Severe Primary Antiphospholipid Syndrome

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Abstract

Antiphospholipid syndrome (APS) is characterised by recurrent venous or arterial thrombosis and/or fetal losses. In APS, the homeostatic regulation of blood coagulation is altered, however, the mechanism of thrombosis is not yet defined and it has varied manifestations. Deep vein thrombosis with or without pulmonary embolism is the most common manifestation followed by arterial occlusion of cerebral, coronary and other arteries including subclavian, retinal, renal and pedal arteries. We report a case of a 42 years old female, with severe primary APS, who presented with symmetrical peripheral gangrene, an uncommon presentation and was treated successfully.

INTRODUCTION

Antiphospholipid syndrome (APS) is an autoimmune disorder, characterised by recurrent venous or arterial thrombosis and/or fetal losses associated with characteristic laboratory abnormalities such as persistently elevated levels of anticardiolipin antibodies, antiphosphatidylserine or their associated plasma proteins, predominantly beta-2 glycoprotein I, or evidence of a circulating anticoagulant. The syndrome occurs in isolation (primary) or in association with connective tissue diseases (secondary), particularly systemic lupus erythematosus. We report a case of 42 years old female with severe primary APS. She presented with symmetrical peripheral gangrene (SPG), along with cardiac involvement.

CASE SUMMARY

A 42 years old female non smoker, presented with complaints of numbness of the digits of both upper and lower limbs followed by progressive blackish discolouration since 2 months. She had similar complaints during previous winters. There was history of abortion (>12 weeks gestation). There was no history of episodic bluish discolouration of digits, difficulty in swallowing, fever, breathlessness, joint pain, hemoptysis or prolonged drug intake. On examination, her pulse was 100/min, regular. All upper limb pulses were normally palpable, bilateral popliteal, dorsalis pedis and posterior tibials were feeble. Blood pressure was 118/76 mmHg. No carotid or renal bruit was heard. On local examination, there was blackish discolouration of middle finger of right upper limb, index and little fingers of left upper limb, fourth and fifth toes of right lower limb and all toes of left lower limb along with a ruptured blister over dorsum of left foot (Fig. 1). There was mild hepatosplenomegaly Rest of the systemic examination were normal.

Investigations revealed, haemoglobin of 10.6 gm/dl, total leucocyte count 5700/mm³, differential leucocyte count P<sub>1</sub>↓↓, L<sub>1</sub>↑↑↑↑↑↑↑, platelet count 1,60,000/mm³ and ESR 50 mm in first hour. Random blood sugar and renal function tests were normal. Urine examination revealed trace protein. 24 hrs urinary protein was 144 mg. Total serum bilirubin was 0.6 mg/dl, serum alanine aminotransferase 61U/l, serum aspartate aminotransferase 66U/l, alkaline phosphatase 253 U/l, total serum protein 7.8 gm/dl (albumin 3.4 gm/dl), prothrombin time 15 sec (control=13 sec), and activated partial thromboplastin time (aPTT) of 44 sec (control=26 sec). Fibrinogen and D-dimer levels were normal. X-ray chest showed cardiomegaly. Ultrasound abdomen was suggestive of mild hepatosplenomegaly. RF, LE cell, CRP, HBsAg, anti-HCV and malarial antigen were negative. Blood and urine cultures were sterile. ELISA for HIV was non reactive. VDRL was reactive (1:4 dilution). Treponema pallidum haemagglutination test, direct and indirect Coombs test were negative. ANA was positive (titre 1:40); anti-dsDNA, p and c-ANCA were negative. ECG showed bifascicular block (first degree heart block with RBBB) with generalised T wave inversion. Echocardiographic study showed normal cardiac valves, RA, RV dilatation, normotensive tricuspid regurgitation (RVSP - 30 mmHg), global hypokinesia with ejection fraction of 32%. There was no evidence of pericardial effusion, intracardiac thrombus or pulmonary hypertension. Cardiac enzymes were normal. Carotid intima media thickness were normal on both sides without any evidence of thrombus or plaque. Arterial colour Doppler of both upper and lower limbs showed normal flow. Anticardiolipin antibodies were positive, kaolin clotting time (KCT) and aPTT were prolonged (Table 1). She also
had cryoglobulinemia.

Diagnosis of severe primary APS was entertained and treated with low molecular weight heparin (LMWH) followed by warfarin, prednisolone, aspirin and pentoxyphylline to which she showed gradual response. During follow-up period of six months her gangrenous part of the digits got autoamputated and at present she is doing well on aspirin, warfarin and prednisolone.

**DISCUSSION**

This patient of severe primary APS, is interesting as she presented with symmetrical peripheral gangrene along with cardiac involvement (global hypokinesia with normotensive tricuspid regurgitation). She showed gradual response to LMWH, warfarin, prednisolone, aspirin and pentoxyphylline.

Diagnostic criteria for APS were revised in 2006, according to which at least one clinical criterion and one laboratory criterion must be present for a patient to be classified as having APS. Virtually any organ and vessel (artery, vein) can be involved. APS usually presents with digital ulcers, gangrene and sometimes mimics Buerger’s disease, however SPG as a presenting manifestation is reported uncommonly.

SPG is a rare clinical condition manifesting with acral ischemic damage in two or more extremities in absence of obstruction or vasculitis of the relevant artery, infection like streptococcus pneumoniae, meningococcus, falciparum malaria and viral gastroenteritis being the most common cause SPG has been reported in DIC, low cardiac output states, Hodgkin’s disease, systemic lupus erythematosus, use of vasopressors, reaction to drugs (sulphamethazine, penicillin), ergotism, acquired hemolytic anemia, decreased levels of protein C and rarely in association with APS.

Treatment plan should be individualized depending on the aggressiveness of disease and type of complications as no modality of treatment is universally accepted in managing SPG. Intravenous nitroprusside, prostaglandins (e.g. epoprostenol), topical nitroglycerine ointment, papavarine, reserpine, streptokinase, dextran, hyperbaric oxygen and sympathetic blockers have been tried with little success. The primary treatment of this condition includes treating the underlying cause.

In general treatment regimens for APS must be individualized according to the patient’s current clinical status and history of thrombotic events. For severe or refractory cases, a combination of warfarin and aspirin may be used. Corticosteroids and intravenous immunoglobulins appears beneficial in severe APS including catastrophic APS. Treatment for significant thrombotic events in patients with APS is generally lifelong. The present case is presented to highlight the importance of early recognition, diagnosis and treatment of an uncommon disease to prevent high morbidity and mortality.

**REFERENCES**