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*Images in Hematology*

# Cholesterol Emboli Associated With Warfarin Treatment

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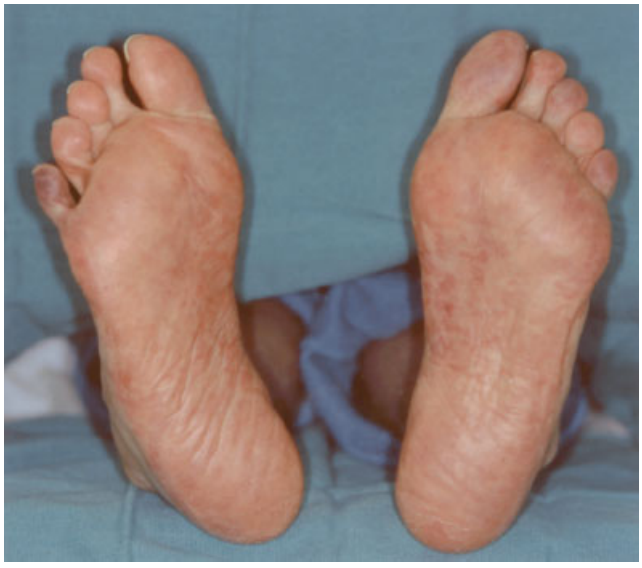

**Image 1.**

A 61-year-old woman with colon cancer presented with painful lesions of the feet that she first noted 1 week following the initiation of warfarin treatment. Five months earlier, she had been found to have stage III colon cancer for which she had undergone incomplete resection of a cecal tumor. Because of subclavian vein thrombosis and pulmonary embolism associated with the presence of a central venous catheter, she had been anticoagulated initially with heparin, followed by warfarin therapy. One week after the warfarin had been started and 2 weeks after the initiation of combined 5-fluorouracil and leucovorin chemotherapy, the patient noticed purple lesions on the soles of both feet. These lesions, which progressed both in number and size over the following 2 months, were sufficiently painful that they made walking difficult. Although the intensity of symptoms did fluctuate, there seemed to be no temporal relationship to subsequent courses of 5-fluoruracil and



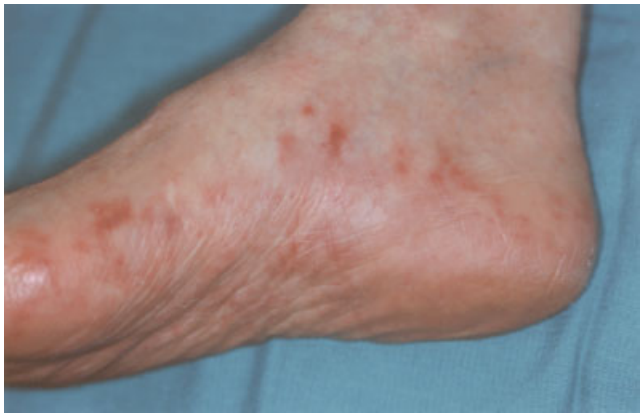

**Image 2.**

leucovorin. A few weeks after the initial lesions had appeared, the patient noted that several of her toes had turned blue. In addition, she described diffuse erythema of her palms, although she observed no discrete lesions or pain of the hands and no rashes or lesions on any other areas of her body.

Two months after the onset of these symptoms, the patient was referred to a coagulationist who found the soles and sides of both feet to have many purple, poorly circumscribed, nonraised, tender lesions. Each foot also exhibited a diffuse, patchy, reddish discoloration that blanched on pressure (see Images 1 and 2), and the fifth digit of the right foot was distinctly purple (see Image 1). The hands showed a diffuse, erythematous,

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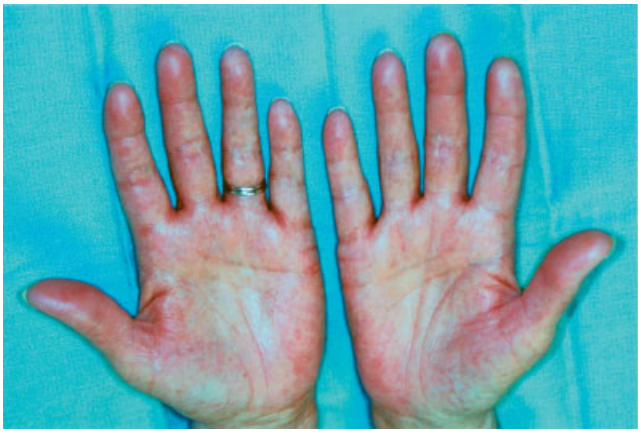

Image 3.

