Cholesterol Embolism: A Case Report and Review of the Literature

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GOAL

To understand the diagnosis and cutaneous manifestations of cholesterol embolism

OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Discuss the clinical symptoms of cholesterol embolism.
2. Describe the risk factors of cholesterol embolism.
3. Explain the cutaneous manifestations of cholesterol embolism.

CME Test on page 270.

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Cholesterol embolism is a serious disease with a poor prognosis. Its diagnostic features are illustrated and discussed, with emphasis on the typical cutaneous findings of blue toes and livedo reticularis.

Cholesterol embolism, also known as atheroembolism, is the occlusion of arteries due to embolism of atheromatous debris that has become detached from an arterial plaque. It usually affects white men older than 50 years;

smokers; and those with diabetes, hyperlipidemia, and peripheral vascular disease. The patient presented here had all of these risk factors. Cholesterol embolism may occur spontaneously or may follow as an iatrogenic complication of invasive vascular procedures or fibrinolytic therapy. Because this plaque is most commonly found in the descending aorta, the kidneys and skin of the lower extremities are the usual sites. However, atheromata of other arteries, such as the ascending aorta or the carotid, may result in emboli, which produce neurologic, retinal, or cardiac symptoms. Skin biopsy may show the cholesterol emboli as needle-shaped clefts within the lumina of small vessels.

Case Report

An 81-year-old white man presented with disorientation that worsened over 2 weeks. He was hypertensive and diabetic and suffered from chronic obstructive pulmonary disease, gout, and chronic renal insufficiency with a baseline serum creatinine level of 1.9 mg/dL. The patient's history revealed that he had abused alcohol and marijuana for 50 years and had recently quit smoking. Four months prior to this admission, he sustained a myocardial infarction. His pedal pulses were absent bilaterally. Results of an ultrasound of the abdomen revealed a 4.2-cm aneurysm in the lower abdominal aorta, with a partial thrombus and atherosclerotic changes in the proximal aorta. He underwent coronary bypass surgery, and his recovery was uneventful until the present episode of disorientation.

On admission, physical examination revealed an afebrile older adult man who was confused but comfortable and had no focal neurologic deficits. The most striking finding was bilateral, cold, purple toes. Blood urea nitrogen and creatinine levels were 125 mg/dL and 8.4 mg/dL, respectively. Total cholesterol was 297 mg/dL; triglycerides, 210 mg/dL; high-density lipoproteins, 50 mg/dL; low-density lipoproteins, 205 mg/dL; and very-low-density lipoproteins, 42 mg/dL. Antinuclear antibody, rheumatoid factor, and anticardiolipin antibody test results were negative. Results of a computed tomography of the brain revealed an old lacunar infarct and cortical atrophy. Echocardiogram results revealed hypokinetic anterior and inferior walls, with an ejection fraction of 30%.

On the fourth day, the patient developed livedo reticularis over the lower extremities (Figures 1 and 2). Results of a skin biopsy taken from the right thigh revealed congestion and cholesterol emboli in the deep arteries of the dermis (Figures 3 and 4), which confirmed the diagnosis of cholesterol embolism. Renal failure worsened, probably from recurrent embolism to the kidneys, and the patient subsequently required dialysis. He went into cardiogenic shock and died on the 16th day of hospitalization.

Comment

Cholesterol embolism is a devastating complication of atherosclerosis. The typical patient is a white man older than 50 years with a history of smoking, hypertension, diabetes,[1] atherosclerosis,[2] and peripheral vascular disease.[3] An atherosclerotic plaque demonstrated on ultrasound, transesophageal echocardiogram, and magnetic resonance imaging signifies an increased risk of atheroembolism.[4] In 50% of cholesterol embolism cases, the lower extremities are involved.[5] It may occur spontaneously or may follow as an iatrogenic complication from invasive vascular procedures[5] during which mechanical fragmentation and dislodgment from the plaques may occur.[6,7] The embolism usually occurs within hours to days following vascular intervention[8]; however, it also may occur up to 16 weeks thereafter.[9] Anticoagulants and fibrinolytic agents[10] also can precipitate as well as exacerbate embolization, which indicates that interference with the healing of eroded plaques may aid the release of atheromatous particles downstream into the circulation.[10,11] In some cases, antineutrophilic cytoplasmic antibody has been implicated as a possible cause of cholesterol embolism[12] and is attributed to vessel damage caused by atherosclerosis.[13]

