Case Report

Thromboangiitis Obliterans (Buerger’s Disease): A Rare Case

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Abstract

Buerger’s disease or thromboangiitis obliterans is an inflammatory, non-atherosclerotic process that affects small and medium-sized vessels and nerves at the extremities. It is manifested by pain and claudication of the fingers, evolving into necrosis and ulceration. Amputation is a reality for many patients.

Buerger’s disease is rare, and the pathophysiological mechanisms that trigger it are not clear. However, there has been good progress in understanding the pathogenesis of the disease and there is a strong association with smoking, immunity, disorders of coagulation and heredity. This is a clear example that exposure to tobacco contributes to the onset and worsening of the disease. Smoking cessation and vasodilator therapy appear to be the best therapeutic strategy.

ABBREVIATIONS

TAO: Thromboangiitis Obliterans; ASO: Ateriosclerosis Obliterans

INTRODUCTION

Thromboangiitis obliterans (TAO) is a segmental occlusive inflammatory condition of arteries and veins, characterized by thrombosis and recanalization of the affected vessel [1]. It is a non-atherosclerotic inflammatory disease affecting small and medium sized arteries and veins of the upper and lower extremities [2]. The disease is found worldwide, but the highest incidence of thromboangiitis obliterans occurs in the Middle and Far East [3]. The prevalence of the disease among all patients with peripheral arterial disease ranges from values as low as 0.5 to 5.6% in Western Europe to values as high as 45 to 63% in India, 16 to 66% in Korea and Japan, and 80% among Jews of Ashkenazi ancestry living in Israel. Part of this variation in disease prevalence may be due to variability in diagnostic criteria [4,5]. The clinical criteria include: current or recent history of tobacco use; presence of distal-extremity ischemia indicated by claudication, pain at rest, ischemic ulcers or gangrenes and documented by non-invasive vascular testing; exclusion of autoimmune diseases, hypercoagulable states and diabetes mellitus; exclusion of a proximal source of emboli by echocardiography or arteriography; consistent arteriographic findings in the clinically involved and non-involved limbs. The only therapy clearly shown to prevent amputation is the complete abstinence of tobacco [6]. Patients may present with claudication of the feet, legs, hands and arms. The pain typically begins in the extremities, but may radiate to more central parts of the body. As the disease progresses, typical calf claudication and eventually ischemic pain at rest and ischemic ulcerations on the toes, feet or fingers may develop [7].

Although Buerger’s disease most commonly affects the small and medium-sized arteries and veins in the arms, hands, legs and feet, it has been reported in many other vascular beds. There are case reports of involvement of the cerebral and coronary arteries, aorta, intestinal vessels, and even multiple-organ involvement. When TAO occurs in unusual locations, the diagnosis should be made only when histopathological examination identifies the acute-phase lesions [8].

CASE PRESENTATION

A 72-year-old man, admitted to the Emergency Department with Raynaud phenomenon with four months of evolution, associated with recurrent edema of the second and third fingers of the left hand. The patient was a construction worker and smoker 1 pack per day since age 16.

He denied known diseases such as Hypertension, Diabetes Mellitus and Dyslipidemia. No usual medication and no allergies.

At physical examination with heliotropical rash, with capillary glycemia of 120 mg / dl and Blood pressure (145/99 mmHg).

In the analytical study performed, hemogram, thyroid function, renal function, liver function without changes and with parameters of infection negative.

Autoimmune and cancer research was negative.
The differential diagnoses were: systemic embolisation or thrombophilia, Buerger’s disease, vasculitis, atherosclerotic arteriopathy (less likely in this age group) and systemic lupus erythematosus-related vasculitis.

The study for thrombophilia and immunology was negative. A possible source of systemic embolism was excluded by transthoracic echocardiogram and carotid-vertebral Doppler. The viral (HIV, hepatitis B virus and hepatitis C virus) and syphilitic serologies were negative. The thoracoabdominopelvic CT was unremarkable.

Capillaroscopy revealed changes compatible with primary Raynaud’s phenomenon. Smoking cessation advised.

Reassumed smoking habits and at the end of two months admitted again to the Emergency Department with necrotic plaques at the level of the fingers. Assumed Buerger disease after diagnostic angiography. Anti-ischemic and vasodilator therapy was optimized without improvement, with Vascular Surgery and Plastic Surgery, opting for amputation of the fingers.

No specific laboratory test for diagnosing Buerger’s disease is available.

Unlike other types of vasculitis, in patients with Buerger’s disease the acute-phase reactions (such as the erythrocyte sedimentation rate and C-reactive protein level) are normal [2].

Recommended tests to rule out other causes of vasculitis include a complete blood cell count; liver function tests; determination of serum creatinine concentrations, fasting blood sugar levels and sedimentation rate; tests for antinuclear antibody, rheumatoid factor, serologic markers for CREST (calcinosis cutis, Raynaud phenomenon, sclerodactyly and telangiectasia) syndrome and scleroderma, and screening for hypercoagulability. Screening for hypercoagulopathy, including antiphospholipid antibodies and homocystein in patients with Buerger’s disease, is recommended.

