Case Report

Massive pulmonary hemorrhage in a Saudi female with primary antiphospholipid syndrome

Mohamed S. Al-Hajjaj, *FRCP(C), FCCP.*

ABSTRACT

The antiphospholipid syndrome is characterized by the presence of antiphospholipid antibodies and the association of protean clinical manifestations as a result of both venous and arterial thrombosis. Because diffuse alveolar hemorrhage leading to acute respiratory failure is a rather unusual complication of antiphospholipid antibodies, this diagnosis may be overlooked or its manifestations are attributed to another disease. Presented here is a young Saudi female with primary antiphospholipid syndrome who recovered after a stormy clinical course of acute respiratory failure in the intensive care unit.

Keywords: Antiphospholipid, alveolar, hemorrhage, respiratory failure.

Saudi Medical Journal 2000; Vol. 21 (8): 777-779

Expectoration of blood (hemoptysis) is a serious albeit non-specific, pulmonary symptom that deserves a thorough diagnostic work-up.[1] Patients with diffuse alveolar hemorrhage (DAH) presenting usually with hemoptysis pose a real diagnostic challenge for the treating physician because of the heterogenous etiologies involved.[2] In the case presented, a relatively rare cause of pulmonary hemorrhage (antiphospholipid syndrome) was reached after exhaustive investigations. In the antiphospholipid syndrome, DAH leading to acute respiratory failure is a rather unusual complication of the syndrome, making it is possible that the diagnosis is overlooked or its manifestations are attributed to another disease.[3] The primary type of antiphospholipid syndrome (APS) (i.e. without underlying disease e.g. systemic lupus erythematosis) is now recognized to be much more common than the secondary type. It is characterized by widespread venous and arterial thrombosis predisposed by the presence of antiphospholipid antibodies.[4] As in the case presented, a patient with primary APS may develop massive pulmonary hemorrhage leading to respiratory failure. However the response to high-dose intravenous glucocorticosteroid treatment was dramatic.

Case Report. A 27 year-old Saudi non-smoker, single female was referred and admitted electively for the work-up of hemoptysis. Her first episode occurred 2 years before this presentation, and was followed by recurrent hemoptysis of variable amounts of 10-50 cc of fresh blood. Eleven months before presentation she had deep vein thrombosis in the left lower limb then in the right lower limb. There was a history of mild shortness of breath but no chest pain, joint pains, hematemesis or melena.

From the Medical Department, College of Medicine, King Saud Unversity, Riyadh, Kingdom of Saudi Arabia.

Received 26th February 2000. Accepted for publication in final form 26th April 2000.

Address correspondence and reprint request to: Dr Mohamed S. Al-Hajjaj, Associate Professor & Consultant Pulmonologist, Medical Department (38), College of Medicine, King Saud University, PO Box 2925, Riyadh 11461, Kingdom of Saudi Arabia. Tel. +966 1 467 1528. Fax: +966 1 467 9496. E-mail: mshajjaj@ksu.edu

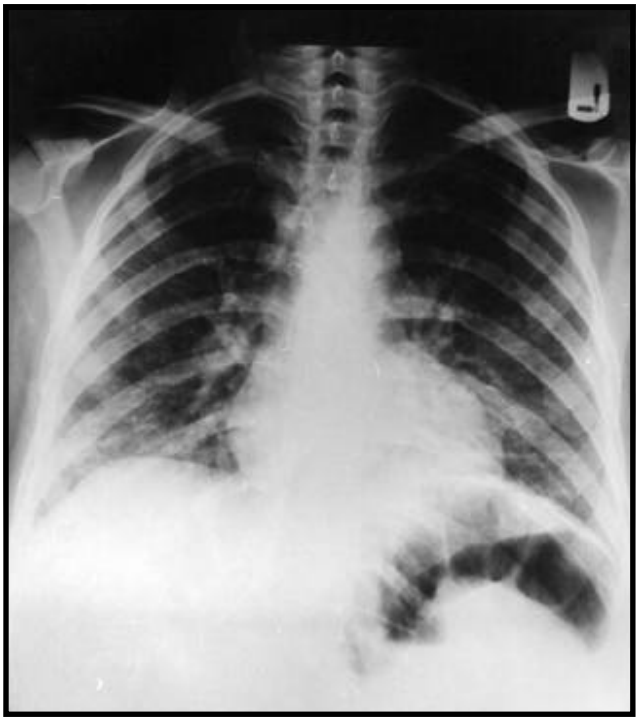

Figure 1 - A chest radiograph showing bilateral air-space disease.

She had been on a high dose of Coumadin. On examination, she was pale and tachypneic, but there was no clubbing, telangiectasia or joint disease. Coarse crackles were present in the chest bilaterally. Both lower limbs were swollen and tender.

