CLINICAL VIGNETTE

Case Report: Blue Toe Syndrome

Jonie Hsiao, M.D.

Case Presentation

A 63-year-old male with a history of ischemic cardiomyopathy and congestive heart failure off all medications for 10 years is sent by his primary care provider to the Emergency Department for concerning physical exam findings on his lower extremities. The patient has multiple scattered cyanotic-appearing lesions on both feet. His feet additionally appear mottled and cool. The patient had mild, if any pain, and states these lesions have been present for a few months.

On physical exam, the patient was afebrile with unremarkable vital signs. His cardiovascular exam is notable for a II/VI systolic murmur without rubs or gallops. His lungs are clear. His abdomen is soft without palpable masses or bruits. His bilateral lower extremities are cool with symmetric 1+ edema. He has bilateral palpable pulses in the dorsalis pedis. The posterior tibialis is not palpable but is biphasic and audible with dopplers. There are multiple scattered 1-2mm purple-dark blue discolorations throughout both feet extending up towards the ankles. The feet appear mottled. There are no other notable lesions or nodules, and no discolorations noted on the upper extremities.

Although the time course and exam were not consistent with acute critical ischemia, vascular surgery was consulted given concern for blue toe syndrome.

Discussion

Blue toe syndrome, also referred to as "trash toe," presents as multiple, spontaneous, scattered cyanotic lesions on the lower extremities, limited to the feet and particularly notable in the toes. This is almost a pathognomonic manifestation of cholesterol embolic syndrome. The clinical finding results from multiple small ischemic insults on the peripheral vascular beds from a proximal embolic source (microemboli). However thrombotic, inflammatory, or obstructive disorders may also impede distal arterial flow, and the mechanisms are not mutually exclusive.[1,2] A few examples of diseases primarily caused by thrombosis would include antiphospholipid syndrome, disseminated intravascular coagulation, and warfarin skin necrosis. Hyperviscosity syndromes, vasculitides, or calcific vasculopathy can also present similarly. In addition, although most embolic cases originate from cholesterol plaques in proximal large vessels, other embolic phenomena, such as endocarditis or intracardiac tumors may be culprit.[1]

Overall, embolism from proximal atherosclerotic plaques is the most common cause of blue toe syndrome.[2] There are 6 key steps in the development of cholesterol embolism syndrome. These include: 1) presence of plaque in a proximal, large-caliber artery; 2) plaque rupture (spontaneous, traumatic, or iatrogenic); 3) embolization of plaque debris; 4) mechanical occlusion of emboli in small vessels; 5) subsequent inflammatory response; and 6) end-vessel or organ damage.[3]

Patients who have risk factors for atherosclerosis are at-risk for cholesterol embolism syndrome. The disease most commonly occurs as an iatrogenic complication from invasive procedures such as angiography and angioplasty. It has also been theorized that anticoagulation or thrombolytic therapy are risk factors for plaque destabilization and rupture. Although this has been reported in the literature, causality is not well-established. The true incidence of the syndrome is unknown as clinical manifestations are often only apparent after significant end-organ damage has occurred, and many more cases are asymptomatic and identified on autopsy.[1,3]

Depending on the location of the embolic source, the clinical findings of cholesterol embolism syndrome can be quite variable. It may include stroke, bowel ischemia, acute renal injury, as well as blue toe syndrome. Given the potential multi-system involvement, the disease can mimic a vasculitis. If the ischemic cutaneous injury is also pronounced, ulceration, tissue loss, gangrene, and infection are possibilities. Apart from blue toe syndrome, another common cutaneous finding is livedo reticularis, a lace-like pattern of mottling that occurs due to increased amounts of desaturated blood in the vascular beds or venodilation from stasis.[1]

The segment most commonly responsible for symptomatic embolization is the aorta-iliac segment. Establishing the source of the embolism through imaging studies is essential. Non-invasive vascular imaging includes ultrasound to detect aneurysms, occlusive disease, and atheromatous plaques. Computerized tomography angiography (CTA) remains the preferred imaging modality for diagnosis.[2,4] However, if the embolic source is at a suprarenal location, renal function may be compromised, and alternative studies such as magnetic

resonance imaging (MRI) or transesophageal echocardiography (TEE), may be considered.

Treatment for blue toe syndrome caused by cholesterol emboli is primarily the supportive care of its clinical manifestations and primary prevention of another event.[3] For the latter, medical therapy is aimed at risk factor reduction for atherosclerosis, including management of hypertension, cholesterol, and smoking. Antiplatelet agents and statins are likely beneficial. As mentioned previously, anticoagulation therapy may theoretically cause cholesterol emboli syndrome from plaque destabilization. However, anticoagulation has also been used as a treatment option, as some theorize that the plaques may be more fibrinoplatelet in nature.[5] Options for surgical removal of the lesions include bypass, endarterectomy, and endovascular techniques, such as intra-arterial stenting.[5]

Clinical Course and Outcome

Initial basic blood work for this patient was only remarkable for mild renal dysfunction. (creatinine 1.30 mg/dL). His lower extremity arterial dopplers were normal, and an ultrasound of the aorta did not show an aneurysm, thrombus, or occlusion. The patient's transthoracic echocardiogram did not demonstrate any valvular lesions. CTA of the chest, abdomen, and pelvis revealed scattered atherosclerotic disease in the thoracic and abdominal aorta without evidence of significant stenosis, thrombus or aneurysm. Antinuclear antibody (ANA) and antineutrophil cytoplasmic antibody (ANCA) were within normal limits. Total cholesterol and LDL were also within normal limits. As imaging studies did not reveal a discrete lesion amenable to surgical intervention, the patient was medically managed with disease modification therapies for prevention of atherosclerosis including a statin and aspirin.

REFERENCES

1. **Hirschmann JV, Raugi GJ**. Blue (or purple) toe syndrome. *J Am Acad Dermatol*. 2009 Jan;60(1):1-20; quiz 21-2. doi: 10.1016/j.jaad.2008.09.038. PubMed PMID:19103358.
2. **O'Keeffe ST, Woods BO, Breslin DJ, Tsapatsaris NP**. Blue toe syndrome. Causes and management. *Arch Intern Med*. 1992 Nov;152(11):2197-202. Review. PubMed PMID: 1444678.
3. **Kronzon I, Saric M**. Cholesterol embolization syndrome. *Circulation*. 2010 Aug 10;122(6):631-41. doi: 10.1161/CIRCULATIONAHA.109.886465. Review. PubMed PMID:20697039.
4. **Sawalhi SI, Hamad H**. Etiology of 'blue toe' syndrome: Emboli versus warfarin therapy. Report of a case. *Journal of Taibah University Medical Sciences*. 2012;7(1):41-44.
5. **Matchett WJ, McFarland DR, Eidt JF, Moursi MM**. Blue toe syndrome: treatment with intra-arterial stents and review of therapies. *J Vasc Interv Radiol*. 2000 May;11(5):585-92. PubMed PMID: 10834489.

Submitted June 2, 2016