Current modalities for the diagnostic and management approach of buerger’s disease: a case report and comprehensive review

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ABSTRACT

Background: Thromboangiitis obliterans (TAO or Buerger’s disease) is a non-atherosclerotic inflammatory vascular disease usually related to smoking. Until now, there is no consensus establishing the diagnosis and standard treatment.

Case Illustration: A 74-year-old smoker woman complained of blackening and painful fingertips in both upper limbs. On upper-extremities examination, we found necrotic gangrene at the 3rd fingertips of the right hand, and the 2nd and 4th fingertips of the left hand, with limitation of the movement at the affected hand, and the 2nd and 4th fingertips of the left hand due to the pain. On laboratory findings, there was a leukocytosis, mild Anemia, no coagulopathy, and normal autoimmune screening. Doppler Ultrasonography showed vascular incompetence of the left palmar arch artery, with no deep or superficial vein thrombosis. Arteriography revealed multiple stenosis of the Left Radial artery and Right Ulnar artery with collateral corkscrew-shaped. The patient was diagnosed with peripheral Critical Limb Threatening Ischemia caused by TAO, which underwent conservative management for 10 days and Percutaneous Trans Angioplasty (PTA) ballooning.

Discussion: Buerger disease commonly affects smoker men between 40-45 years old. Several clinical criteria were used to establish TAO, including Shinoya and Olin’s criteria. There are still no specific management guidelines for TAO, and smoking cessation is the only accepted effective treatment to prevent the progression of the disease and avoid amputation, followed by conservative and interventional management for patients with Critical Limb Ischemia.

Conclusions: Awareness of the entity and familiarity with the clinical, angiographic, and pathologic features are the keys to a prompt and correct diagnosis of TAO. Although still controversial, endovascular intervention is regarded as a potentially efficacious approach in TAO with critical limb ischemia management.

Keywords: buerger’s disease, management, outcome, artery.


INTRODUCTION

Thromboangiitis obliterans (TAO or Buerger’s disease) is one of the peripheral vascular diseases that most commonly affects the small and medium-sized arteries, veins, and nerves of the arms and legs, and is usually related to smoking. It is a nonatherosclerotic, segmental, and inflammatory vasculitis, due to obstruction of cellular clout through the blood vessel, while relatively respecting the structure of the mural surfaces.¹² TAO is found all over the world and is more common in Asian races than in others.¹³ 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.¹⁴ Until now, the underlying pathology and etiology of the disease remain unclear, and there is no consensus establishing the diagnosis, so the diagnosis is based on clinical criteria (excluding other causes) as well as angiography.¹ The management is also controversial since there is no standard treatment guideline for the disease and PTA ballooning become a popular modality for TAO. Here we report a case of a 74-year-old smoker woman with TAO manifestation on the 3rd fingertips of her right hand and the 2nd and 4th fingertips of her left hand.

CASE PRESENTATIONS

A 74-year-old female complained of blackening and painful fingertips. The lesion began as a small non-healing wound for one month and became swollen and purulent. Two weeks before admission, the fingertips started to blacken and became more painful. She denied having chest pain and shortness of breath but has a history of dyspnea during activity. The patient was a smoker for five years. At presentation, she was in moderate pain of her left hand. The patient was a smoker for five years. On upper-extremities examination, the fingertips started to blacken and became more painful. She denied having chest pain and shortness of breath but has a history of dyspnea during activity. The patient was a smoker for five years. On upper-extremities examination, the patient was in moderate pain of her left hand.
hand, followed with limitation of the movement at the affected finger due to the pain (Figure 1). The pulsation of the radial and ulnar arteries of the left hand was palpable but weak, whereas the brachial arteries of both hands were palpable. And the Ankle Brachial Index examination was 0.9 for both extremities.

Electrocardiography was performed and showed a sinus rhythm with rates around 88 beats per minute (bpm), Left Axis Deviation, and Left Ventricle Hypertrophy (Figure 2). The chest X-ray result was Cardiomegaly with a Cardiotoracic Ratio of 64%, and aortic knob calcification suggested an aortosclerosis (Figure 3). Laboratory findings showed leukocytosis (White Blood Cells of 11,580/uL), mild Anemia (Haemoglobin of 10.5mg/dL), with normal coagulation state and no abnormality in autoimmune test screening of indirect immunofluorescence anti-nuclear antibody (ANA-IF). Limited study transthoracic echocardiography showed normal heart dimension with concentric left ventricular hypertrophy, normal systolic function of the left and right ventricle, and grade 1 diastolic dysfunction of the left ventricle, global normokinetic on segmental analysis, normal valvular function with estimated right atrial pressure 8 mmHg and there was no thrombus in cardiac chamber. Doppler ultrasonography of the left hand showed vascular incompetence of the left palmar arch artery without deep or superficial vein thrombosis (Figure 4). Angiography revealed multiple stenosis at the left radial artery, with minimal presentation of left palmar arch runoff from the left radial artery, accompanied by a collateral corkscrew appearance (Figure 5).