Hemoglobin was 94 g/L, mean corposcular volume (MCV) 71 (80-94), mean corpuscular hemoglobin (MCH) 25 (27-32), platelets 148 x 10^9/L, erythrocyte sedimentation rate (ESR) 40 mm/hr, Prothrombin Time (PT) 19.4 sec, Activated Partial Thromboplastin Time (APTT) 53 sec, International normalized ratio (INR) 1.3, Fibrinogen assay 4.3 g/L, Protein S activity 38% (65-140%), Protein C, anti-thrombin III activity, and factor XIII were normal. Rheumatoid factor, anti-nuclear antibodies (ANA), anti-deoxyribonucleic acid (DNA) were negative. Pulmonary function tests showed a restrictive pattern and decreased diffusion of lung carbon monoxide (DLCO), [forced vital capacity (FVC) = 2.28L (66% predicted), forced expiratory volume in one second (FEV_1) = 2.04L (70%), Ratio = 89%, total lung capacity (TLC) = 2.91L (68%) and DLCO = 10.6 ml/min/mmHg (39%)]. Doppler ultrasound and a venogram of the legs confirmed extensive ileo femoral deep vein thrombosis and a ventilation/perfusion V/Q scan showed low probability of pulmonary embolism (matched ventilation/perfusion defect in the right base and matched irregularity of ventilation and perfusion in the rest of the right lung and in the left lung indicating parenchymal disease). Bronchoscopy showed fresh blood in the airways with structural abnormality. Chest radiography (Figure 1) showed bilateral air-space disease and computerized tomography (CT) scanning (Figure 2) showed diffuse ground glass opacification in both lung fields. A video-assisted thoracoscopic biopsy revealed pulmonary hemosiderosis, marked intra-alveolar fresh and old hemorrhage with numerous hemosiderin-laden macrophages and organizing thrombi in small blood vessels but no vasculitis (Figure 3). The patient was diagnosed to have protein S deficiency, extensive deep vein thrombosis, and secondary pulmonary hemosiderosis. She was treated with low molecular weight heparin (has a lower risk of bleeding), persantin, iron and folic acid supplements and was discharged when her clinical condition improved.

Four months later, the patient was re-admitted with recurrent hemoptysis, progressive shortness of breath, and severe hypoxia. Investigations at this time showed iron deficiency anemia with a hemoglobin of 9.6 g/L. Chest radiography showed bilateral air-space consolidation and lung CT scanning showed diffuse ground glass opacification

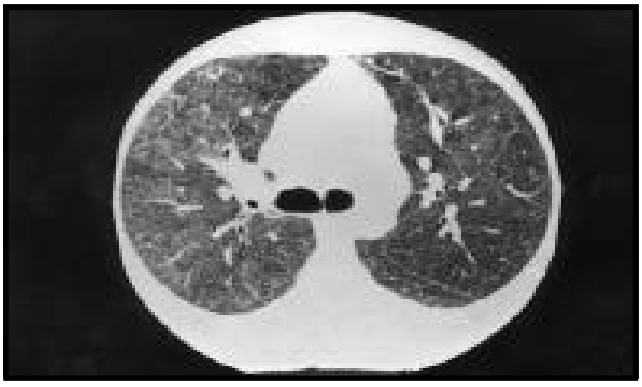

Figure 2 - CT scan of chest parenchymal window showing diffuse ground glass appearance of pulmonary hemorrhage.

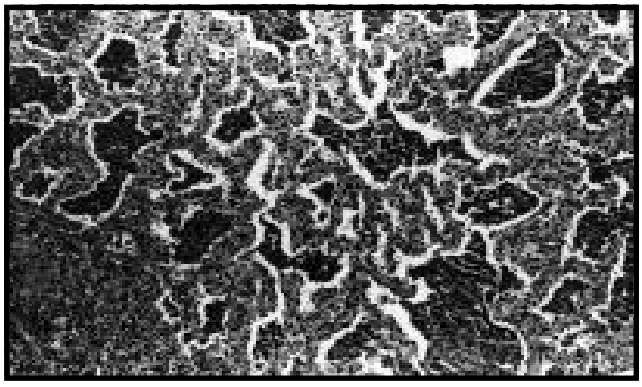

Figure 3 - Pulmonary hemosiderosis. Numerous hemosiderin laden macrophages are seen within alveolar lumina. (H & E stain x 100).

of both sides. Arterial blood gases on admission were: PH: 7.42, PO_2 37.5 mmHg, PCO_2 35 mmHg and O_2 saturation was 68%. By this time the results of a previously sent blood tests were obtained. Antiphospholipid antibody (IgG): > 100 (N < 12 U/ml, antiphospholipid antibody (IgM) < 6 (N 16 U/ml). Venereal disease research laboratory (VDRL) and lupus anticoagulant were positive. A diagnosis of antiphospholipid syndrome (APS) was made and the patient was transferred to the intensive care unit where she was intubated, ventilated and treated with supportive therapy and intravenous methylprednisolone 200mg daily and cyclophosmanide 750 mg. Subsequently hemoptysis abated and the patient had steady improvement with clearing of the chest radiograph. She was later discharged and given maintenance immuno-suppressive therapy.

