An unlikely cause of shortness of breath

Introduction

The following case features a presentation of sudden onset dyspnoea, a relatively common presentation to the emergency department. Investigations revealed a cardiovascular problem with an unexpected underlying pathology of the mitral valve. This case highlights the importance of thorough investigation of symptoms which are common and thus may seem to be trivial.

Discussion

This is a complex case featuring an autoimmune thrombotic pathology strongly suggestive of primary antiphospholipid syndrome. This did not meet the full clinical criteria required for a definite diagnosis and was thus labelled as 'probable primary antiphospholipid syndrome'. Regardless, the patient suffered severe complications requiring a mitral valve replacement at a young age. This highlights the importance of early diagnosis of such autoimmune conditions, which may not fulfil all the criteria and at times overlap with each other, which may further delay treatment

Ruis-Irastorza et al (2010) define primary antiphospholipid syndrome as a systemic autoimmune thrombophilic disorder characterized by recurrent thrombosis and/or obstetric morbidity in the presence of persistently positive anti-phospholipid antibodies.

Asherson (2006) described several primary antiphospholipid syndrome-related clinical scenarios:

1. Definite antiphospholipid syndrome – antiphospholipid syndrome satisfying laboratory criteria (positive anti-phospholipid antibodies) and clinical criteria (major thrombotic event and/or pregnancy morbidity)
2. Asymptomatic patients with positive anti-phospholipid antibodies – patients fulfilling the laboratory criteria but not clinical criteria for antiphospholipid syndrome
3. Probable antiphospholipid syndrome – positive serology with the presence of manifestations known to be associated

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CASE REPORT

A previously healthy 38-year-old woman presented to the emergency department with a 1-week history of progressive dyspnoea. She was tachypnoeic at rest with oxygen saturations of 96% on room air, on chest examination bilateral, inspiratory crepitations were heard at lung bases. On auscultation, a pansystolic murmur was found. Her lower limbs showed no signs of deep vein thrombosis or oedema. The patient had no prior medical history. She had had two uncomplicated pregnancies, and had no history of past miscarriages or significant family history of thrombosis.

Investigations revealed a thrombocytopenia, mildly impaired renal function and raised inflammatory markers. Three sets of blood cultures were negative. A morning urinalysis was positive for microalbuminuria. Abdominal ultrasonography showed normal kidneys and mild splenomegaly. Electrocardiogram showed a sinus tachycardia while chest X-ray demonstrated pulmonary congestion. Echocardiography revealed severe mitral regurgitation, likely chronic with a dilated left atrium and pulmonary systolic pressures of 36+10 mmHg. A large vegetation was seen on the posterior leaflet of the mitral valve.

On closer review, a purplish net-like rash characteristic of livedo reticularis was seen on her hands, which prompted screening for a connective tissue disorder such as systemic lupus erythematosus and antiphospholipid syndrome. ANA and anti-dsDNA were both negative and complement levels were normal. Antiphospholipid antibody screen was strongly positive (B2-glycoprotein IgG >100 U/ml, IgM 20 U/ml and anti-cardiolipin antibody IgG 92.9 GPL, IgM 21.8 MPL).

At this point the differential diagnosis consisted of infective endocarditis *vs* an autoimmune endocarditis. The three negative blood cultures and normal white cell count argued against infective endocarditis.

The age and gender of this patient as well as the appearance of livedo reticularis supported a diagnosis of systemic lupus erythematosus and/or antiphospholipid syndrome with an underlying Libman–Sachs endocarditis or primary antiphospholipid syndrome. The absence of Raynaud's, mouth ulcers, alopecia or arthritis, together with negative ANA and anti-dsDNA, argued against a diagnosis of systemic lupus erythematosus.

The clinical picture of mitral valve thrombus, renal microangiopathy, livedo reticularis, thrombocytopenia and the strongly positive serology for antiphospholipid syndrome made primary antiphospholipid syndrome the most likely diagnosis. Despite lacking the clinical criteria required for a definite diagnosis of antiphospholipid syndrome (previous major thrombotic event or pregnancy morbidity), primary antiphospholipid syndrome predisposed this patient to thrombotic events with the formation of a thrombus on the mitral valve leading to severe mitral regurgitation.

