Painful ear nodules

Was there a connection between our patient's drug use and the appearance of his ears, which were turning black?

Katherine Winter, MD; Rhianna Ritter, MD; Anthony J. Viera, MD
University of North Carolina Family Medicine, Chapel Hill

kwinter@unch.unc.edu

DEPARTMENT EDITOR
Richard P. Usatine, MD
University of Texas Health Science Center at San Antonio

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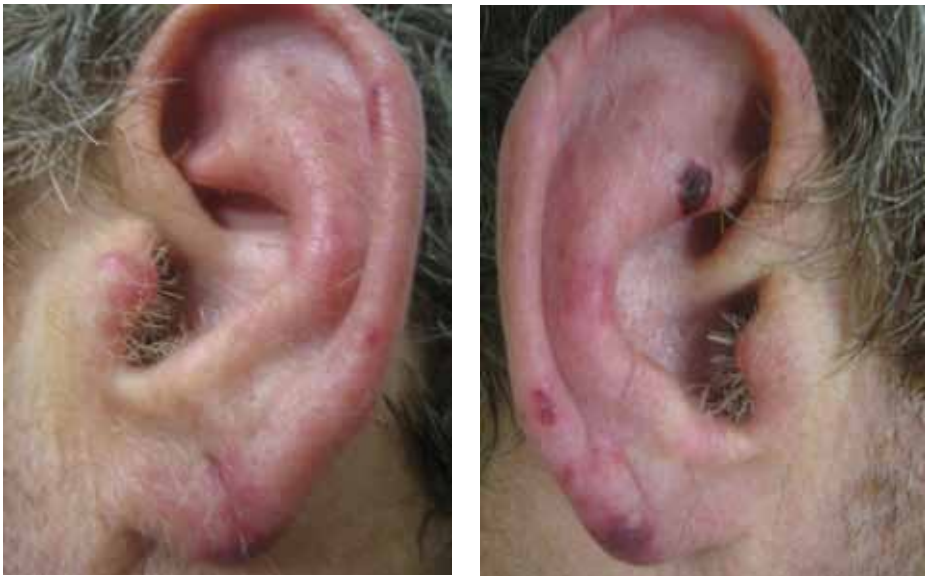
A 49-YEAR-OLD MAN with a history of hypertension, hypercholesterolemia, polysubstance use, recurrent methicillin-resistant *Staphylococcus aureus* skin infections, and chronic hepatitis C infection sought care at our emergency department (ED) because parts of his ears had started turning black 3 days earlier. They were also painful to the touch. He denied fever, any similar skin lesions, injury to his ears, or a history of easy bleeding or bruising. A recovering alcoholic, he admitted to regular marijuana use and twice-weekly cocaine use. He had last used cocaine 3 days ago.

The patient was thin and in no acute distress. His vital signs and cardiopulmonary exams were normal. Examination of his ears revealed bilateral violaceous firm, tender purpura on the pinnae (**FIGURE**).

A complete blood count (CBC) revealed mild leukopenia (white blood cell [WBC] count, 2.0×10^9/L), neutropenia (0.9×10^9/L), and a normal platelet count (264×10^9/L). A chemistry panel, liver function tests, and prothrombin time were normal. Erythrocyte sedimentation rate (ESR) was elevated to 69 mm/h. The patient's cholesterol level was not elevated. Urine toxicology was positive for cocaine and opioids. A human immunodeficiency virus test was negative.

- WHAT IS YOUR DIAGNOSIS?
- HOW WOULD YOU TREAT THIS PATIENT?

FIGURE
Tender purpura on the pinnae



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Lesions typically appear on the ears and the cheeks, although they can appear anywhere on the body.

Diagnosis: Levamisole toxicity

The patient was diagnosed with levamisole toxicity based on his clinical presentation and the fact that he had used cocaine around the time his ear lesions appeared.

Levamisole—primarily a veterinary antihelmintic medication—is used on rare occasions to treat nephrotic syndrome in children.[1] Levamisole is frequently added to cocaine or heroin to increase the street drug's potency. The Drug Enforcement Administration reports that 69% of seized cocaine lots in the United States contain levamisole.[2]

The compound is thought to cause a vasculitis and bone marrow suppression resulting in neutropenia. The vasculitis targets small vessels, resulting in thrombosis, which can lead to tissue necrosis.[1]

Other possibilities in the differential Dx

The differential diagnosis includes a variety of vasculitides and other microvascular pathologies.

