CANNABIS USE: INCREASING RISK OF THROMBOANGIITIS OBLITERANS (BUERGER’S DISEASE)

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ABSTRACT

Thromboangiitis obliterans (TAO) is most commonly associated with tobacco exposure and Cannabis induced from thromboangiitis obliterans. It is a non-atherosclerotic inflammatory vasculitis. Which is resulting in small and medium sized arteries and commonly affecting the upper and lower limbs of young men who smoke. The clinical criteria include: age under 45 years; current or recent history of tobacco or cannabis use; Necrosis of the toe, Narrowing of the left tibial–peroneal artery, Involvement of digital arteries, lower limb or juvenile arteriopathies, claudication indicated by distal extremity ischemia presence, pain at rest, gangrenes or ulcers which are documented by non-invasive vascular testing, proximal source of emboli by arteriography. Non-involve limbs are the findings of arteriography. The disease is world widely distributed among all patients with peripheral arterial disease is 0.5 to 5.6% in Western Europe countries, 45 to 63% in India, and 16 to 66% in Asia and 80% among Ashkenazi Jews. Initiation inflammatory response resulting in lesions and progression of disease is due to use or exposure to cannabis, but in thromboangiitis obliterans is unknown. It is essential to stop smoking immediately and completely to reduce the incidence of amputation and to prevent in order to prevent progression of disease. And other effective treatments include supportive measures and vasodilating agents or antibiotic, analgesia drugs, surgical revascularization or sympathectomy. Spinal cord stimulation and vascular growth factor gene therapy have is beneficial in alleviating ischemic pain and have been used experimentally in patients with Buerger’s disease with promising results.

KEYWORDS: Thromboangiitis obliterans, arteriopathies, and sympathectomy.
INTRODUCTION
Thromboangiitis obliterans (TAO) is a segmental occlusive inflammatory condition of vasculitis, which is characterized by thrombosis and recanalization of the affected vessels.\(^1,2\) It is a non-atherosclerotic inflammatory vasculitis. Which is resulting in small and medium sized arteries and commonly affecting the upper and lower limbs of young men who smoke.\(^3\) A hyper cellular thrombus fills the lumen. The disease is almost exclusively associated with tobacco use. Although rare, use of cannabis has similarly been implicated as a causative agent in the inflammatory response resulting in lesions consistent with Buerger’s disease. Unfortunately, the great majority of cannabis users who develop Buerger’s type lesions are concomitant users of tobacco.\(^4\)

Epidemiology
Although disease is worldwide distribution, it has more prevalent and highest incidence occurs in Middle East, North East and Western Europe.\(^5\) In general population of japan the prevalence of the disease as estimated at 5/100,000 persons in 1985.\(^6\) Among all patients with peripheral arterial disease is 0.5 to 5.6% in Western Europe countries, 45 to 63% in India, and 16 to 66% in Asia. According to the United Nations Office of Drugs and Crime, there are some 165 million users of cannabis worldwide, making it the most widely used illicit drug.\(^7\) The prevalence due to variability in diagnostic criteria.\(^8\)

Clinical Presentation
Buerger’s disease is most commonly seen in young men (i.e., 20-40 years of age) it begins with ischemia of the distal small vessels of the arms, legs hands and feet. Rarely occurs in the absence of occlusive disease of the small vessels and involvement of large arteries is unusual.\(^9\) The pain typically begins in the extremities and radiates to central parts of the body. Limbs that are clinically not affected but presents with arteriographic abnormalities. Cannabis arteritis, Necrosis of the toe Showed in Figure 1, Narrowing of the left tibial–peroneal artery, Involvement of digital arteries, lower limb or juvenile arteriopathies, Parasthesias or cold sensation or cyanosis occurs in limbs or fingers, approximately 15% plantar claudication and 16% of sural claudication occurs, 19% of ulceration or gangrene occurs on the distal phalanges, the lower limb is often painful and eventually ischemic pain.\(^10\) Other signs and symptoms includes numbness and/or tingling in the limbs, 12.5% may have recurrent episodes of large joint arthritis before their arterial occlusion presentation, recurrent
superficial thrombophlebitis of either the arms or legs, and Raynaud’s phenomenon occur in 40%.

There are case reports of involvement of digital arteries, involvement of the coronary arteries, aorta, intestinal vessels, cerebral and even multiple organ involvement. Although Buerger’s disease affects most commonly in the arms, legs and feet. When TAO occurs unusually, diagnosis should be made only when acute phase lesions identifies.

![Figure 1: Necrosis of the toe](image)

**Diagnostic criteria**

Diagnostic criteria should be discussed from clinical point of view. It is important to first exclude other vascular diseases, such as atherosclerosis, emboli and autoimmune disease before diagnosing Buerger disease. Diagnosis is often made after the exclusion of other vascular diseases. The absence of diabetes mellitus, hypertension, and hypercholesteremia and the presence of venous thrombophlebitis is a common feature of history.

Several different criteria have been proposed for the diagnosis of thromboangiitis obliterans.

