Reminder of important clinical lesson

Rapidly progressive pulmonary haemorrhage in a case of microscopic polyangiitis

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Correspondence to Dr James MacKay, jw.mackay@gmail.com**Summary**

A 77-year-old gentleman, a holidaymaker in the area, presented with a 2-month history of cough productive of rust-coloured sputum and exertional dyspnoea. His initial chest x-ray showed bibasal interstitial shadowing. He then deteriorated rapidly to type 1 respiratory failure with acute renal failure. A CT chest showed bilateral alveolar haemorrhage. Testing for p-anti-neutrophil cytoplasmic antibody was strongly positive, with an anti-myeloperoxidase antibody titre of 198 units/ml (normal range 0–6 units/ml). A diagnosis of microscopic polyangiitis was made. Following treatment with plasma exchange, cyclophosphamide and steroids, he made a good recovery.

BACKGROUND

Reminder of an important clinical lesson: the diagnosis of pulmonary haemorrhage is difficult in the acute medical setting. However, it should be considered as part of the differential diagnosis in patients who present with respiratory symptoms (especially with concurrent renal impairment) not resolving with treatment for more common conditions.

In this case the early consideration of this differential and performance of the relevant investigations lead to a definitive diagnosis which allowed the correct treatment to be administered when the patient deteriorated.

CASE PRESENTATION

A 77-year-old gentleman presented with a 2-month history of cough productive of rust-coloured sputum and

Figure 1 Initial chest x-ray.

Figure 2 Repeat chest x-ray.

exertional dyspnoea. He denied chest pain, orthopnoea and ankle oedema. He had noticed some frank blood on blowing his nose recently, but denied haemoptysis. No further symptoms were detected on systemic enquiry.

His medical history was remarkable for ischaemic heart disease, hypertension, type-2 diabetes mellitus, diverticular disease, hiatus hernia and chronic kidney disease 3. His medications included aspirin, omeprazole, simvastatin, tolbutamide, bisoprolol, amlodipine and ramipril. He was an ex-smoker with a 20 pack/year history, having given up 30 years ago, and drank alcohol only very occasionally. He was a retired builder and reported previous occasional exposure to asbestos. He lived alone and was usually fully independent. There was no family history of note.

On examination, the patient was haemodynamically stable, with oxygen saturations of 88% on room air. Systemic examination was remarkable for bilateral fine inspiratory crackles heard at both lung bases. Urinalysis showed ++++ proteinuria and +++ haematuria. Arterial blood gas performed on admission showed a compensated metabolic acidosis, with a base excess of -5.9 mmol/l.

A chest x-ray was performed which showed bibasilar interstitial shadowing (figure 1). Initial blood results revealed a normocytic anaemia (haemoglobin 9.6 g/dl) and acute on chronic renal failure with a urea of 22.5 mmol/l and creatinine of 413 µmol/l (baseline 178 µmol/l). Erythrocyte sedimentation rate was elevated at 73 mm in the first hour. Echocardiography was performed and revealed good biventricular systolic function.

Over the next few days the patient deteriorated, developing type 1 respiratory failure requiring continuous

positive airway pressure (CPAP) to maintain his oxygen saturations. His renal function remained stable, however, his haemoglobin continued to drop and he required transfusion of a single unit of red blood cells. Repeat chest x-ray revealed worsening of the bibasilar shadowing seen on the initial film (figure 2), and a non-contrast CT chest demonstrated bilateral diffuse pulmonary haemorrhage (figure 3).

At this point, the results of his autoantibody screen became available. They showed a strongly positive anti-myeloperoxidase titre of 198 units/ml (normal range 0–6 units/ml). The patient was transferred to a nearby intensive care unit for urgent plasmapheresis.

INVESTIGATIONS

Anti-neutrophil cytoplasmic antibody (ANCA) testing revealed a strongly positive p-ANCA with an anti-myeloperoxidase titre of 198 units/ml.

DIFFERENTIAL DIAGNOSIS

Microscopic polyangiitis

The initial differential diagnosis included heart failure, atypical pneumonia, interstitial lung disease, vasculitides (Wegener's granulomatosis, microscopic polyangiitis) and Goodpasture's disease.

TREATMENT

The patient was treated on intensive treatment unit (ITU) with seven plasma exchanges, intravenous cyclophosphamide and intravenous methylprednisolone. He also required CPAP to maintain his saturations while on ITU.

Figure 3 Non-contrast chest CT showing diffuse bilateral alveolar haemorrhage.

Figure 4 Histology from renal biopsy.

OUTCOME AND FOLLOW-UP

Following the treatment described above, the patient made a good recovery and was discharged from hospital. A renal biopsy was performed during admission, showing a focal segmental glomerulonephritis with crescents (figure 4). The patient continues to be seen in the rheumatology outpatient clinic where he is receiving pulsed intravenous cyclophosphamide. He is also on maintenance prednisolone, 40 mg orally once daily.

DISCUSSION

Pulmonary haemorrhage is often life-threatening, and provides a significant diagnostic challenge in the acute setting. The most common initial clinical features are cough, dyspnoea and fever, thus recognition and diagnosis require a high-degree of clinical suspicion. Haemoptysis is often absent at time of presentation, as the alveoli have the capacity to absorb a large volume of blood without extension into higher order airways.

Findings on examination are generally non-specific, although the presence of a rash or other vasculitic stigmata may indicate the underlying diagnosis. The typical chest x-ray will show bilateral patchy or diffuse alveolar shadowing. CT scanning of the chest is said to be more sensitive in differentiating pulmonary haemorrhage from other causes of alveolar shadowing.¹ Measurement via spirometry of κ CO (carbon monoxide transfer co-efficient) is a sensitive indicator of pulmonary haemorrhage, however, its utility in the acute setting is limited as the patient may be too unwell to perform spirometry.

The presence of concurrent renal impairment and/or an abnormal urine dip should prompt consideration of a diagnosis of pulmonary-renal syndrome. This term describes co-existent pulmonary haemorrhage and glomerulonephritis. The most common cause of this syndrome is a systemic vasculitis.² If such a diagnosis is being considered, performance of the relevant autoantibody tests and involvement of a renal physician at an early stage are vital.

Microscopic polyangiitis is a systemic small-vessel vasculitis associated with necrotizing glomerulonephritis and pulmonary capillaritis. Pulmonary haemorrhage has been reported as a feature of this condition in between 10–50% of patients.³

Other organ system involvement is common. Glomerulonephritis (classically a focal crescentic glomerulonephritis) is the most common feature, being present in

90% of patients. Other affected sites are the nervous system (60–70% of patients), lungs (50–70%), gastrointestinal tract (30%) and heart (10–15%). Upper airways disease is rare, distinguishing the condition clinically from Wegener's granulomatosis.³

Testing for anti-myeloperoxidase antibody (p-ANCA) is positive in between 50–80% of patients.⁴

As the pathogenesis of this condition has been shown in animal models to be closely linked to the action of the anti-myeloperoxidase antibody, the rationale for plasma exchange therapy is the removal of these antibodies from the circulation.⁵

Learning points

- In patients presenting with atypical pulmonary symptoms and new onset renal impairment, a diagnosis of pulmonary-renal syndrome should be considered.
- Vasculitides can present with a rapidly progressive course, with associated high mortality and morbidity.
- Early consideration of the diagnosis and performance of the relevant investigations allows accurate, prompt and potentially life-saving treatment to be administered.
- In patients with suspected pulmonary haemorrhage, early involvement of the intensive care team is important as plasma exchange may be necessary.

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Competing interests None.

Patient consent Obtained.

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