A Middle-aged Woman Suffering Buerger’s Disease

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ABSTRACT

A 48 years old woman complains of numbness on her fingers and toes. Her 4th and the 5th right fingertips were painful and then blackened. She had no diabetes and hypertension history. She didn’t smoke, but her husband and son were smokers. On local examination there were necrotic gangrenes on the 4th and the 5th fingertips of the right hand. Laboratory examination results (including immunology marker) were within normal limit. Doppler ultrasound and arteriography showed segmental stenosis and partial occlusion of distal arteries on all extremities. We assessed the patient with Buerger’s disease. The managements were oral analgesic and vasodilator medication. Endoscopic thoracic ganglion sympathectomy was performed, followed by amputation of the necrotic fingers. We did not perform a biopsy, so according to all examinations and also by Shionoya and Olin’s criteria, the patient was more likely to suffer from Buerger’s disease than other peripheral occlusive diseases.

Introduction

Thromboangiitis obliterans (TAO) or Buerger’s disease is a non-atherosclerotic, segmental inflammatory disease that most commonly affects the small and medium-sized arteries, veins, and nerves of the arms and legs. Von Winiwarter first described a patient with thromboangiitis obliterans in 1879. Twenty-nine years later, Leo Buerger provided a detailed and accurate description of the pathological findings in 11 amputated limbs [1]. The disease is found all over the world, but the highest incidence is found in the Middle East. TAO is said to be more common in Asian races than others [2]. The prevalence of the disease among all patients with peripheral arterial disease ranges from as low as 0.5 to 5.6% in Western Europe to values as high as 45 to 63% in India and 16 to 66% in Korea and Japan [3].

Buerger’s disease is common in young men (between 40-45 years of age) who smoke. However, the patient’s spectrum of TAO has changed; the ratio of men to women decreases, the number of older patients increase, and the
involvement of the upper limb become more frequent \[1,2\]. Although the disease has been described since more than 100 years ago, the underlying pathology and etiology of the disease remain unclear \[3\]. The use of cigarettes or exposure to cigarettes is still the essence of the occurrence and the progressivity of this disease. Some researchers believe that TAO can also happen to non-smokers (although only <5% of cases). TAO cases on non-smokers can be driven by cold, frostbite, trauma to the extremities, or the misuse of sympathomimetic drugs \[1,5\]. Until now there is no consensus establishing the diagnosis and there were no specific markers, so the diagnosis is based on clinical criteria (by excluding other causes) as well as angiography \[1-3\].

Here we report a case of middle-aged non smoker woman with Buerger’s disease. The clinical manifestations were gangrene at the fourth and fifth fingertips of her right hand. The patient underwent amputation of the gangrenous fingertips and thoracic ganglion sympathectomy.

**Case Presentation**

A Javanese woman, aged 48 years, came to Soetomo General Hospital because her 4th and the 5th right fingertips were painful and then blackened. She complained of frequent numbness at her fingertips and feet since 6 months before. Then gradually, the fourth and fifth fingertips of her right hand started to blackened and shrink. She had no history of hypertension, diabetes, and joint pain. She was not a smoker, but the patient lived in a smoker's environment (her husband and son were both smokers).

From the physical examination she was in good condition, blood pressure of 150/90 mmHg, heart rate of 90 times/minute, breathing of 20 times/minute, and the temperature of 36.5 °C. On extremity examinations, we found ischemic gangrene at the 4th fingertips of the left hand that was already healed and necrosis gangrene at 4th and 5th fingertips of the right hand (figure 1). The pulsation of the radial was palpable but weak, whereas brachial arteries of both hands were palpable.

![Figure 1. healed ischemic gangrene at the 4th fingertips of the left hand and necrosis gangrene at 4th and 5th fingertips of right hand.](image-url)
ECG and chest X-ray results were within normal limit. On laboratory examination, we found mild leukocytosis (11.100 /μL), mildly elevated cholesterol level, no coagulation abnormalities, and immunology test for autoimmune screening were also within normal limit. Transthoracic echocardiography was performed and the result was within normal limit. Doppler US scans showed that there was moderate stenosis at the left palmaris artery. From the pulse wave Doppler, there were biphasic wave form at brachial artery, radial, and ulnar artery indicating a stenosis.

Arteriography result showed astenosis at radial and distal ulnar artery of the left hand. At the right hand, there was partial occlusion at ulnar artery and no flow at digital artery. From the arteriography of the right inferior extremities, we found an occlusion of the anterior tibial artery and no flow at dorsalis pedis and metatarsal artery with collateral branches. Below are the pictures of the angiographic finding.
Initial assessment of this patient was Severe Raynaud Phenomenon with differential diagnoses of Peripheral Arterial Disease. The management was Captopril 12.5 mg tablet three times daily for the hypertension, Simvastatin 20mg once daily, Acetyl Salicylic Acid 100 mg once daily, Cilostazole 50mg twice daily, and Morfin Sulfate 10mg for pain management. We added Beraprost 20 mcg twice daily and Fluoxetine 10 mg for the Raynaud Phenomenon.