A high degree of clinical suspicion is necessary to make a diagnosis of atheroembolism because the clinical findings may vary depending on the site of involvement[14] or may be nonspecific like weight loss, pyrexia, altered mental status, and increased blood pressure. Cutaneous manifestations occur in over one third of atheroembolism cases[5] and include, in order of frequency, blue toe syndrome, livedo reticularis, gangrene, ulceration, nodules, and purpura.[6] These cutaneous manifestations are usually acute and asymmetric. Blue toe syndrome consists of purple or blue discoloration of some of the toes, which may have a reticulated margin. The toes are painful, tender, and colder than the rest of the feet, and pedal pulses may be normal. The differential diagnosis includes local trauma, peripheral vascular disease such as diabetic ischemia (which may produce gangrene), Kaposi sarcoma, acrocyanosis, vasculitis, and acral-lentiginous melanoma. Livedo reticularis is a persistent, lacy, purple mottling caused by slow blood flow through the horizontally arranged superficial venous plexus of the skin, which allows more time for deoxygenation of the blood to occur.[15] An important differential diagnosis is livedoid vasculitis, a chronic, segmental, hyalinizing vasculopathy of the small

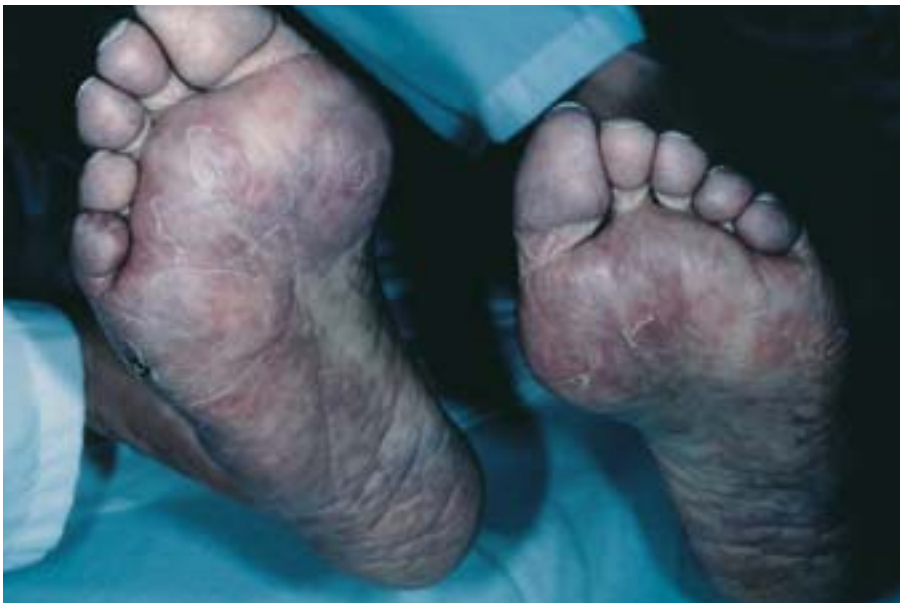

Figure 1. Mottled purple soles of the feet.

