Thromboangiitis Obliterans - Case Report

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Rezumat

Trombangecta obliterantă - prezentare de caz

Trombangecta obliterantă (boala Buerger) este o boală inflamatorie a arterelor și venelor mici ale extremităților care determină tromboza și obstrucția parțială sau totală a vaselor. Afectarea este predominantă la sexul masculin cu debut sub vârsta de 40 de ani. Particularitatea cazului nostru este prezentarea unei paciențe în vârstă de 62 ani, veche fumătoare, cu trombangectă obliterantă neglijată și debut în jurul vârstei de 48 de ani. Aspectul clinic, cu afectare concomitentă și severă atât a membrelor inferioare, cât și a celor superioare, precum și tabloul arteriografic sunt deosebit de sugestive, subliniindu-se posibilitatea apariziei bolii Buerger și la sexul feminin.

Cuvinte cheie: trombangecta obliterantă, tabloul clinic, diagnostic, tratament

Abstract

Thromboangiitis obliterans (Buerger's disease) represents an inflammatory disease of limbs’ small arteries and veins causing vascular thrombosis, and partial or total obstruction. It affects mostly male gender aged < 40 years old. The peculiarity of our case is underlined by presenting a 62 years, chronic tobacco user and not compliant female patient known with thromboangiitis obliterans for almost 15 years. The arteriographic and clinical features with concomitant and sever affected upper and lower limbs are highly suggestive, emphasizing the possibility of Buerger's disease development even in female patients.

Key words: thromboangiitis obliterans, clinical features, diagnosis, treatment

Introduction

Thromboangiitis obliterans represents an inflammatory disease of small-sized arteries and veins, with secondary thrombosis and partial or total vessels obstruction, in the absence of or with minimal presence of atherosclerosis (1). It was first described by von Winiwarter, in 1879, but the terminology and detailed pathophysiological features were published by Leo Buerger, in 1908 (2).

The disease frequently affects the population of Middle East, South East Asia and Eastern Europe (1,2).

The etiology remains unclear, but several risk factors are strongly associated with the disease (1-4):

- heavy-smokers represent 99% of patients diagnosed
with Buerger’s disease, and cessation can slow down its progression. The direct toxic effect of carbon monoxide on vascular wall, the vasoconstrictive effect of nicotine and hypersensitivity to tobacco may represent the inducing mechanisms of the disease;
- male gender (over 90% of the patients are males);
- young age onset (20 – 40 years old) is typical and represents the differential characteristic to the atherosclerosis obliterans;
- a hypercoagulable state is present, but it is difficult to assess whether it is primary or a consequence of the disease;
- cellular hypersensitivity to collagen I and III (normal constituents of the arteries) (2,5);
- genetic predisposition is supported by increased prevalence of HLA-B5 and HLA-A9.

The pathophysiology, clinical aspects and laboratory tests of Buerger’s disease present unique features which determine the positive diagnosis, differentiate thromboangiitis obliterans of other possible causes and establish the adequate treatment management (Table 1) (1-7).

Case report

62 years old female patient was admitted in the Department of Nephrology and Dialysis for typical manifestations of low urinary tract infection (frequency, dysuria, and cloudy urines) that initiated some days before. Simultaneously, the patient complained of severe left forefoot pain, which onset happened several months ago and the need of daily use of nonsteroidal anti-inflammatory drugs (NSAIDs) and opioid analgesics (tramadol). Additionally, 4 years ago, our patient was diagnosed with hypertension, being under treatment with angiotensin-converting enzymes (ACEs) and thiazides. She was a heavy-smoker (over 20 years and 30 cigarettes per day). Without emphasizing the urinary disorder that was rapidly managed, we present the chronology of Buerger’s disease lesions.

The onset was at the age 45 – 48 with severe algic symptomatology of distal phalanges of both hands, but she was unable to specify when Raynaud phenomenon started. The patient self-administrated various NSAIDs and analgesics. During disease progression, initially distal phalanges ulcerations developed and later on bone necrosis and gangrene that led to loss of distal phalanges of index, middle and fourth finger (left hand), and distal phalanges of index and middle finger (right hand). When necrosis occurred, the patient self-treated using antiseptic bonding until lesions cicatrization. The first documented images were dated August 2011 (Fig. 1), when the patient wanted international help, declaring that she had consulted different physicians for several times without receiving an efficient treatment, except the symptomatic one.

In the last 3 years, additionally to the upper limbs lesions, nocturnal rest pain and intermittent claudication of lower limbs occurred, manifestations followed by bone necrosis and function loss. As in hands, these lesions presented scars, and distal phalanx absence of left hallux, and distal and middle phalanges amputation of right second digit could be also noticed (Fig. 2). Lesions progression continued until April 2012, when the patient referred to our Department complaining of low urinary tract infection and severe left forefoot pain; moist gangrene of the entire hallux was revealed (Fig. 3).

