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IMAGING VIGNETTE

INTERMEDIATE

CLINICAL VIGNETTE

Detecting Free Cholesterol Crystals in a Patient With Spontaneous Cholesterol Embolization Syndrome

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ABSTRACT

Spontaneous cholesterol embolization is thought to be due to aortic plaque-derived shower emboli; however, flowing cholesterol crystals have not been detected. Free multilayer cholesterol crystals obtained from the femoral artery were observed using polarized light microscopy. Detection of these crystals may indicate the occurrence of spontaneous shower emboli. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2020;2:615-8) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

A 90-year-old man with chronic heart failure, atrial fibrillation, and hypertension was admitted with reported appetite loss. Cyanotic lesions were found on the toes and distal phalanges (**Figure 1A**), but he did not express pain, because of a recent history of cerebral infarction. Blood flow, detected using vascular ultrasound, was decreased in bilateral lower arteries; however, there was no significant common iliac, superficial femoral, or popliteal artery stenosis. Serum creatinine level was increased from 1.48 to 2.60 mg/dl, and spontaneous cholesterol embolization syndrome was suspected. Computed tomography showed severe calcification but no ectasia or aneurysmal change in the aorta. Circumferential calcification was detected at the infrarenal abdominal artery and bilateral common iliac arteries.

To confirm cholesterol embolization syndrome, free cholesterol crystals (CCs) in the femoral artery were scanned using 2 methods. Blood was sampled from the right femoral artery and spread on filter paper (pore size 7 μm). A lamé-like reflection, suggesting the presence of crystals (1), was observed both with the eye (**Figure 1B**) and using a microscope (**Figure 1C**). The filter paper was rinsed with distilled water, and this water was scanned using polarized light microscopy as previously described (filter-paper rinse method [1]). The blood was also spread on a glass slide and cover-slipped. The sample was instantly frozen for hemolysis and scanned using polarized light microscopy (instant-freeze method). Free multilayer CCs were detected using both the filter-paper rinse (**Figure 1D**) and instant-freeze methods (**Figure 1E**).

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, or patient consent where appropriate. For more information, visit the *JACC: Case Reports* author instructions page.

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ABBREVIATIONS AND ACRONYMS

CC = cholesterol crystal

Spontaneous embolism, including blue toe, has been termed cholesterol embolization syndrome (2) despite the lack of CCs detected in images. Needle-shaped ghost-cell hematoxylin and eosin–stained entities have been pathologically regarded as CCs (2). However, renal or skin biopsies are required to observe embolized tissues, and free CCs have not yet been detected. By detecting free CCs from spontaneous ruptured aortic plaques (1), innumerable free CCs could easily be sampled from the femoral artery in patients with spontaneous cholesterol embolization syndrome (**Figure 1C**). More CCs than detected are assumed to continuously flow to the toes. CCs trapped in end arteries and muscles may decrease their function via mechanical obstruction and inflammasome pathway activation (3).

After intravenous methylprednisolone administration, the patient's serum creatinine level decreased to 1.34 mg/dl, and the blue toe gradually recovered.

Cholesterol embolization syndrome is considered to be mainly iatrogenic because of interventional or operative procedures (2). Detection of aortic plaques using computed tomographic angiography and transesophageal echocardiography has been attempted; however, spatial resolution is limited. Recent advances in nonobstructive general angioscopy have enabled the detection of spontaneous ruptured aortic plaques. Screening of the aorta using nonobstructive general angioscopy revealed that spontaneous ruptured aortic plaques have an incidence of 80.9% among patients with or suspected to have coronary artery disease, which is quite higher than the reported incidence (<5%) (1). Thus, spontaneous cholesterol embolization syndrome may be more easily diagnosed by detecting free CCs and/or spontaneous ruptured aortic plaques.