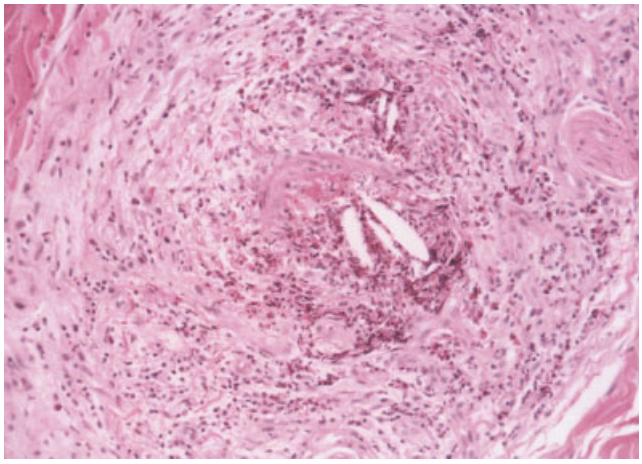

Image 5.

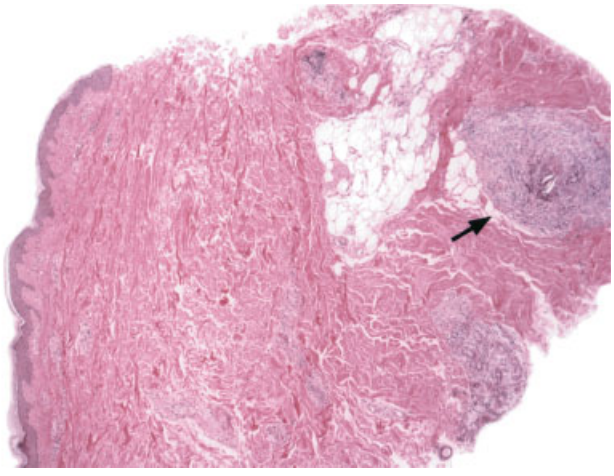

Image 4.

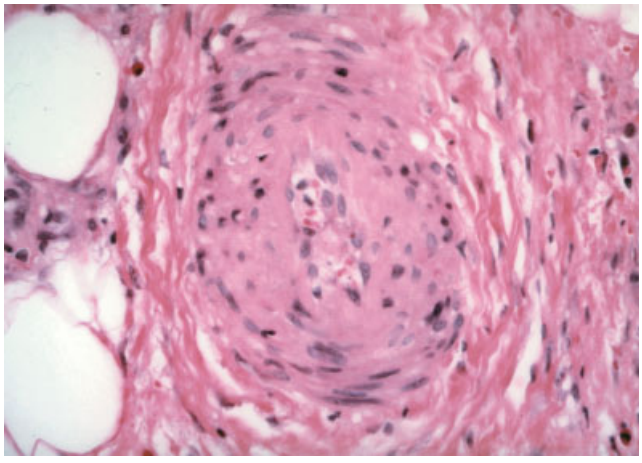

Image 6.

blanching rash along with a few discrete lesions similar to those on the feet (see Image 3). A faint rash was noticed over the right buttock. The serum creatinine was normal (0.7 mg/dL), and no circulating eosinophilia was present.

A biopsy of the involved area of the right buttock showed evidence of an intra-arterial atheroembolus (see Images 4 and 5). A biopsy of the right foot obtained from the area of a purplish lesion showed fibrin and red cell fragments within the lumen of a small artery (see Image 6), suggesting the possibility of an additional atheroembolus. However, evidence of atheroembolism was not found in any of the histologic sections from this foot.

Based on these pathologic findings and on the clinical features of this case, the diagnosis of cholesterol emboli was made. Because no arterial manipulations had been performed that could explain these emboli, they were felt to be etiologically related to the warfarin. It is well known that warfarin can produce a violaceous, painful discoloration of the toes and the sides of the feet that is commonly referred to as the "purple toe syndrome". This syndrome is thought to be caused by cholesterol emboli that are due either to hemorrhage into atheromatous plaques or to weakening of the fibrin meshwork that overlies the atheromatous lesions. Evidence of cholesterol embolization in other skin areas has also been reported. While the diffuse redness of the hands of our patients also raises the possibility of cutaneous toxicity caused by 5-fluorouracil, neither the clinical presentation of this case nor the findings of cholesterol emboli support the diagnosis of chemotherapy-induced palmar–plantar erythrodysesthesia syndrome (hand–foot syndrome).

Because of the recent history of pulmonary embolism, a decision was made to continue anticoagulation with warfarin. Over the ensuing several weeks, the patient improved considerably, and 6 months after the onset of symptoms, she had become completely asymptomatic, and her feet had returned to normal.