Based on arteriography results and Olin and Shionoya criteria, we concluded that the patient was suffering from Buerger disease. We ceased Captopril, Cilostazole, and Beraprost medication and we gave the patient Sildenafil 25 mg three times daily and Nifedipine 5 mg three times daily. The patient was then consulted to the Thoracic and Vascular Surgery Department. Endoscopic thoracal ganglion sympathectomy (ETS) was performed, followed by amputation of the necrotic fingers without any complication. The patient was discharged without any complains of ischemic gangrene after the surgical procedure.

Discussion

Since it was proposed by Buerger in 1908, the pathogenesis of Buerger's disease, or known as Thrombo angiitis obliterans (TAO), is still not clarified yet and the unity as a disease is still in debate. Men are exposed more often and there is a strong connection between smoking and this disease [4]. As mentioned earlier, the specific etiology is unknown. Secondary etiology that has a positive effect on this disease are age, gender, race, hereditary factors (HLA phenotype), autoimmune processes, occupation, and changes in blood components (coagulability, anticardiolipin antibodies, homocysteine and smoking) [5].

According to an immunohistochemical study, TAO is an endarteritis due to cellular immunity mediated by T-cell and humoral immunity mediated by B cell and associated with activation of macrophages or dendritic cells in the intima wall [2]. Other factors which are considered to accelerate the disease are high levels of lipoprotein, degradation of elastin, antibody anticardiolipin, serotonin, and diabetes mellitus [5]. The most frequent clinical symptom is felt on the lower limb. There is no adequate data about the very early stages of TAO. Most patients who seek help have undergone ulceration (38-85%) and or pain at rest (50-89%).

Frequent super infections and lesions develop into the distal necrosis and gangrene. Ischemia on the upper extremities occurs in 40-50% patients. Some might be detected in 63% of patients with Allen's test, and 91% of patients were detected with an arteriogram of the forearm. Raynaud's phenomenon is usually unilateral, found in half of TAO patients, and superficial thrombophlebitis is found in 40-60% of cases. Raynaud's phenomenon occurs because of reversible spasm of the peripheral arterioladue to response to cold or stress. Critical ischemia can occur and particularly very painful, which lead to ulceration or gangrene. [2,6,7]

In this case, the patient was a woman, unlike most cases, and she did not smoke, but lived in a smoker's neighborhood. She sometimes felt numbness and her fingers turned pale or blue during cold exposure. This condition led to Raynaud's phenomenon or Raynaud's disease, that's why at first we diagnosed the patient with severe Raynaud's phenomenon with critical ischemia.

There is no specific laboratory examination to diagnose Buerger's disease. Unlike other vasculitistypes, in patients with Buerger disease, an acute-phase reaction such as LED and CRP are usually normal [3]. A complete examination should be done to exclude other causes of vasculitis.
Including complete blood test, liver and renal function test, fasting blood sugar, CRP, ANA test, Rheumatoid factor, serological marker for CREST syndrome (Calcinosis cutis, Raynaud's phenomenon, Sclerodactyly, Telangiectasia, and Scleroderma), and screening for hypercoagulability, including examination of antiphospholipid antibodies. The embolic source at the proximal should be removed with an echocardiography and arteriography examination \[1,3\].

In this patient, the history of previous mechanical trauma was unclear, and she had no history of diabetes mellitus. On laboratory result there was only mildly slipidemia. Immunology or auto immune process was unlikely to be the cause, because the level of IgG ACA was 8.6 (negative anticardiolipin antibody, cut off point 10). Echocardiography findings revealed no thrombus inside cardiac chambers.

Imaging examination such as Duplex Ultrasound and arteriography would provide a useful tool for correct diagnosis. The Colour Duplex Ultrasound (CDU) examination can be used to assist with the diagnosis of TAO, but due to the usual unusually vascular lesions distribution, it is important to combine the clinical assessment of patients with CDU's invention. CDU examination characteristics in TAO are: 1) Occlusion of the distal calf or pedis artery; 2) Occlusion of the arterial palmaris arch, forearm or digital arteries; 3) The arteries in the proximal of the occlusive lesions are normally obtained; 4) Serpiginous collateral Formation or crock-screw overview; 5) The walls of blood vessels that are intrigued in the thrombotic occlusion area, sometimes free of calcification.

The supporting examination such as digital subtract angiography (DSA) is a method of radiology inspection that provides the most thorough information and is even considered to be the gold standard. Characteristics of TAO angiography findings are: stenosis and multiple occlusion, bilateral, symmetrical, segmental, distal local arteries of the legs and forearm with a picture of smooth and regular blood vessels, and non-atherosclerotic.

There is usually a corkscrew collateral around the obstruction with an image such as a crock-screw, tree root, or spider's leg: Martorell's sign. But unfortunately, the collateral-like image of this screw is not pathognomonic for Buerger's disease, as this image can be seen in Systemic Lupus Erythematos Scleroderma, CREST syndrome, other small vascular occlusion disease, and in a cocaine, amphetamine or marijuana abuser \[1,6,8\]. The CT or MRA does not currently have a role in the diagnosis of Buerger's disease. Some researchers believe that both modalities lack of spatial resolution to detect pathological conditions in small arteries \[9\].

