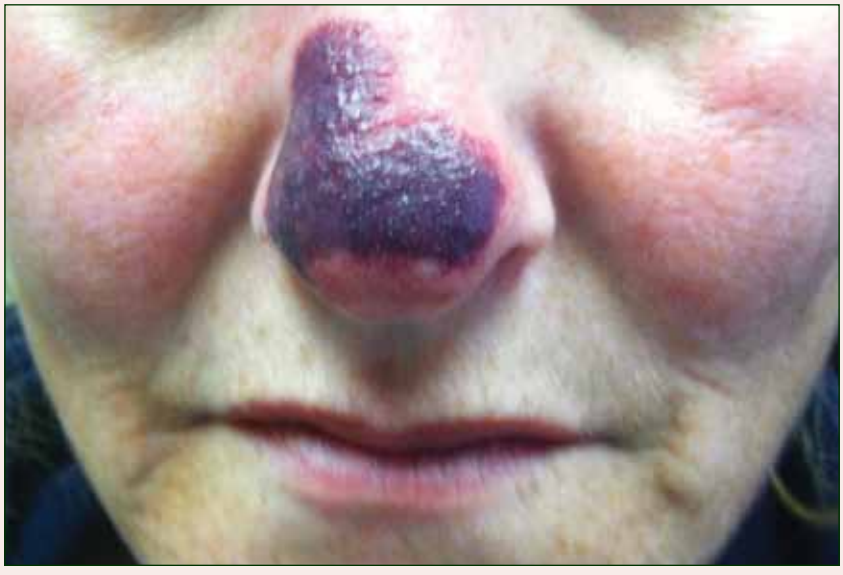
Painful Purpura and Cutaneous Necrosis

What's the diagnosis?



A 44-year-old woman with a history of hepatitis C virus and cocaine abuse presented with painful bruising and skin breakdown. Three weeks prior she was treated at an urgent care clinic with oral clindamycin for a recurrent *Staphylococcus* infection of her finger. One week later she started developing purpura and painful skin necrosis and ulceration. Most notable was the purpura on the tip of the nose. She also reported arthralgia and low-grade fever.

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The Diagnosis: Levamisole-Contaminated Cocaine

Physical examination revealed scattered palpable purpura including the nasal tip and large necrotizing skin lesions with bullae (Figure 1). Retiform purpura was noted on the patient's trunk and legs. Purpuric plaques in various stages of necrosis were identified on the arms, trunk, breasts, and thighs, with an early lesion involving the left ear (Figure 2). Vitals revealed a blood pressure of 151/79 mm Hg and a temperature of 37.3°C. Although the patient initially denied illicit drug use, she later admitted to smoking crack cocaine prior to the skin eruption.

Levamisole, an agent used in the veterinary setting to deworm cattle and pigs, is a common additive found in nearly 77% of the seized cocaine supplies in the United States.[1] Because of its immunomodulator effects, the agent was once used in humans to treat conditions such as colon cancer, rheumatoid arthritis, and nephritic syndrome. Therapeutic levamisole use has been associated with purpura on the external ears, cheeks, and nasal tip. The predilection for purpura on the ears was first described in children using levamisole as treatment of nephritic syndrome.[2] Antinuclear cytoplasmic antibodies (ANCA) and antiphospholipid antibodies also were associated with therapeutic use.[3] Reported effects of levamisole in cocaine users include fever, agranulocytosis, and infection. The mechanism is currently unknown but is thought to be an immunological process as evidenced by the presence of positive autoantibodies.[4] Characteristic purpura in a cocaine abuser should alert the physician to consider levamisole as the culprit.

The diagnosis is largely a clinical one and other serious etiologies must be ruled out. The differential should include purpura fulminans, a rare hemorrhagic condition caused by severe infection, such as meningococcemia or deficiency of the vitamin K–dependent anticoagulants protein C and protein S. Given our patient's history of hepatitis, purpura fulminans could have been likely. Purpura fulminans is rapidly progressive and is usually accompanied by disseminated intravascular coagulation. Coagulation studies and evidence of a consumptive coagulopathy such as thrombocytopenia, prolonged partial thromboplastin time, and activated partial thromboplastin time would favor this diagnosis. These studies as well as protein C and protein S were normal in our patient. Mixed cryoglobulinemia also should be suspected in a patient with hepatitis C virus who presents with vasculitis and arthralgia. An undetectable viral load in addition to a negative assay for cryoglobulins and normal complement (C3 and C4) levels make this diagnosis unlikely. Further, the purpura in