If a proximal source of embolization is suspected, transthoracic or transesophageal echocardiography and arteriography should be performed. Angiographic findings include severe distal segmental occlusive lesions.

While the clinical criteria of TAO are relatively well defined, there is no consensus on the histopathological findings [8]. It is particularly difficult to distinguish morphologically TAO from atherosclerosis obliterans (ASO). Histopathological findings are also known to vary according to the duration of the disease. The findings are most likely to be diagnostic in the acute phase of the disease, most commonly at biopsy of a segment of a vessel with superficial thrombophlebitis [7]. Other histopathological phases, such as intermediate (subacute) and end-state (chronic) phases, have been described.

**DISCUSSION**

Buerger’s disease is rare, and the pathophysiological mechanisms that trigger it are not clear. However, there is a strong association with smoking, immunity, disorders of coagulation and heredity.

One hundred years after the original description by Leo Buerger, the aetiology of the disease remains unknown [9,10]. However, use of or exposure to tobacco is central to the initiation and progression of the disease [11].

The clinical criteria for TAO, edited by Olin in 2000 include: current or recent history of tobacco use; presence of distal extremity ischemia, indicated by daudication, pain at rest, ischemic ulcers or gangrenes and documented by non-invasive vascular testing; exclusion of autoimmune diseases, hypercoagulable states and diabetes mellitus; exclusion of a proximal source of emboli by echocardiography or arteriography; consistent arteriographic findings in the clinically involved and non-involved limbs [12].

Superficial thrombophlebitis and Raynaud’s phenomenon occurs in approximately 40% of patients with TAO [12]. Migrating phlebitis (phlebitis saltans) in young patients is therefore highly suggestive of TAO and may parallel disease activity.

TAO may begin with joint manifestations such as recurrent episodes of arthritis of large joints, with transient, migratory single-joint episodes accompanied by local signs of inflammation. The wrists and knees are the most frequently involved joints. The arthritis is non-erosive. Joint problems precede the diagnosis of TAO by about 10 years on average.

TAO usually begins with ischemia of the distal small arteries and veins. As the disease progresses, it may involve more proximal arteries. Large arteries involvement is unusual and rarely occurs in the absence of small-vessel occlusive disease. However, it has been reported in many other vascular beds. There are case reports of cerebral, coronary, renal, mesenteric, pulmonary, iliac and aorta arteries involvement; even multiple-organ involvement may exist.

TAO is more common in males (male-to-female ratio, 3:1); its incidence is believed to be increasing among women, and this trend is postulated to be due to the increased prevalence of smoking among women. It has been postulated that TAO is an ‘autoimmune’ reaction triggered by some constituents of tobacco [7,8,9]. Patients with the disease show hypersensitivity to intradermally injected tobacco extracts, have increased cellular sensitivity to types I and III collagen, elevated serum antiendothelial cell antibody titres and impaired peripheral vasculature endothelium-dependent vasorelaxation. Increased
prevalence of HLA-A9, HLA-A54 and HLA-B5 is observed in these patients, which suggests a genetic predisposition to the disease.

Currently, there is no specific treatment for TAO. Absolute discontinuation of tobacco use is the only strategy proven to prevent the progression of Buerger’s disease. Smoking as few as 1 or 2 cigarettes daily, using chewing tobacco, or even using nicotine replacements may maintain the disease activity. Selective cannabinoid receptor antagonists, such as rimonabant, which shows promise as a treatment for helping patients to stop smoking, open up interesting new perspectives for this disease strongly related to tobacco use [10,11].

Prostaglandins, in particular the intravenous iloprost, represents one of the more valid treatments in the TAO. It has been shown to be effective in improving symptoms, accelerating resolution of distal extremity trophic changes, and reducing the amputation rate.

Recent studies have suggested that vascular damage caused by endothelin-1 may trigger peripheral arterial occlusive disease. The anti-inflammatory, antifibrotic and selective vasodilatory properties of bosentan (endothelin-1 receptor antagonist) have been shown to alleviate pain at rest and reduce the size of ischaemic ulcers caused by damage to the microcirculation.

This is a clear example that exposure to tobacco contributes to the onset and worsening of the disease. Smoking cessation and vasodilator therapy appear to be the best therapeutic strategy. It is therefore essential that patients diagnosed with Buerger’s disease stop smoking immediately and completely in order to prevent progression of the disease and avoid amputation. Despite the very strong correlation between smoking cessation and the decline of clinical manifestations of TAO, patients may continue to have claudication or Raynaud’s phenomenon after complete cessation of tobacco usage [2].

The new paradigm of an immunopathogenesis of Buerger’s disease might improve knowledge and prognosis in the future. To achieve better clinical results, integrated care in multidisciplinary and trans-sectoral teams with emphasis on lifestyle changes such as smoking cessation, pain control, wound management, and social care by professionals, social workers, and family members is necessary.

REFERENCES