

Case Report

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Regression of Thromboangiitis Obliterans Induced Finger and Toe Ischemia with Medical Cannabis Therapy

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Citation: Dror Robinson, (2017) Regression of Thromboangiitis Obliterans Induced Finger and Toe Ischemia with Medical Cannabis Therapy. Int J clinical & case. 1:6, 125-128

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Received: July 21, 2017; **Accepted:** August 08, 2017; **Published:** September 27, 2017.

Abstract

The current case report describes regression of digital ischemia in thromboangiitis obliterans patient following high-dose medical cannabis therapy (MCT). MCT therapy was instituted as a pain-mitigating treatment when the patient refused amputation due to ischemic and infected foot. Three years later the digital ischemia has resolved leaving minimal scarring. The mechanism of action might be related to the anti-tobacco use effects of MCT as well as the anti-inflammatory action of CBD.

The endocannabinoid system is important in vascular system function via the CB-1 and CB-2 receptors that are widely distributed in the vascular system⁽¹⁾. The relationship between cannabis usage and vascular problems has not been fully elucidated. The current state of knowledge does not support a statistical association between increased incidence of myocardial infarction and cannabis use⁽²⁾. Some authors have found that cannabis use is associated with cardiovascular problems and there is a 3.5 odds ratio of being a cannabis user in patients with thromboangiitis obliterans⁽³⁾. However, this might not be causative but rather an attempt at therapy by the patients. In fact, a mechanism of action by activation of CB-2 receptors is likely to mitigate atherosclerosis. The possible mechanism involves CB2 receptors playing an important compensatory role in controlling tissue inflammation and injury in infiltrating monocytes/macrophages and leukocytes during various pathological conditions of the systems such as atherosclerosis and restenosis⁽⁴⁾. These receptors limit inflammation and associated tissue injury. The current case report describes the use of high-dose cannabis (Medical Cannabis Therapy, MCT) as a therapy for severe thromboangiitis obliterans and results three years later.

Keywords: Thromboangiitis Obliterans, Critical Limb Ischemia, Burger Disease, Cannabis therapy

Case Report

A 59-year-old heavy smoking patient was admitted due to infected and ischemic foot.

Previous medical history included heavy smoking, hyperlipidemia, and hypertension. BMI was 29. Physical examination revealed ulcers at several finger tips on both hands as well as the obviously infected foot. Pulses were not palpable below the popliteal fossae and the cubital fossae and oxygen saturation was 61% at the

toes. Doppler-determined leg-brachial index was 1.04 at the upper thigh, 1.01 at the lower thigh, 0.77 at the upper leg, and 0.38 at the ankle. An angiogram demonstrated occlusion of the popliteal artery with refilling via collaterals in the leg apparently via the tibialis anterior artery, the tibialis posterior and peroneal arteries were completely cut-off (Figure 1).



Figure 1 Representative images from an angiography performed in 2014. The blood supply under the knee is greatly limited. Typical cork-screw appearance of the vessels is observed.

The results were considered indicative of Burger's disease. Intravenous antibiotic therapy was begun for 4 days, with signs of worsening infection and progression of the erythema and edema up to the ankle. The patient's involved foot had minimal toe motion, no sensation over the plantar surface of the toes and forefoot, and the toes were beginning to deform into hammer-toes. Erythema extended to the ankle with metatarsophalangeal septic arthritis due to penetrating ulcer between the third and fourth toes (osteomyelitis was not identified on X-rays). Due to severe infection

(Figure 2, left hand panel, CRP 35 [norm<0.5), WBC 23,000 cells per ml), the suggested therapy was below knee amputation. The patient declined the surgery and decided to self-medicate with cannabis (~10% CBD not less than 10% THC) and cannabis oil (30-50% CBD) of the wounds applied twice a day. He also received oral antibiotics for 6 weeks (Augmentin 875 mg twice a day and ciprofloxacin 750 md twice a day). Off-loading was not used due to patient lack of compliance.



