CASE REPORT

Antiphospholipid Syndrome with Pulmonary Artery Embolism and Multiple Venous Thromboses

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SUMMARY

We report a case of a 21 year-old university student with underlying lupus nephritis who presented with recurrent symptoms of fever, haemoptysis, and pleuritic chest pain. CT pulmonary angiogram confirmed pulmonary embolism in the right subsegmental pulmonary arteries. One week later, she developed left renal vein and left common iliac vein thromboses, with new emboli in the left subsegmental pulmonary arteries. We hereforth discuss the diagnostic issues of a patient with systemic lupus erythematosus (SLE) on corticosteroids therapy, and also treatment of the antiphospholipid syndrome.

KEY WORDS:
Antiphospholipid syndrome (APS), Pulmonary embolism, Thrombosis, Systemic lupus erythematosus (SLE)

INTRODUCTION

Antiphospholipid syndrome (APS) is diagnosed when at least one clinical and one laboratory criteria are met, based on the Sapporo Classification Criteria[1]. Clinical criteria include arterial, venous, or small vessel thrombosis, or the presence of pregnancy morbidity. Laboratory criteria include: a.) presence of lupus anticoagulant antibody, b.) medium or high titre (or >99th percentile) IgG/IgM anticardiolipin antibody, or c.) IgG/IgM anti-β2 glycoprotein-I antibody (titre >99th percentile).

Measurement of the above antiphospholipid antibodies must remain consistent on two or more occasions of at least 12 weeks apart, to fulfill the laboratory criteria.

This syndrome can be further subdivided into primary APS when it occurs alone, or secondary APS when it occurs in association with other conditions, such as SLE. We herein report a case of secondary APS presenting with pulmonary artery embolism and multiple venous thromboses.

CASE REPORTS

A 21 year-old single university student first presented with nephrotic syndrome in July 2007. Physical examination only revealed a malar flush which she claimed to have been present since childhood. There were no past miscarriages or any features of thromboses present. Her prothrombin time (PT) was normal, but the activated partial thromboplastin time (APTT) was deranged at 68-69 seconds, which was only partially correctable to 55 seconds with a mixing test. Lupus anticoagulant antibody was positive and anticardiolipin IgG was normal.

Serum complement levels (C3, C4) were low, and anti-nuclear antibody (ANA) was high at 1:1280 but the anti-dsDNA was normal. A renal biopsy performed subsequently on 7/9/07 confirmed histological features of membranous lupus nephritis (WHO Class V). Hence, she was diagnosed with lupus nephritis secondary to SLE. She was commenced on azathioprine on top of prednisolone and perindopril.

Following treatment, her proteinuria resolved and she was well until one year later when she presented with recurrent episodes of fever, cough, haemoptysis, and pleuritic chest pain. Her chest radiograph (Figure 1) and sputum culture were normal. Her sputum direct smear for acid-fast bacilli (AFB) was negative and her Mantoux test yielded a skin induration of 8mm. An electrocardiogram was normal and her pulse oxymetry test in room air was 98%.

Based on the clinical symptoms, pulmonary embolism was suspected and this was confirmed by a CT pulmonary angiogram on 3/9/08 (Figure 2a) which revealed multiple filling defects in the right subsegmental pulmonary arteries. Bronchoscopy was also performed to rule out pneumonia or pulmonary tuberculosis. Broncho-alveolar lavage fluid from the postero-basal segment of the right lower lobe was slightly bloody and its laboratory investigations were all reported as normal, except for some excess red cells.

On 5/9/08, she fell off her motor-cycle and developed left leg swelling. A Doppler ultrasound of the left lower limb revealed left common iliac vein thrombosis. On admission to the ward that day, she also complained of acute left loin pain. An urgent contrasted CT scan of the abdomen confirmed left renal vein and left common iliac vein thromboses. This repeat CT scan (Figure 2b) also showed new left-sided embolism/ filling defects in the left subsegmental pulmonary vessels.

She was discharged on 26/9/08 with prednisolone 5mg daily, warfarin anticoagulation, and hydroxychloroquine on top of her usual azathioprine. A week later however, she developed blurring of vision in both eyes, lasting less than 24 hours. Assessment by the ophthalmologist showed slightly

This article was accepted: 24 August 2010
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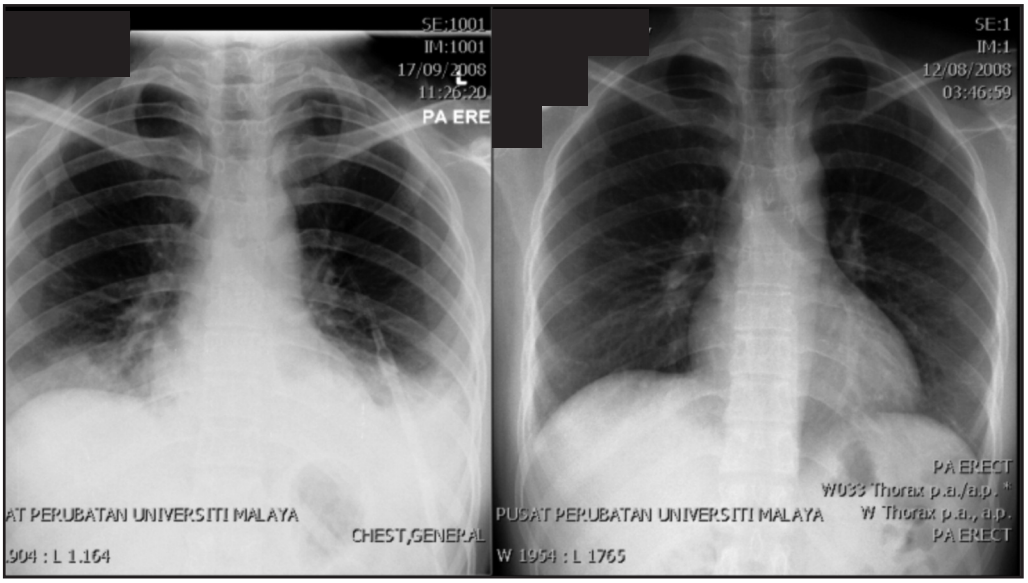