The patient was diagnosed with peripheral chronic limb-threatening ischemia caused by TAO with hypertensive heart disease and dyslipidemia. Initially, the patient was treated with conservative management with unfractionated heparin (UFH) 5000 IU intravenous bolus followed by 20000 UFH in 24 hours, cilostazol 50 mg twice a day, sodium beraprost 20 mcg three times a day, hypertension therapy, simvastatin 20 mg daily, paracetamol 1000 mg three times for ten days. For the next two months, the patient underwent percutaneous trans angioplasty (PTA) ballooning as the further management for her upper left limb and a good improvement in her clinical condition.

**DISCUSSION**

This case presented a 74-year-old smoker woman with necrotic wounds on her fingertips, an unusual TAO epidemiologic. TAO commonly affects men with age between 40–45 years old who smoke. At first, TAO incidence was more common in men, but recently, the incidence of TAO in women has increased due to an escalation in smoking behaviors among women. Tobacco used is postulated to trigger an autoimmune reaction in TAO patients, supported by a study that showed an increase of cellular sensitivity to type I and III collagen, elevated serum anti-endothelial cell antibody titers, and impaired peripheral vasculature endothelium-dependent vasorelaxation. Genetic factors, infection related to oral hygiene, hypercoagulability state, and immunologic mechanisms leading to a progression of vascular tissue inflammation are thought to be other etiologies of the disease.

Diagnosis of TAO is established through anamnese, physical examination, and further examination, such as several laboratory examinations, serologic profiles, Doppler ultrasonography, and angiography by ruling out the trauma to the extremities or the misuse of sympathomimetic drugs. Tobacco used
differential diagnoses of TAO, including atherosclerosis, emboli, autoimmune diseases, and other types of vasculitis. Biopsy is usually needed for patients with an unusual characteristic, such as large artery involvement or age greater than 45 years. However, there are no definitive markers and guidelines for diagnosing TAO. Consequently, various clinical criteria such as Shionoya, Olin, and Papa criteria are used to assess the diagnosis of TAO. For this case, the diagnosis of TAO was established through Shionoya and Olin's criteria. The Shionoya criteria consist of five criteria related to the occurrence of disease, including smoking history, disease onset before the age of 50, obstruction of the infrapopliteal artery, involvement of the upper extremities or phlebitis migrans, and the absence of risk factors for atherosclerosis other than smoking. Meanwhile, Olin's Criteria encompass several factors, including an age below 45 years, a current or recent history of tobacco usage, the presence of distal extremity ischemia as indicated by symptoms such as claudication, pain at rest, ischemic ulcers, or gangrene, and confirmed through non-invasive vascular testing. Additionally, autoimmune diseases, hypercoagulable states, and diabetes mellitus should be excluded as potential causes. Furthermore, the presence of a proximal source of emboli is ruled out through echocardiography or arteriography. And lastly, consistent arteriographic findings are observed in both the clinically affected and unaffected limbs. In the presented case, the patient fulfilled all the criteria, except age and hypertension as risk factors, and considering the patient was a heavy smoker with delayed wound healing despite no evidence of underlying disease.

Figure 3. Chest X-ray revealed cardiomegaly with a Cardio-Thoracic Ratio of 64%, calcification of the aortic arch indicating an aortosclerotic, without any pulmonary abnormality.

Figure 4. The Duplex Ultrasonography revealed a monophasic waveform flow in the radial, ulnar, and palmar arch arteries of the Left hand.
The total amputation rate for patients with TAO is as high as 33%. For the initial treatment, angiography was performed to assess the blood flow in the upper extremities and confirm vascular problems. TAO can be identified when young smokers exhibit peripheral ischemia and recurrent superficial thrombophlebitis affecting the upper limbs without any associated risk factors, such as diabetes or atherosclerosis. Therefore, TAO is characterized by distal vascular disease without calcification, segmental occlusive lesions, or the formation of corkscrew collaterals observed on angiography.10–12

According to Choi et al., TAO patient has a poor prognosis related to amputation incidence, which is as high as 33% for the total amputation rate for patients treated conservatively.13 There are still no specific management guidelines for TAO, and smoking cessation is the only accepted effective treatment to prevent the progression of the disease and avoid amputation.10,12–16 For the initial treatment, conservative management can be an option for TAO patients. In the present case, conservative treatment, including UFH, cilostazol, sodium beraprost, amlodipine, simvastatin, and paracetamol, was given for 10 days and improved clinical condition. Bed rest is essential for patients with critical limb ischemia. Despite the lack of clinical evidence demonstrating the effectiveness of vasodilators, thrombolytics, anticoagulants, and corticosteroids, several studies still suggest their potential for symptomatic relief. The efficacy of calcium channel blockers as vasodilators appears to be significant in patients with vasospasm. The administration of vasodilator therapy is believed to induce dilation of blood arteries located proximal to the stenotic or occlusive lesion, as well as the vessels that run parallel to the lesion, leading to an improvement in blood circulation to the adjacent vascular bed.6,7,17