The clinical criteria of Shionoya are

1. Smoking history
2. Onset of before the age of 50 years
3. Infra-popliteal arterial occlusions
4. Phlebitis migrans or either arm involvement

The clinical criteria of Olin are

1. Less than 45 years
2. Current history of smoking
3. Presence of distal extremity ischemia
4. Pain at rest
5. Ischemic ulcers or gangrene
6. exclusion of a proximal source of emboli by echocardiography or arteriography
7. Consistent arteriographic findings in the clinically involved and non-involved limbs.

**Diagnostic methods**

In case of physical examination people with Critical ischemia presents with gangrene or rest pain lasting >2 weeks, ankle pressure <50 mmHg and with non-critical ischemia presents with either new onset of rest pain or claudication. A sinus heart rhythm is detected and Gangrene or ulceration may be noted. Upper limb involvement is the clinical evident in 50% of patients.

Allen test should be performed to assess the circulation in the hands and fingers. A negative allen test reveals no ulnar or radial artery occlusion and positive test indicate presence of upper limb disease.[14]

Laboratory investigations is recommended to rule out other causes of vascular disease. Blood glucose should be normal and buerger’s disease can be excluded in patients with diabetes Biochemical evidence of renal failure suggests that presence of an autoimmune disease. ESR, complete blood count, liver function test, erythrocyte sedimentation rate, antinuclear antibody, rheumatoid factor, antinuetrophilic cytoplasmic antibody (ANCA), serologic markers for CREST syndrome and complement measurements should be normal. If a proximal source of embolization is suspected, Tran’s esophageal echocardiography, transthoracic or arteriography should be performed. Thrombophilia screen should exclude protein C, protein S, and antithrmbin III deficiencies.[15]

Arterial Doppler test confirms the absence of infrapopliteal, brachial, or distal pulses. Modern methods also includes such as Arterial duplex, computerized tomography (CT) and magnetic resonance imaging (MRI), angiography identify diseased vessels. Tissue biopsy may aid diagnosis but should avoided in ischemia tissue.[16]

**Differential diagnosis**

The distal nature of TAO and the involvement of the arms and legs for longstanding will helps to differentiate this disease from atherosclerosis. In contrast to systemic vasculitis, the
elastic lamina and the media are preserved in which disruption of these lamina is usually striking. \[18\]

However abnormal result can also be present in other types of occlusive diseases, of the hand, emboli, Hypercoagulable state, Raynaud phenomenon, rheumatoid vasculitis, Systemic lupus erythematous CREST syndrome. \[17\]

**Complications**

As the tissue democrats, Gangrene develops in a few days with an acutely ischemic leg. Often a gangrenous toe is present. 19% major amputation rate, who continues to smoke. In case disease progression for longer periods like more than 8 years has been associated with premature atherosclerosis. \[10, 18\] lower limb or juvenile arteriopathies.

**Management**

The most effective treatment for buerger’s disease is immediate smoking cessation. It is essential to stop smoking immediately and completely to reduce the incidence of amputation and to prevent in order to prevent progression of disease. \[3, 19\] Supportive measures includes Gentle massage to increase circulation, avoid sitting or standing for longer periods in one position, walking with a bare foot to avoid injury, avoiding tight clothing or restrictive clothing. Early treatment is also important, because buerger’s disease may provoke that influence quality of life. A return to smoking only 1 to 2 cigarettes a day, using smokeless tobacco (chewing tobacco), or using nicotine replacement therapy may keep the disease active. Physician must educate and counsel their patients repeatedly about their importance of smoking cessation. \[20\]

In case of critical ischemia vasoactive dilation is done with nifedipine, buflomedil, prostaglandins along with any debridement of gangrenous tissue. Severe forms can be treated with sympatholytics, hyperbaric oxygen therapy, thrombolysis, or a distal rescue bypass. Based on the severity of ischemia and degree of pain, pentoxifylline and cilostazol have had shown a good effect in healing ischemic ulcers. \[21\] Antibiotics are indicated in the presence of infection or wet gangrene, treatment regimens includes pencillin plus metronidazole or ciprofloxacin. In ischemic pain Tramadol is sufficient to relieve, superficial venous thrombophlebitis can also be treated with the NSAIDS. In case of non-critical ischemia along with vasoactive dilators oral antibiotics are sufficient to treat infections and wet gangrene with Amoxicillin/clavulanate or ciprofloxacin, penicillin plus metronidazole. \[22\]
Due to the lack of patent distal vessels, arterial revascularization is usually not an option. The benefit of bypass surgery to distal arteries also remains controversial because of the high incidence of graft failure, however in case of severe ischemia and there is a distal target vessel, bypass with the use of autologous vein should be considered. Spinal cord stimulation and vascular growth factor gene therapy have is beneficial in alleviating ischemic pain and have been used experimentally in patients with Buerger’s disease with promising results.\textsuperscript{23, 24} Sympathectomy is often used in more severe cases where there is a tissue loss and in case of no revascularization.

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