While the mainstay of treatment in thrombotic antiphospholipid syndrome is long-term anticoagulation, in cases of probable primary antiphospholipid syndrome one needs to weigh the pros and cons of anticoagulation in the short and long term, as data on the efficacy of anticoagulation on microangiopathic nephropathy and valvular heart disease are unclear. This patient had several poor prognostic signs and risk factors for a thromboembolic event including high-level triple positivity for antiphospholipid antibodies, severe mitral valve disease with a vegetation, and renal impairment. She was anticoagulated with heparin and warfarin.

Four months later renal function improved and the mitral valve vegetation was no longer visible on echocardiography. However, there was still evidence of severe mitral regurgitation and she was referred for mitral valve replacement.

with antiphospholipid syndrome but not satisfying clinical criteria for definite antiphospholipid syndrome.

The concept of probable antiphospholipid syndrome is a relatively new one and the literature is limited. Asherson et al (2007) have reported patients presenting with heart valve lesions, chorea, renal microangiopathy, thrombocytopenia, fetal loss or livedo reticularis. These patients exhibit clear features of a systemic microangiopathy but lack the clinical criteria of large vessel thrombosis or pregnancy morbidity for a diagnosis of definite antiphospholipid syndrome. These patients may develop further clinical signs in the future and eventually be diagnosed with definite antiphospholipid syndrome.

Moyssakis et al (2007) report that valvular abnormalities in antiphospholipid syndrome are usually asymptomatic and often discovered incidentally. However, significant valvular dysfunction and consequent heart failure may occur. Moreover, valvular abnormalities can be complicated by secondary infective endocarditis and embolization from vegetations leading to widespread systemic complications such as strokes, pulmonary and renal infarcts.

This patient underwent a mitral valve replacement with good result and is on lifelong anticoagulation. She is under rheumatology, cardiology and nephrology follow up. **BJHM**

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Moyssakis I, Tektonidou MG, Vasilliou VA, Samarkos M, Votteas V, Moutsopoulos HM (2007) Libman-Sacks endocarditis in systemic lupus erythematosus: prevalence, associations, and evolution. *Am J Med* **120**(7): 636–642. https://doi.org/10.1016/j.amjmed.2007.01.024

LEARNING POINTS

- In the acute setting it can be difficult to be certain of the cause of a new valvular lesion and often one has to cover for infective endocarditis by starting empirical antibiotics, to prevent irreversible valvular damage.
- Antiphospholipid syndrome treatment remains a challenge both in terms of timely diagnosis and management.
- Consideration of 'probable antiphospholipid syndrome' with the redefining of antiphospholipid syndrome criteria to include important outcomes such as valvular lesions and antiphospholipid syndrome nephropathy is warranted to ensure early diagnosis and prevent long-term sequelae.

Ruiz-Irastorza G, Crowther M, Branch W, Khamashta MA (2010) Antiphospholipid syndrome. *Lancet* **376**(9751): 1498–1509 https://doi.org/10.1016/S0140-6736(10)60709-X

Supraclavicular aneurysm as a presentation of alpha-1 antitrypsin deficiency

A 50-year-old woman presented to the outpatient clinic because of the appearance of a supraclavicular lump. She had experienced several months of weight loss and difficulties swallowing solids. She was on atorvastatin and clopidogrel because of an unexplained ischaemic cerebral stroke. Apart from a deep non-pulsatile tumour which was adherent on examination, physical examination, gastroscopy and abdominal ultrasound scan were normal. A computed tomography scan showed a 4 cm diameter ovoid mass, closely related to the right subclavian artery. Angiography of the aortic and supra-aortic branches was both diagnostic and therapeutic (*Figure 1*).

Apart from a mild cholestatic pattern (bilirubin 1.73 mg/dl and gamma-glutamyl transferase 69 U/litre), blood cell count, proteinogramme, tumour markers, anti-nuclear antibodies, anti-neutrophil cytoplasmic antibodies and viral serologies were normal. Given the clinical scenario of cholestasis, an early acute stroke and the presence of aneurysms there was a broad differential diagnosis ranging from infections, neoplasms, genetic disorders, thrombophilias to autoimmune diseases. All investigations came back negative except alpha-1 antitrypsin which was 10 µmol/litre (normal range 20–53 µmol/litre). A ZZ genotype mutation was found in the alpha-1 antitrypsin gene and vascular phenomena related to the alpha-1 antitrypsin deficiency were diagnosed. **BJHM**

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Figure 1. Angiography showing partially-thrombosed pseudoaneurysm undergoing supraselective embolization.