Anticoagulants are believed to possess efficacy in reducing claudication. Cilostazol, a specific inhibitor of phosphodiesterase type III, effectively hinders the activity of cyclic adenosine monophosphate (cAMP) phosphodiesterase. This inhibition results in the prevention of platelet aggregation and relaxation of smooth muscle cells. In a randomized experiment, prostacyclin analog (iloprost) is more advisable and perceived to have greater efficacy than oral aspirin. Research has demonstrated its efficacy in enhancing symptoms, accelerating the resolution of distal extremity trophic changes, and reducing the amputation rate in TAO patients.6 Nevertheless, revascularization as a treatment option for critical limb ischemia individuals should be considered, along with smoking cessation, due to the adverse impact of this condition on patient quality of life.10,15,18 Treatment modalities including endovascular angioplasty, surgical bypass, lumbar sympathectomy, and spinal cord stimulation, have also been reported to give benefit in several studies. However, there is a lack of agreement on the best approach and there are no data about the efficacy and cost of these treatments in TAO.10,18 There is no medical evidence supporting the efficacy of sympathectomy or spinal cord stimulation in terms of enhancing survival rates or reducing the rate of amputations. However, the inhibition of sympathetic vasoconstriction is thought to improve peripheral microcirculation and enhance superficial blood flow to the skin, consequently contributing to the healing process of ischemic ulcerations.6,7,17,18

Surgical revascularization should be a considered option if bypass surgery is technically feasible. However, the feasibility of surgical intervention in TAO is often limited by several factors, including the absence of suitable distal targets for bypass, the inflammatory characteristics of the disease, and the presence of luminal thrombotic lesions, resulting in technical challenges with a high incidence of failure.11,12,15 According to Soliman et al., after a 10-month follow-up period, all bypass graft interventions failed due to the advancement of the disease, both distal and proximal to the location of the anastomosis. Although controversial, endovascular interventions, such as percutaneous transluminal angioplasty (PTA) ballooning, can be considered a therapeutic option for TAO. However, it presents technical difficulties due to diffuse segmental inflammatory process involvement of small distal arteries.11,12,15 However, the present study demonstrates a higher rate of clinical improvement and pain relief among patients with endovascular intervention than other treatment methods.18 PTA ballooning has been documented to exhibit favorable outcomes in terms of technical success and safety, reducing amputation rates and sustained clinical improvement during subsequent monitoring periods.13,16,18,19 According to Lee et al.,11 with the implementation of
comprehensive endovascular treatment, 95% of patients achieved technical success, and about 84% of patients demonstrated sustained clinical improvement during the 2-year follow-up period, showing the effectiveness of revascularization procedures in enhancing patients’ quality of life. In a study conducted by Ghoneim et al.18 observed that over a 12-month follow-up period, 66.7% of patients who underwent endovascular management exhibited clinical improvement. Continuation of smoking habit and disregarded medical advice was noted to be the reason resulting in the intermittent activity of the disease and exacerbation of TAO occurred in 33.3% of patients in the endovascular intervention.

Now, a promising new approach is a gene transfer technique to stimulate therapeutic angiogenesis in TAO patients using implantation of autologous bone marrow mononuclear cells or mesenchymal stem cells derived from human umbilical cord blood into ischemic limbs, which postulated can restore the limb function by promotes the development of new collateral vessels.7

CONCLUSION
A rapid and accurate diagnosis of TAO relies on the awareness of the entity and familiarity with the clinical, angiographic, and pathologic characteristics of TAO. The diagnosis of TAO is often missed in patients with old age or female gender. Therefore, it is important not to dismiss the possibility of TAO based solely on these patient demographics. Currently, there is no specific treatment for TAO. Absolute discontinuation of tobacco use is the only strategy proven to prevent disease progression. Endovascular intervention or PTA ballooning is considered a technically viable and potentially efficacious approach in TAO with critical limb ischemia management. This intervention can be offered as a final alternative management for limb salvage in individuals who already use other management options. Smoking cessation is also mandatory for the long-term sustainability of outcomes, and it is advisable to closely monitor patients and consider further interventions to sustain clinical advantages, particularly in individuals who persist in smoking.

DISCLOSURE
Funding
None.

Conflict of Interest
The author reports no conflicts of interest in this work.

Author Contribution
Agung Pradnyana Suwirya is involved in concepts, clinical studies, definition of intellectual content, manuscript review, and guarantor.

Putu Eka Diangi Putri is involved in the design, literature search, manuscript preparation, and manuscript editing.

I Gusti Ayu Wijayanty Permatasari involved in concept, clinical studies, and data acquisition.

Bagus Ari Pradnyana is involved in clinical studies, definition of intellectual content, manuscript review, and guarantor.

Acknowledgments
None.

Ethical consideration
The Current report obtained signed written informed consent from the patient and legal guardian regarding publication of medical data in scientific medical journals with confidentiality to personal information.

REFERENCES