Discussion. Antiphospholipid syndrome is a relatively newly recognised syndrome of clinical manifestations and complications of venous and arterial thrombosis predisposed by the presence of antiphospholipid antibodies (anticardiolipin antibodies and lupus anticoagulant).[5] The patient had a primary type of the disease because there was no evidence of systemic lupus erythromatosis or other collagen vascular disease.[6] Pulmonary complications of APS has been reviewed by Asherson and Cervera.[7] They doubted the association of intra-alveolar pulmonary hemorrhage (PH) and APS. However more recently, several case reports (including the case presented) had shown that although pulmonary hemorrhage is not common in the APS, nevertheless, its presence should alert the treating physician to pursue the diagnosis of APS.[8,9]

The exact mechanism by which hemorrhage occurs is unknown. However, it is possible that the antiphospholipid antibodies are directed against a variety of plasma proteins and proteins expressed on the surface of platelets or vascular endothelial cells leading to microvascular thrombosis with or without capillaritis.[10,11] Clinically, the diffuse nature of the pulmonary hemorrhage in this patient which led to acute respiratory failure did simulate acute respiratory distress syndrome (ARDS). The good response to treatment and the quick recovery as well as the unexplained drop in hemoglobin points to the correct diagnosis of PH rather than ARDS. Although ARDS has been reported as a complication of APS. The possibility of intra-alveolar bleeding from APS should always be considered in the differential diagnosis of unexplained ARDS, because the outcome of the treatment as in this case, is much more favourable than ARDS.[12]

Treatment of diffuse alveolar hemorrhage in APS has not been definitely established. However, based on previous case reports, steroids are effective and should probably be given intraparentally in the acute phase of the disease.[9,10] Cyclophosphamide with or without plasmapheresis has been used and appears to be useful particularly in severe cases.[13] In many patients, like the case presented, simultaneous presence of bleeding and thrombosis occurs. The recommended approach for treatment in this situation is to withhold anticoagulation where there is active bleeding but to re-institute therapy as soon as the pulmonary status had improved.[14]

References

1. Strickland B. Investigating haemoptysis. Br J Hosp Med 1986; 35: 242, 246-251.
2. Hillerdal G, Hagg A, Licke G, Wegenius G, Scheibenpflug L. Intra-alveolar haemorrhage in the anticardiolipin antibody syndrome. Scand J Rheumatol 1991; 20: 58-62.
3. Gertner E. Diffuse alveolar hemorrhage in the antiphospholipid syndrome: spectrum of disease and treatment. J Rheumatol 1999; 26: 805-807.
4. Kandiah DA, Sali A, Sheng Y, Victoria EJ, Marquis DM, Coutts SM et al. Current insights into the "antiphospholipid" syndrome: clinical, immunological, and molecular aspects. Adv Immunol 1998; 70: 507-563.
5. Petri M. Pathogenesis and treatment of the antiphospholipid antibody syndrome. Med Clin North Am 1997; 81: 151-177.
6. Asherson RA, Khamashta MA, Ordi-Ros J, et al. The "primary" antiphospholipid syndrome: major clinical and serological features. Medicine (Baltimore) 1989; 68: 366-374.
7. Asherson RA, Cervera R. Review: Antiphospholipid Antibodies and the Lung. J Rheumatol 1995; 22: 62-66.
8. Kerr JE, Poe R, Kramer Z. Antiphospholipid Antibody Syndrome Presenting as a Refractory Noninflammatory Pulmonary Vasculopathy. Chest 1997; 112: 1707-1710.
9. Maggiorini M, Knoblauch A, Schneider J, Russi EW. Diffuse microvascular pulmonary thrombosis associated with primary antiphospholipid antibody syndrome. Eur Respir J 1997; 10: 727-730.
10. Leatruman JW, Davies SF, Hoidal JR. Alveolar hemorrhage syndromes: diffuse microvascular lung hemorrhage in immune and idiopathic disorders. Medicine (Baltimore) 1984; 63: 343-361.
11. Sammaritano LR, Gharavi AE, Lockshin MD. Antiphospholipid Antibody Syndrome: Immunologic and Clinical Aspects. Semin Arthritis Rheum 1990; 20: 81-96.
12. Ghosh S, Walters HD, Joist JH, Osborn TG, Moore TL. Adult respiratory distress syndrome associated with antiphospholipid antibody syndrome. J Rheumatol 1993; 20: 1406-1408.