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Recurrent anti-GBM disease with pulmonary artery aneurysms

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Lesson
We present the first known case of pulmonary artery aneurysms as a feature of Recurrent Anti-Glomerular Basement Membrane disease.

Keywords
Acute renal failure, renal medicine

Case report

A 39-year-old Caucasian man presented with a four-week history of haemoptysis, haematuria and general malaise. There were no other specific symptoms, in particular, oral or genital ulceration or arthralgia. He smoked more than 40 cigarettes per day. His previous medical history was unremarkable, as was his family history. He was not taking any regular prescribed or non-prescribed medications. On examination, his blood pressure was 161/76 but there were no clinical features to suggest Behçet's disease, polyarteritis nodosa, a collagen-vascular disorder, or signs of right heart disease. In addition, there was no clinical evidence of venous thromboembolism. Dipstick urinalysis revealed haematuria (4+) and proteinuria (1+). Initial investigations showed impaired renal function with a serum creatinine of 1359 µmol/L, and a normocytic anaemia with a haemoglobin. of 8.0 g/dL and an MCV of 90 fL. His chest radiograph was consistent with pulmonary haemorrhage. Serology revealed a positive anti-GBM titre 124 AU/ml (Normal range <15) and a negative Anti-neutrophil cytoplasmic antibody.

He was commenced on haemodialysis and was treated with 17 sessions of plasma exchange and a three-month course of pulsed intravenous cyclophosphamide. Plasma exchange was continued for three weeks, due to ongoing haemoptysis. Anti-GBM titres were undetectable on at least six occasions during the next six months. He remained dialysis-dependant throughout the duration of his treatment.

Six months after his first negative anti-GBM titre and after finishing cyclophosphamide, he re-presented with recurrent episodes of haemoptysis. His anti-GBM titres were again raised (174 AU/ml). A chest radiograph (Figure 1) revealed an abnormal area in the right hilum, and a computed tomography of the pulmonary arteries (CTPA) confirmed a 2.5 cm aneurysm of the right pulmonary artery, supplying the lower lobe, and two further adjacent aneurysms (Figure 2). Pulmonary function tests revealed a mild restrictive ventilation defect.

In view of the recurrence of anti-GBM titres and the pulmonary aneurysms, it was suggested he might have a co-existent small vessel vasculitis. He was commenced on azathioprine and prednisolone immunosuppressive therapy, following which the anti-GBM titres became negative. Clinical examination did not reveal any evidence of another vasculitis, and serum ANCA remained negative.

Discussion

Anti-GBM disease is a disorder with an incidence of one per million in the United Kingdom and is caused by autoantibodies directed against the non-collagenous domain of the α3 chain of type IV collagen found predominantly within glomerular and alveolar basement membranes. It manifests as a rapidly progressive glomerulonephritis associated with pulmonary haemorrhage. Pulmonary haemorrhage appears to be commonest in young Caucasian men, especially smokers.[1]

Anti-GBM disease is diagnosed by a combination of positive anti-GBM antibodies and detecting linear IgG deposits on the glomerular basement membrane on renal biopsy. Treatment consists of removing the antigen with plasma exchange, and suppressing its ongoing production with immunosuppression, by cyclophosphamide. Plasma exchange is continued until haemoptysis resolves and, in cases where a renal recovery is predicted, when anti-GBM titres are undetectable on at least two occasions.[2]

Anti-GBM disease is usually a monophasic illness in that it does not recur once a successful treatment course has been completed. Anti-GBM antibodies are

Figure 1. Plain chest radiograph showing abnormal right hilum.

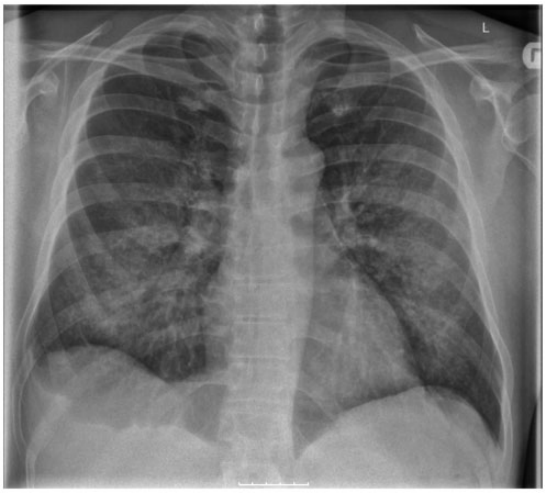
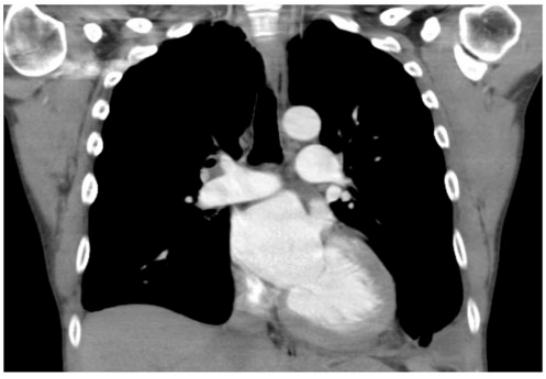


Figure 2. CTPA showing pulmonary aneurysms.



usually undetectable after treatment with plasma exchange and immunosuppressive therapy and are undetectable at 12 months in untreated disease.[3] Recurrence is rare and tends to happen after the initial symptoms have been controlled but before the antibody titre has been fully suppressed. The antibody has not been reported to occur in the absence of disease.[4] This case is unusual in that it recurred following numerous negative anti-GBM titres, but has similarities with previously documented cases where haemoptysis is the main feature of recurrence, and may have been triggered by pulmonary oedema.[5]

Aneurysms of the main pulmonary arteries are rare with an estimated incidence of 1 in 14,000 from post-mortem studies.[6] Most cases are due to trauma – often iatrogenic, infection (mycotic endocarditis, syphilis, tuberculosis), or Behçet's disease.[7] Less common causes include pulmonary hypertension, congenital cyanotic heart disease, neoplasia and connective tissue disease.

This case provided a diagnostic challenge as an association between recurrent anti-GBM disease and pulmonary artery aneurysms has not previously been described in the literature, and the differentials of pulmonary artery aneurysms were not present in this case. There was no clinical or serological evidence of infection or neoplasia, and there is no history of preceding trauma or congenital heart disease. Clinical features of a connective tissue disorder were not present and there was no peripheral thromboembolism, thus excluding Hughes-Stovin syndrome. This case had none of the major diagnostic criteria of Behçet's disease.[8] Co-existent polyarteritis nodosa was considered as this is a vasculitis that occurs with aneurysm formation in many organs,[9] but pulmonary arterial aneurysms have not been described in PAN, and no aneurysms were found within intra-abdominal organs on computed tomography angiogram in this case.

This case has a typical epidemiological profile and clinical presentation of anti-GBM disease. This case does not have clinical, serological or radiological features to suggest a co-existent disorder associated with pulmonary artery aneurysms. In conclusion, the combination of anti-GBM disease and pulmonary artery aneurysms is likely to represent either a new association of anti-GBM disease (possibly due to a recurrent hit causing the development of pulmonary artery aneurysms) or a newly described variant of anti-GBM disease.

Declarations

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Guarantor: HW

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