We found biphasic pulse wave form at the brachial artery, the ulnar artery, and the left palmar artery of both hands. The palmar arteries of the right hand could not be evaluated. The result of this CDU indicated the presence of moderate stenosis on the left Palmaris artery, and there was no thrombus found causing arterial occlusion. Then the patient underwent arteriography, with the results of occlusion and stenosis in the distal artery in the four extremities where there were no image of atherosclerosis or thrombus. After all of the supporting examinations were done, we also made exclusion criteria using Olin and Shionoya as listed below. The patient met 3 of the 4 Shionoya criteria and fulfilled 4 of the 6 criteria of Olin. We diagnosed the patient with Buerger disease.

Diagnostic criteria of Shionoya (1998) \[3\]: Smoking history; Onset before the age of 50 years; Infrapopliteal arterial occlusions; Either arm
involvement or phlebitis migrans; Absence of atherosclerotic risk factors other than smoking. Diagnostic criteria of Olin (2000) [3]: Age under 45 years; Current or recent history of tobacco use; The presence of distal extremity ischemia indicated by claudication, pain at rest, ischemic ulcers or gangrene 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.

Management for Buerger's disease includes conservative, interventional, and surgical therapies. The most effective and ultimate therapy is to discontinue the use of cigarettes. Even smoking one or two cigarettes per day, using smokeless cigarettes (chewing tobacco), or using a nicotine substitute can cause the disease to remain active [1,2].

If there is Raynaud phenomenon, the management includes vasodilators that have antiplatelet effect and decrease oxidative stress such as calcium channel blockers (Nifedipine 10-30 mg oral, Amlodipine 5-20 mg tab or Diltiazem); Angiotensin II receptor antagonists, or Selective serotonin reuptake inhibitors (SSRIs) such as Fluoxetine.

Raynaud's phenomenon that has undergone critical ischemia requires Prostaglandin in analog administration (such as Iloprost 0.5-2 ng/kg/min), intravenous administration of nitroglycerin, phosphodiesterase inhibitors such as Cilostazol, Sildenafil, Endothelin Receptor inhibitors (Bosentan), or Beraprost although they are still in debate [7]. In Japan, where TAO's prevalence rate is quite high, there is a shift from surgical therapy to medical approaches due to the presence of prostaglandin analogue [9,10]. Immuno suppressive therapy may be useful in some TAO patients such as glucocorticoid and Azathioprine in addition to antiplatelet therapy and vasodilator. They significantly lowers the amputation rate [2]. Interventional therapy is performed if there is an occlusion of the arteries. Surgical management includes sympathectomy and revascularization.

Clinical experience suggests that Raynaud's phenomenon in the legs can be repaired with sympathectomy [2]. It is said that sympathectomy might cure ischemic ulceration, reduce pain, but does not prevent or reduce the amputation rate [1,9]. Thoracic sympathectomy has long been used for the treatment of various kinds of upper limb disorders such as hyperhidrosis, Raynaud's phenomenon, and post-traumatic pain syndrome.

The study by Matsumoto et.al from 1992 to 2001, showed healing of digital ulceration of 7 patients after the ETS (Endoscopic Thoracic Sympathectomy), reportedly there was no visible recurrence in the digit ulceration and formation of new ulcers during observation (12-91 months after surgery). Arterial bypass therapy can be done if there is occlusion in the upper segment of the knee, because when the level drops below the knee, bypass procedure will lead to decreasing flow, as well as the number of its patency [1,10].

Surgical reconstruction of the arteries is not suitable for Buerger's disease, because the characteristic of the disease is inflammation [2]. The patient initially received antiplatelet and vasodilator (Beraprost and Fluoxetine). After the diagnosis leads to the Buerger's disease, Beraprost was switched to Sildenafil 3x25 mg and Nifedipine 3x5 mg orally. Subsequently, this patient underwent left and right Thoracalis II and IV ganglion sympathectomy. She also underwent amputation of digit IV and V of her right hand. The post surgery condition of the patient was good without any complications. Additional
treatments were antibiotic and pain killer intravenously. Unfortunately, we didn’t performa biopsy of the affected finger, so that we couldn’t determine the anatomic pathological abnormality findings to this patient’s arteries.

Smoking cigarettes have an important role in the progression and prognosis of the disease. The newly associated ischemic lesions occur in patients who continue to smoke or start smoking again (after the quit-smoking period) [6]. Since the patient was not an active smoker, but a passive smoker, we encouraged her husband and son to cease smoking. The patient was lost to follow up, but at least there was no recurrent ischemic necrotic occurrence until discharge.

**Conclusion**

Shionoya and Olin’s criteria helped us exclude other disease. The managements were analgesic and oral vasodilator medication combined with surgical. Endoscopic thoracal ganglion sympathectomy was performed and followed by amputation of the nacrotic fingers. Then the next treatment was focused on dilating the small arteries, reduce the pain, and education to avoid smoke exposure.

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