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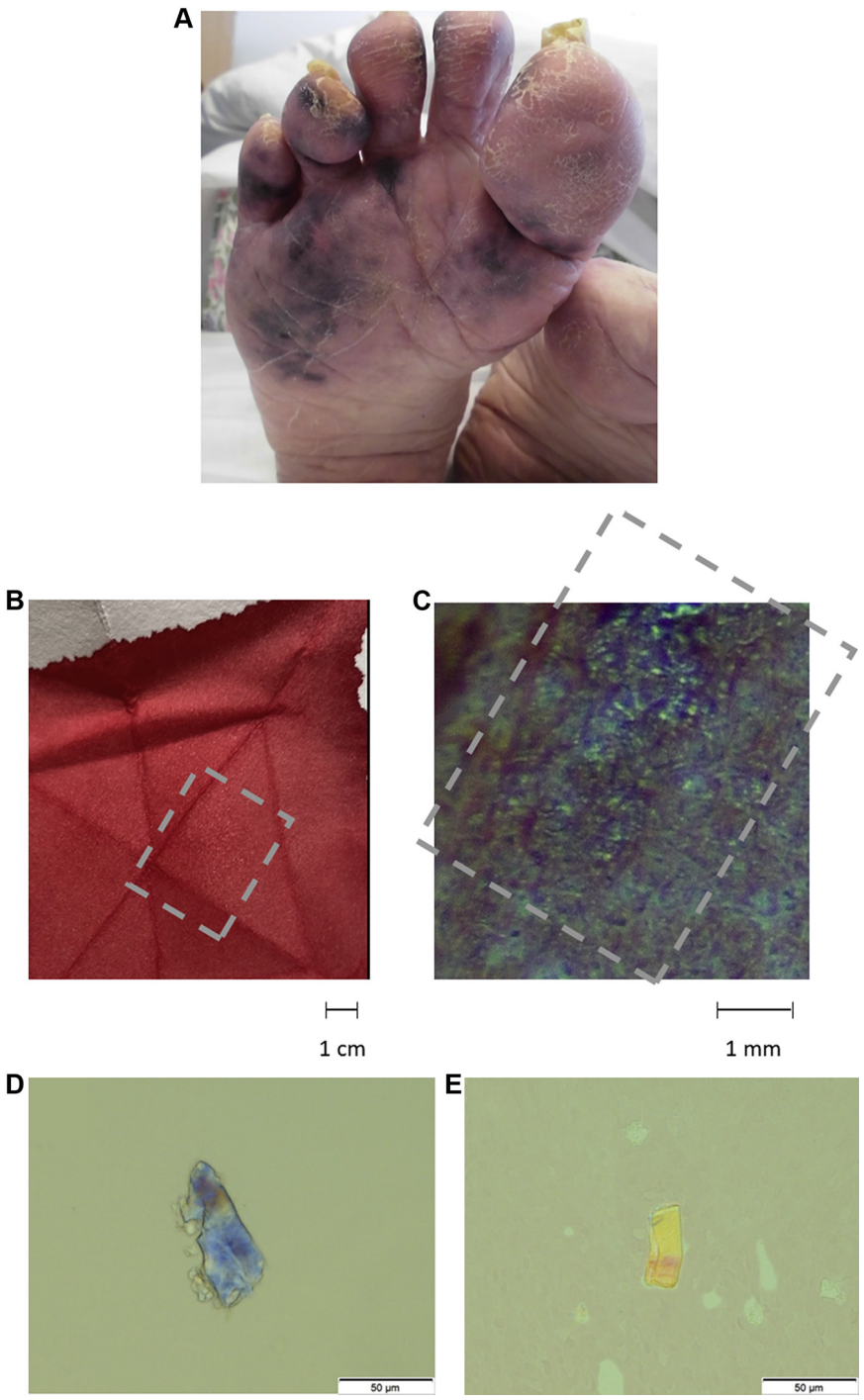
FIGURE 1 Images in a Patient With Spontaneous Cholesterol Embolization Syndrome



(A) Clinical image of cholesterol embolization syndrome. **(B)** Five milliliters of blood spread on filter paper. A slight lamé-like reflection (highlighted within the **rectangle**) was seen. Scale bar: 1 cm. **(C)** A digital microscopic image of the lamé-like reflection (highlighted within the **rectangle**). Scale bar: 1 mm. **(D)** Free multilayer cholesterol crystals obtained using the filter-paper rinse method. Cholesterol crystals appear blue on polarized light microscopy. Scale bar: 50 μm. **(E)** Free multilayer cholesterol crystals obtained using the instant-freeze method. Cholesterol crystals appear orange on polarized light microscopy. Erythrocytes are also seen in the background. Scale bar: 50 μm.

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KEY WORDS blue toe, cholesterol crystals, cholesterol embolization syndrome