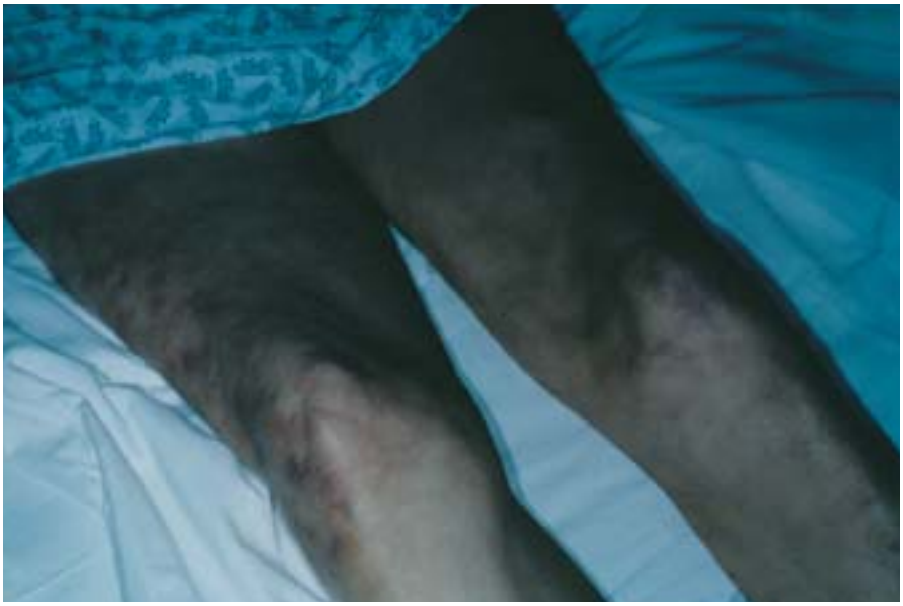

Figure 2. Livedo reticularis of the thighs. Skin biopsy site is visible on the right thigh.

blood vessels that presents clinically as painful lesions of the legs that ulcerate, heal slowly, and leave atrophic scars. In addition to the idiopathic and cholesterol embolic types, livedo reticularis also can be associated with a variety of causes. It may occur as a drug eruption, especially from amantadine. Some other causes of livedo reticularis are connective tissue diseases (eg, systemic lupus erythematosus), infections (eg, human parvovirus B19), dysproteinemias (eg, cryoglobulinemia), and Sneddon syndrome. Renal, bowel, bladder, or mesenteric involvement may be seen.[5] Renal involvement may be diagnosed clinically when renal functions worsen after known inciting factors.[16] Ophthalmoscopy may reveal Hollenhorst plaques, which result from ischemia or infarct.

The patient may have an elevated erythrocyte sedimentation rate, eosinophilia, eosinophiluria, anemia, thrombocytopenia, or hypocomplementemia.[16] Imaging of the aorta by an ultrasound, Doppler scan, transesophageal echocardiogram, or magnetic resonance imaging may reveal atherosclerotic involvement of the vessels.[4] Clinical diagnosis can be confirmed by a biopsy, which

