and lower respiratory tract, focal necrotising glomerulonephritis and generalised focal necrotising vasculitis involving both arteries and veins.²

Wegener's granulomatosis most commonly occurs in Caucasians and affects men and women equally. The mean age at diagnosis is 40 years, but the disease can develop at any age.⁶ The lungs are the most commonly affected organ, with evidence of respiratory involvement in over 90% of patients during the course of the disease; in 9% of patients, it is the only organ affected.⁵

Alveolar haemorrhage may be the presenting manifestation of Wegener granulomatosis in approximately 8% of patients with the disease.⁷ The sensitivities of C-ANCA testing for overall Wegener granulomatosis ranged from 34% to 92%, and the specificities ranged from 88% to 100%. Thus, although C-ANCA test results may serve clinicians as adjunct evidence for the diagnosis of Wegener granulomatosis, these results must be viewed in the context of the patient's clinical picture and disease activity and the prevalence of Wegener granulomatosis in the clinical setting in which the patient is seen.⁸

Types of antineutrophil cytoplasmic antibodies are generally measured using ELISA and indirect immunofluorescence.

- P-ANCA, or perinuclear antineutrophil cytoplasmic antibodies, shows a perinuclear staining pattern. The target antigen is most commonly myeloperoxidase. It is associated with microscopic polyangitis, Churg Strauss

syndrome and focal necrotising and crescentic glomerulonephritis.

- C-ANCA, or cytoplasmic antineutrophil cytoplasmic antibodies, shows a diffusely granular, cytoplasmic staining pattern. The target antigen is most commonly proteinase 3. It is associated with Wegener's granulomatosis.
- x-ANCA, or atypical antineutrophil cytoplasmic antibodies, may be seen in many disease processes, but is most commonly found in chronic inflammatory bowel disease (ulcerative colitis and Crohn's disease).⁹

Learning points

- ▶ Limited form of granulomatosis with polyangitis (Wegener's) presenting as diffuse alveolar haemorrhage is rare.
- ▶ Timely and active management is vital for reducing the morbidity and mortality associated with this disease.
- ▶ Steroids (prednisolone) and cyclophosphamide institute the primary line of treatment in this disease.

Competing interests None.

Patient consent Obtained.

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Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Vaishnav KU, Bhatt C, Desai A. Diffuse alveolar haemorrhage in granulomatosis with polyangitis (Wegener's) with coexistent rheumatoid arthritis. *BMJ Case Reports* 2012;10.1136/bcr.2012.006184, Published XXX

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