INTRODUCTION

Thromboangiitis obliterans (TAO), or Buerger's disease, is a vascular occlusive disease associated with cigarette smoking. It typically affects medium sized vessels of extremities. Basic pathology of TAO is described to be endothelial activation with highly inflammatory intraluminal thrombosis preserving internal elastic membrane. Cryoglobulins are immunoglobulins that precipitate in the cold and dissolve on re-warming. Cryoglobulinemic vasculitis is a typical small vessel disease associated with cryoglobulinemia commonly bearing typical purpuric skin lesions. An association of TAO with cryoglobulinemia is not reported yet. We report a 34-year-old male heavy cigarette smoker seen for extremity pain and cyanosis of left little finger along with skin rashes characteristic of small vessel disease. Initial presentation of his symptoms at winter and unusual purpuric skin lesions led to search for cold-agglutinating globulins in his plasma. He had severe cryoglobulinemia while the other laboratory tests were normal. TAO associated with cryoglobulinemia merges as a possibility.

CASE REPORT

A 34-year-old male with history of 20 pack/year cigarette smoking was referred for severe ischemic pain in extremities especially feet. He suffered from myalgia, fatigue, coldness of fingers and blue discoloration of left little toe for 1 month. He denied Raynaud phenomenon. Physical examination, vital signs and general physical examination were unremarkable. Coldness of left foot and cyanosis of left little toe and absent left posterior tibialis and dorsalis pedis arterial pulses were evident. Crops of skin ischemic areas were observed in medial aspect of his left foot (Figure 1a). There were splinter hemorrhages in several nail beds of the fingers and superficial phlebitis on his right arm. Alen test was negative in upper limbs.

Ultrasonic investigations of internal organs including transesophageal echocardiography were unremarkable. Laboratory tests including CBC, ESR, C-reactive protein, fasting blood sugar, lipid profile, rheumatoid factor, anti-cardiolipin profile, anti-CCP, ANA, ANCA (c,p), serum protein electrophoresis, complement components, anti-HIV-1-antibody, HBVs antigen, HCV-antibody, along with liver and kidney function tests had normal results. Posteroanterior chest radiograph was also normal. However, Magnetic Resonance Angiography (MRA) of lower extremities showed cut-off in his left posterior and anterior tibialis along with mild tortuosity in common peroneal arteries (Figure 1b). Cryoglobulins was assayed due to onset of his vascular symptoms in a cold season that showed highly positive results after two days (Figure 2).

The patient was asked to stop smoking and mini-pulse of 500 mg intravenous prednisolone, 1000 mg cyclophosphamide, oral prednisolone 30 mg/d, diltiazem 30 mg BID, heparin 1000 U/h, warfarin 5 mg/d morphine
2 mg/TID, pentoxifylline mg 400 mg/tid and iloprost (2 ng/kg/minute, 6 hourly for 21 days) were started with short-term favorable response. Epidural bupivacaine infusion was given because of intractable pain and excessive morphine requirement. The patient refused further invasive diagnostic and therapeutic. Hospitalization in another center resulted in below knee amputation after 10 days. Revision of necropsy results of amputated tissue showed intraluminal inflammatory thrombi without significant infiltration of vessel wall typical of thromboangiitis obliterans. Diagnosis of TAO was based on the Olin criteria.

DISCUSSION

Clinical features of TAO include claudication of the affected extremity, Raynaud phenomenon and superficial vein thrombophlebitis. Important physical findings include decreased or absent pulses distal to the obstruction, reduced skin temperature. Pallor or cyanosis is frequent. Claudication is usually limited to the calves and feet or the forearms and hands. Trophic nail changes, painful ulcerations and gangrene may develop at the tips of the fingers or toes. Physical examination shows normal brachial and popliteal pulses but reduced or absent more peripheral pulses. Arteriography is helpful in making the diagnosis. Smooth, tapering segmental lesions in the distal vessels are characteristic but not constant feature as are collateral corkscrew vessels at sites of vascular occlusion.7 Corkscrew pattern reported to be seen in 27% of TAO patients. Proximal atherosclerotic disease is usually absent as in our patient. The diagnosis can be confirmed by excisional biopsy and pathology examination of an involved vessel after amputation. Clinical findings of this case were consistent with TAO and fulfilled the Olin criteria.

In the initial stages of TAO, polymorphonuclear leukocytes infiltrate the walls of the small and medium-sized arteries and veins. The internal elastic lamina is preserved (which differentiates it from other classic vasculitides) and a cellular, inflammatory, thrombus develops in the vascular lumen. As TAO progresses, mononuclear cells, fibroblasts, and giant cells replace the neutrophils. Later stages are characterized by perivascular fibrosis, organized thrombus and recanalization.

The basis for treating TAO is smoking cessation but this goal is almost never achieved. Most reports of anti-coagulation, anti-platelet and anti-inflammatory drugs are disappointing with a few exceptions.9 Use of synthetic prostaglandin-I2 (Ilomedin) is reported to be of benefit by some authors.9 Autologous bone marrow mononuclear cell transplantation showed benefit in several studies but needs confirmation.10 Treatment of cryoglobulinemic vasculitis depends on the type of cryoglobulin, underlying disease and severity of symptoms. Some patients with cryoglobulinemia suffer from mild, recurrent crops of lower extremity purpura that require no therapy. More extensive vasculitis associated with autoimmune diseases or essential cryoglobulinemia may respond to prednisone, cyclophosphamide or both.

A causal relationship between TAO and cryoglobulinemia could not be proved but it might be the case.

REFERENCES