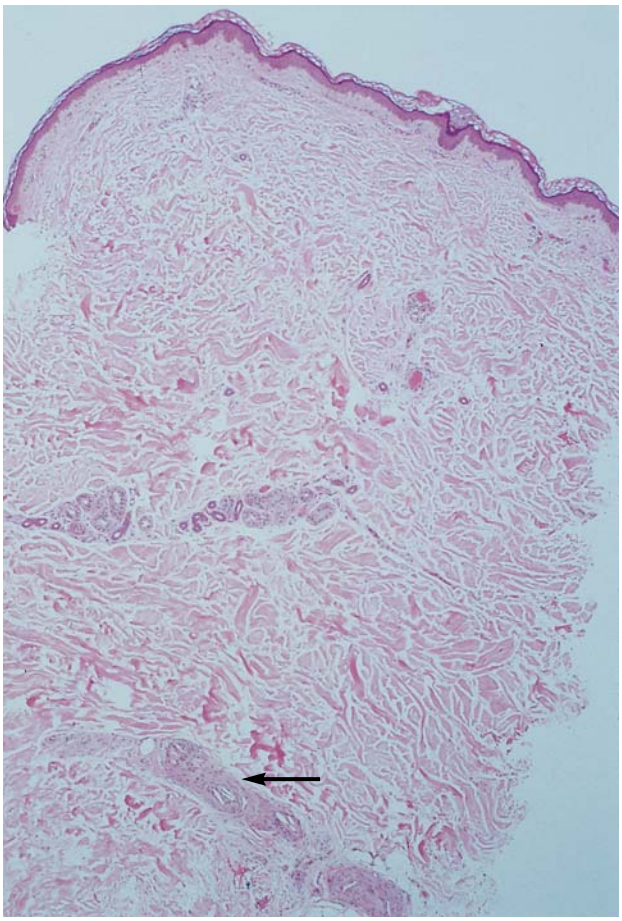

Figure 3. Skin biopsy results showing atheroemboli with cholesterol clefts in the small arteries of the deep dermis (arrow)(H&E, original magnification ×4).

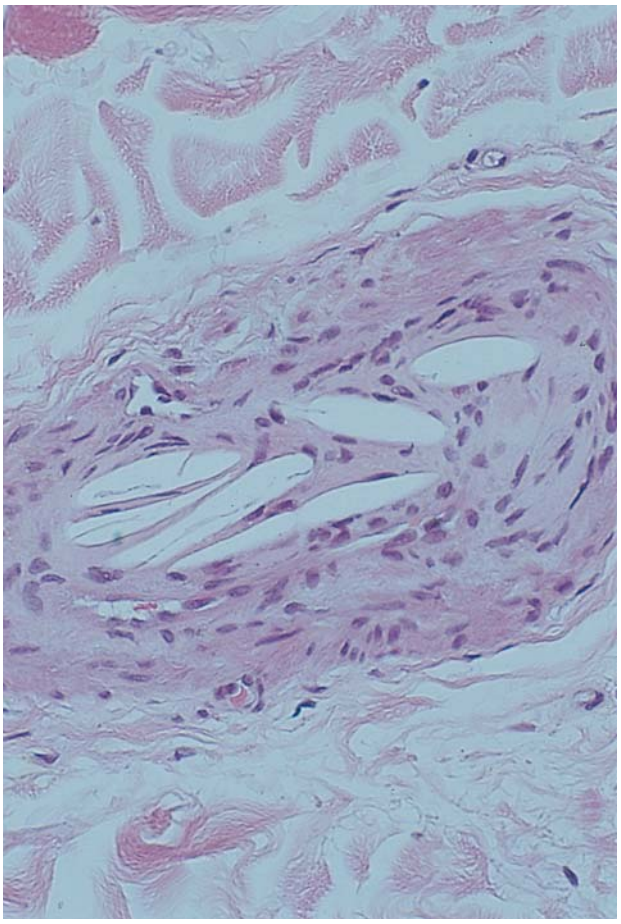

Figure 4. Higher magnification of skin biopsy results showing occlusive atheroemboli (cholesterol emboli) in a deep dermal artery (H&E, original magnification ×40).

shows pathognomonic needle-shaped clefts in small arterioles, which may be accompanied by inflammation of the vessel wall.[17] If skin lesions are not available for biopsy, a kidney or muscle biopsy can be performed, which may show similar histologic changes.[7]

The prognosis of cholesterol embolism is poor, with a mortality rate of 72% to 80%.[5,6] Cardiac failure is the leading cause of death in patients with cholesterol embolism.[13] Renal failure secondary to embolization leads to worsening of renal function, and cardiac failure subsequently occurs. The increase in peripheral vascular resistance due to clogging of the peripheral arterioles with cholesterol emboli is the other mechanism precipitating cardiac failure.[18]

Conclusion

Risk factor modification alters the outcome from atherosclerosis significantly and is worthwhile.[16] Only 30% of cholesterol embolism cases are diagnosed before death,[5] and the treatment of atheroembolism is still controversial. We present this case to emphasize the role of clinical judgment and skin biopsy in the early diagnosis of cholesterol embolism.

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