Cholesterol emboli arise when cholesterol crystals are released from atherosclerotic plaques, typically after invasive cardiac procedures. In addition, anticoagulants can cause the release of these crystals by inhibiting the formation of protective clots around unstable plaques.[3] These emboli can seed the microvasculature anywhere, but the kidneys and skin are most frequently affected. These crystals not only clog the vasculature, causing tissue ischemia, but also activate the complement cascade, triggering a series of inflammatory responses that can lead to luminal fibrosis and narrowing.[3]

Affected patients have a history of atherosclerotic disease or predisposing factors such as hypertension or diabetes. Ulcerations or frank cyanosis may be found at the tips of the fingers or toes. In severe cases, gangrene will form in these regions. Patients may also have livido reticularis, a lace-like hyperpigmented rash over the lower extremities. Laboratory analysis may indicate acute renal failure or eosinophilia.[3]

Bacterial endocarditis results from the seeding of bacterial emboli primarily from the mitral or tricuspid valves.[4] Streptococci are the primary infectious agent, with staphylococci being more common among intravenous drug users. High-risk populations include patients with artificial valves, the elderly, and the immunocompromised.[4]

Clinical manifestations include Janeway lesions (asymptomatic hemorrhagic papules on the palms) and Osler's nodes (tender nodules on the fingertips). Splinter hemorrhages, or linear nonblanching lesions, may be present within the nail beds. Palpable purpura and petechiae may also be found.

Patients may have positive blood cultures, leukocytosis, an elevated ESR, or vegetations on a transesophageal echocardiogram.[4] The physical exam may reveal a new cardiac murmur.

High circulating levels of cryoglobulins can arise in the setting of hepatitis C infection, but can also be seen in a number of autoimmune disorders and other infectious diseases.[5] Cryoglobulins are immune complexes that are deposited into the lumen of microvasculature. In cold temperatures, these cryoglobulins precipitate, resulting in vasculitis. While most patients are asymptomatic, cutaneous findings in the distal extremities can include palpable purpura, ulcerations, and livido reticularis.[5] Patients may complain of arthritis or symptoms consistent with Raynaud's phenomenon.

Detection of specific serum cryoprecipitates isolated by immunofixation is pathognomonic for this condition, provided the sample is collected in a warm tube. Elevated rheumatoid factor and decreased complement levels may also be seen.[5]

Henoch-Schönlein purpura (HSP) is a small vessel vasculitis caused by IgA deposition that predominantly affects children. HSP has a host of systemic symptoms, often preceded by a benign upper respiratory infection, consisting of palpable purpura, arthritis, abdominal pain, and glomerulonephritis.[6] Palpable purpura will generally be found in dependent portions of the body—especially the buttocks and lower legs.

While the diagnosis is primarily clinical, serum IgA levels and ESR can be elevated, urinalysis may demonstrate hema-

turia or proteinuria, and a CBC may reveal a leukocytosis with normal platelets.[6]

Suspect levamisole toxicity in patients using cocaine

Patients with levamisole toxicity present with sudden-onset tender plaques or bullae with necrotic centers within days of cocaine use. Case reports cite lesions primarily on the ears and cheeks. However, they can appear almost anywhere on the body.[2,7-9] Physicians should have a high index of suspicion for levamisole toxicity in patients using cocaine who present with unexplained neutropenia or vasculitis.

Laboratory tests. If needed, tissue biopsy and urine detection of levamisole can be used to confirm the diagnosis.[1]

Management is straight-forward, but not simple

Skin lesions have been reported to improve several weeks after discontinuing use of contaminated cocaine[1] (strength of recommendation [SOR]: **C**). Known users should be referred to drug treatment centers and counseled on the risks of use.

Our patient required hospitalization

When our patient came into the ED, he also complained of left thigh pain and swelling. A computed tomography scan revealed a deep sartorius abscess. The patient was admitted for ultrasound-guided aspiration of the abscess and IV antibiotics. His bilateral painful ear nodules persisted throughout his hospitalization, although his neutropenia resolved after 3 days. JFP

CORRESPONDENCE
Katherine Winter, MD, 101 Manning Drive, Chapel Hill, NC 27514; kwinter@unch.unc.edu

Strength of recommendation (SOR)

- **A** Good-quality patient-oriented evidence
- **B** Inconsistent or limited-quality patient-oriented evidence
- **C** Consensus, usual practice, opinion, disease-oriented evidence, case series

Lesions improve several weeks after discontinuing use of contaminated cocaine.

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