Table 1. Buerger’s disease

<table>
<thead>
<tr>
<th>Etiology</th>
<th>unknown</th>
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<tbody>
<tr>
<td>Risk factors</td>
<td>smoking, male gender, young adults (20 – 40 years old), hypercoagulable state, HLA-B5 and HLA-A9, Asian population</td>
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<td>Symptomatology</td>
<td>lower limbs intermittent claudication, upper limbs involvement, Raynaud phenomenon, superficial thrombophlebitis</td>
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<tr>
<td>Clinical exam</td>
<td>skin trophic disorders secondary to ischemia and gangrene development (toes and/or fingers amputations), migratory thrombophlebitis, great arteries permeability and pulse absence in small and medium-sized arteries</td>
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<tr>
<td>Laboratory tests</td>
<td>Doppler exam – distal artery blood flow stream absence</td>
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<td></td>
<td>Arteriographic hallmarks – distal small-sized artery obstruction; distal artery fragility; “corkscrew collaterals” surrounding the obstruction area; normal aspect of great vessels</td>
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<td>Positive diagnosis</td>
<td>young heavy-smoker male patient, presenting distal popliteal artery obstruction +/-, upper limbs involvement +/-, Raynaud phenomenon, recurrent superficial thrombophlebitis</td>
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<td>Differential diagnosis</td>
<td>atherosclerosis obliterator, vasculitis, arterial emboli</td>
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<tr>
<td>Treatment</td>
<td>medium forms – smoking cessation, vasodilator therapy, anticoagulants in case of thrombophlebitis association</td>
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<td>severe forms – regional sympathectomy, amputation of necrotic lesions</td>
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In addition, the clinical exam highlighted the lesions progression both in upper limbs (Fig. 4) and in right forefoot as well (Fig. 5).

Laboratory findings showed a slight increase of serum cholesterol (252 mg/dL), fibrin monomer test (FMT) ++++, erythrocyte sedimentation rate (ESR) = 50 mm/1h, C-reactive protein (CRP) = 3.04 mg/dL (normal range 0.01 – 1 mg/dL), fibrinogen = 6.39 mg/dL; the urinalysis indicated an alkaline pH, leukocyturia and no bacterial cultures. The bacterial culture of lesions showed the presence of Acinetobacter calcoaceticus-baumannii complex and Staphylococcus aureus. The other usual laboratory tests were in normal range. Chest X-ray and standard EKG were normal. No immune tests were performed.

**Diagnosis**

Although the clinical features were pathognomonic for a positive diagnosis (heavy-smoker patient, upper and lower
limbs involvement, presence of Raynaud phenomenon), arteriographic procedure was performed to establish lesions amplitude and therapy management. The findings were hallmark for thromboangiitis obliterans (Fig. 6): the bilateral permeability of iliac, femoral and popliteal arteries, bilateral occlusion of anterior and posterior tibial and peroneal arteries, “corkscrew collaterals” surrounding the obstruction. Only the infrarenal aorta presented minimal atheromatous plaques, without artery caliber decreasing.

**Treatment**

The patient was transferred to the Department of Vascular Surgery where left lumbar sympathectomy (L2 - L4) and partial left forefoot amputation were performed. 4 days postoperative, the evolution was favorable (Fig. 7). Perioperative, antibiotics therapy was initiated. On discharge the recommen-
Discussions

Buerger’s disease presents some typical unique characteristics (1,4,7-9):
- macroscopically: inflammation associated with thrombosis, without vessel wall necrosis, involving small and medium-sized arteries (sometimes even small and medium veins);
- microscopically: endothelial proliferation and intima vessel infiltration with lymphocytes and fibroblasts induce caliber lessening of affected blood vessels (acute phase). During the sub-acute phase, intraluminal thrombosis and microabscesses develop. The end-stage of the disease is characterized by fibrotic lesions.

In thromboangiitis obliterans there are no signs of arterial wall necrosis; the internal elastic layer is not affected and aneurism development is rare – the characteristic patterns that differentiate it from other arteriopathies (e.g.: vasculitis, atherosclerosis obliterans, polyarteritis nodosa) (2,4).

In concordance with literature data, our patient presented the same pathophysiological pattern that led to severe lesions of upper and lower limbs.

Furthermore, according to international medical reports the positive diagnosis can be established when there is a young smoker male presenting peripheral ischemia signs, episodes of recurrent superficial thrombophlebitis, with involvement of upper limbs, and absence of diabetes or other typical signs of extensive atherosclerosis (1); the arteriographic findings indicate normal great vessels aspect, and the presence of distal arteries structural changes (1-4). In contrast, we presented the case of a female heavy-smoker patient, with old age onset of the disease (45 – 48 years old) and the absence of migratory thrombophlebitis. Additionally, her arteriographic images showed minimal atheromatous plaques of infrarenal aorta, but without artery caliber decreasing. These findings can be in agreement with Tamai et al study (10), which concluded that Notch signal pathway, responsible of atherosclerosis inflammatory state, may be involved in the pathophysiology of Buerger’s disease.

The differential diagnosis of our patient excluded other possible causes: arteriopathies (e.g.: atherosclerosis obliterans, vasculitis, and arterial emboli), Raynaud or neoplastic disease, which are also emphasized by medical literature (2,4,7).

As we already presented, the elected therapy was left lumbar sympathectomy (L2 – L4), partial left foot amputation and several recommendation on discharge: smoking cessation, vasodilator and antiaggregant treatment. Our therapeutically measures were in concordance with the treatment management reported by several international studies (7):
- smoking cessation (1,11),
- vasodilator therapy – alprostadil (2,3,6).
- anticoagulants during the acute phase or when thrombophlebitis is associated (1).
- advanced forms – regional sympathectomy and necrotic lesions amputation; because of the distal lesions localization, arterial reconstruction is rarely performed (1,2,4).
- genetic manipulation – experimental phase (2,4,6).

Conclusions

The case represents a neglected form of thromboangiitis obliterans in a known heavy-smoker female patient. From the classic Buerger’s disease features, two of them: young age onset (below 40 years) and migratory thrombophlebitis are missing. The particularity of the case is represented by the lack of an early diagnosis and the occurrence of the disease in a 45 years old female patient; this last aspect is in accordance with international data which highlight an increased incidence of Buerger’s disease even in women, due to nicotine addiction (3,4,12).

References