Figure 2 Clinical photos of the involved foot at 2014 and at last available follow-up at 2017

The patients pain at rest decreased from 9 on the VAS (visual analogue scale) to 7 after 2 months. The pain intensity continued to decrease to 7 at 6 months, 5 at 12 months and finally 4 during the current examination at 36 months after beginning of MCT therapy. The tobacco smoking amount decreased from 2 and a half packs a

day at the time of presentation, to 1 pack a day at 12 months and none at later time points. Scars remained at the finger tips (Figure 3) and slight skin discoloration at the toes (Figure 2 right hand panel). Oxygen saturation at the toes is currently 95%.

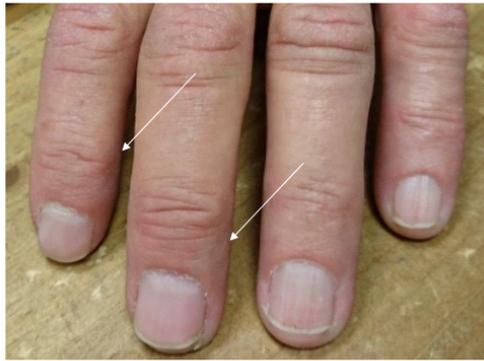


Figure 3 Clinical photo of the hand at last available follow-up at 2017, white arrows

MCT use was not quantified for the first six months, until the patient received a license to consume cannabis. During that time-period the usage was illicit. However, since the license was issued the MCT dose was 20 grams per month for the first six months, 30 grams per month for the next 6-months period. The dose was increased to 40 grams per month later, and to 50 grams per month during the last year. The medication had a minimal content of 10% CBD and less than 5% THC.

The patient returned to gainful employment after one year (gardening technician), his work includes a physical component requiring walking, and some ladder climbing.

Conclusion

The current case report describes a novel treatment regimen of critical limb ischemia in thromboangiitis obliterans using MCT. The favorable result might be related to two separate factors: Stopping tobacco use due to the usage of MCT as well as a possible inflammation moderating effect. Regarding the first factor, the relationship between cannabis recreational use and cigarette smoking is apparently bilaterally facilitatory with cannabis use leading to cigarette smoking and vice versa⁽⁵⁾. The interaction of cannabis usage and tobacco usage is apparently dependent on the reasons for cannabis use. Individuals who used cannabis for conformity reasons were more likely to successfully quit smoking, however, individuals who used cannabis for coping reasons were less likely to quit smoking⁽⁶⁾. This finding might explain the rather confusing literature about co-usage of these two substances. It is likely that in MCT users the drug acts to decrease cigarette smoking, while recreational users often tend to have a multi-substance abuse habit. Cannabis usage (especially daily use) leads to taste alterations, the taste alteration can affect tobacco smoking⁽⁷⁾ and lead to decrease of tobacco consumption. On the molecular level, cannabis increases the upregulation of $\alpha 4\beta 2^*$ nicotinic acetylcholine receptors, a well-established effect of chronic cigarette smoking on the brain⁽⁸⁾. This might act to decrease the need for tobacco abuse. The other factor that might be related to the surprisingly beneficial effect of MCT in this case, is the anti-inflammatory effect of cannabis. This effect is mainly mediated via cannabidiol a cannabis

constituent with anti-inflammatory activity mediated by enhancing adenosine signaling⁽⁹⁾. Apparently, CB-2 receptor activation can decrease tissue fibrosis as well by decreasing TGF-beta⁽¹⁰⁾. The authors hypothesize that the combination of decreased inflammation and fibrosis might act to reverse the ischemia in Burger syndrome as seen in this case. This conclusion is of course debatable as some authors have suggested that an association exists between cannabis use and arteritis⁽¹¹⁾. However, other authors have concluded that the association between cannabis use and arteritis is not clear with concurrent tobacco use a major confounder^(12, 13). Further prospective clinical series is needed prior to performance of a formal randomized clinical trial of MCT in limb ischemia.

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