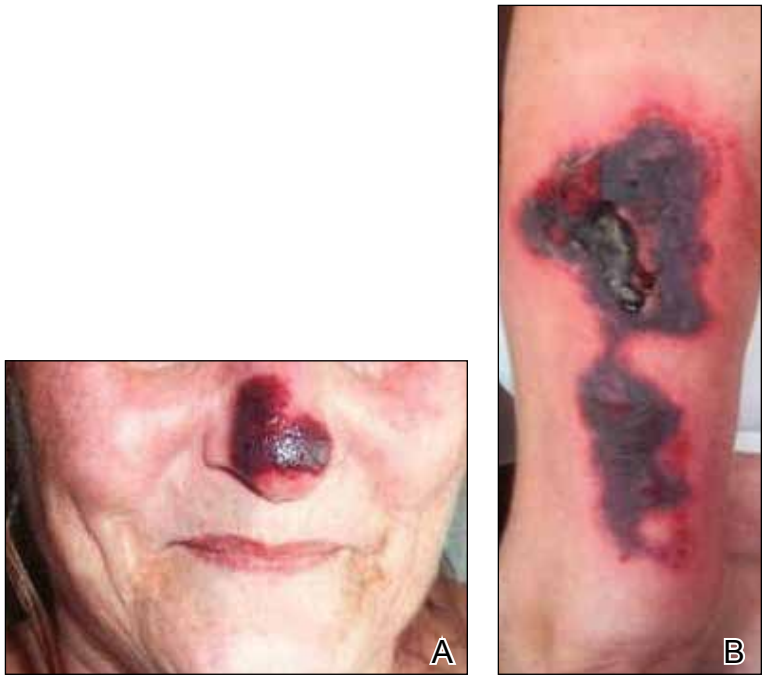

Figure 1. Scattered palpable purpura including the nasal tip (A). Large necrotizing skin lesions with bullae on the arm (B).

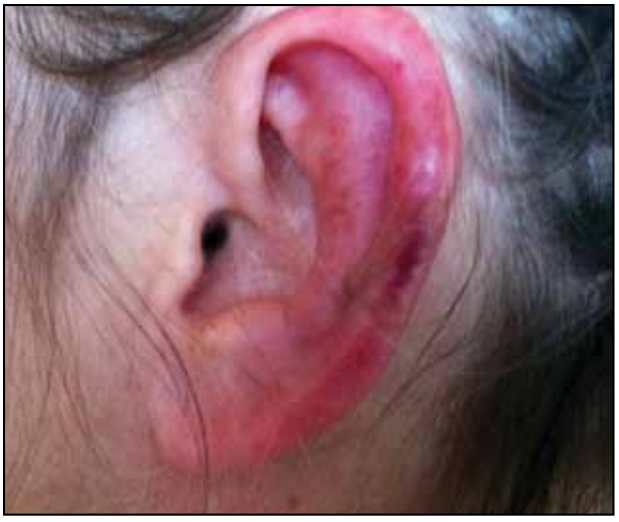

Figure 2. An early purpuric plaque on the left ear.

cryoglobulinemia is typically confined to the lower extremities.[5] Warfarin-induced skin necrosis also should be considered in patients who are taking warfarin.

Laboratory tests can be used to confirm the presence of infection, agranulocytosis, and coagulopathy. Although urine drug screen can confirm exposure to cocaine, levamisole is not detected in routine toxicology screening. Its half-life is between 5 and 6 hours; therefore, detection in blood or urine should be done within 48 hours of exposure.[3,4] Unfortunately, our patient presented 2 weeks after cocaine use, making detection of levamisole unfeasible. Rheumatologic screening also is appropriate in cases of suspected vasculitis. Our patient had a negative antinuclear antibody but tested positive for lupus anticoagulant and perinuclear ANCA. IgA and IgG anticardiolipin were negative with an indeterminate IgM anticardiolipin level. The literature supports these findings, as ANCA antibodies occurred in more than 90% of reported cases.[3] Further, IgM anticardiolipin antibodies and lupus anticoagulant were positive in 65% and 51% of cases, respectively.[3] Leukocyte and neutrophil count were normal in our patient.

Management of these patients is mainly supportive. Complete avoidance of the offending agent is absolutely essential for resolution and avoidance of recurrence. Provided that the patient abstains from cocaine, the skin findings typically resolve in 2 to 3 weeks.[3,6] The antibodies, however, may be present for up to 14 months.[2,3,6] Treatment with steroids and other immunosuppressants has been reported, but evidence is lacking on their role in the resolution of the lesions.[3] In patients who develop a temporary antiphospholipid syndrome, aspirin may be recommended as a preventative measure.[6] Pain management, treatment of secondary infection especially in situations with agranulocytosis, and surgical debridement of wounds are all potential problems that can arise.

Our patient had complete resolution of the purpura involving the nose and ear over the course of 3 weeks. She did, however, have to undergo surgical debridement of the nonhealing full-thickness necrotic lesions on her legs and arms.

The 2013 National Survey on Drug Use and Health estimates 1.5 million individuals aged 12 years or older were current (within the last month) users of cocaine.[7] With levamisole becoming more prevalent in cocaine supplies, clinicians should be aware of this emerging condition. Rapid recognition can spare the patient unnecessary testing and inappropriate treatment regimens. Because testing for levamisole is difficult and not routinely performed, this case highlights the importance of clinical clues and an accurate social history in clinching the diagnosis.

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