Fig. 1: Initial chest radiograph (12/8/08) which was normal subsequently showed consolidation in both lung bases in association with a left-sided pleural effusion on several chest radiographs done later (17/9/08).

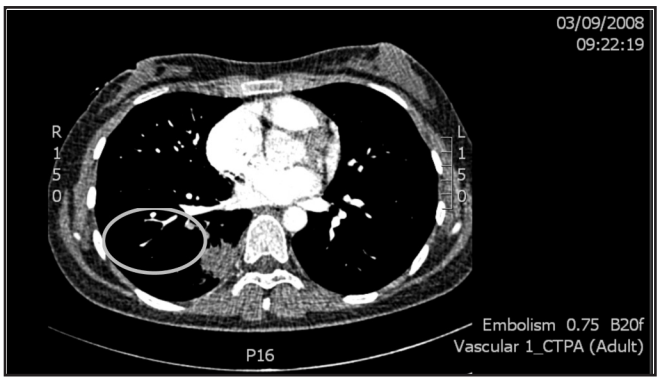

Fig. 2a: CT pulmonary angiogram shows filling defects in the subsegmental pulmonary arteries of the right lower lobe, confirming the diagnosis of pulmonary embolism; with consolidation in the corresponding region.

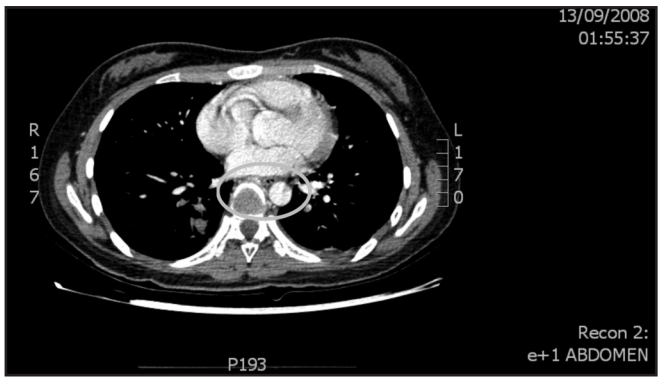

Fig. 2b: New filling defects noted in the left subsegmetal pulmonary arteries on a later CT scan.

hyperaemic optic discs. CT scan of the brain was normal, giving an impression of a transient ischaemic attack. A brain MR angiogram was also normal, with no evidence of intracranial vasculitis.

DISCUSSION

This young lady with underlying SLE had been on treatment for the past one year prior to the chest symptoms. In view of her underlying disease, SLE vasculitis/ interstitial lung disease was considered as an important differential diagnosis. Being in a region where tuberculosis (TB) is still endemic, pulmonary TB is another possibility, especially since she was on immunosuppressive medications. Nonetheless, recurrent pulmonary embolism was highly probable based on the nature of her clinical presentation.

The confirmatory diagnosis of secondary APS was further reinforced when she also developed renal and common iliac vein thromboses, in association with a positive lupus anticoagulant antibody (LA). Apart from that, involvement of the cerebral circulation resulting in the recent transient ischaemic attack should also be noted.

The mainstay of treatment for patients with positive antiphospholipid antibodies (aPL) is with anticoagulant or antiplatelet therapy, depending on the risk of thrombosis. Khamashta *et al.*[2] in 1995 suggested that treatment with high-intensity warfarin (INR≥3) was significantly more effective in preventing further thrombotic events than low-intensity warfarin (INR<3). However, two later randomised trials[3,4] have shown that high-intensity warfarin is not better than moderate-intensity warfarin (INR 2-3) in preventing recurrent venous thrombosis. Compared with placebo or untreated

control, moderate-intensity warfarin reduces the risk of recurrent venous thrombosis by 80-90% irrespective of the presence of aPL[5].

The optimal duration of anticoagulation for prevention of recurrent thrombosis in patients with aPL is still unknown. Certainly, the rate of recurrence of venous thrombosis was highest (1.30 events per patient-year) during the first six months after cessation of warfarin therapy[2]. The reported recurrence rate[2] was 69%, over a 10-year retrospective study. Prospective studies of patients with APS receiving antithrombotic therapy reported an incidence of recurrent thrombosis of 3% to 24% per year[3,4]. Thus, the general consensus favours treating patients with APS and venous thrombosis with an indefinite duration of anticoagulation.

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