

Levamisole Toxicity From Adulterated Cocaine

Volume 59 - Issue 1 - January 2019

Authors:

Carmen A. Julian, DO

Chief Resident, Philadelphia College of Osteopathic Medicine (PCOM)/North Fulton Hospital Medical Campus Dermatology Residency, Roswell, Georgia, in affiliation with the Georgia Campus of PCOM

Marcus B. Goodman, DO

Dermatologist, Goodman Dermatology, PC, and Program Director, PCOM/North Fulton Hospital Medical Campus Dermatology Residency, Roswell, Georgia

Citation:

Julian CA, Goodman MB. Levamisole toxicity from adulterated cocaine. *Consultant*. 2019;59(1):22-24.

A 40-year-old woman presented with fever, cough, hemoptysis, and an asymptomatic rash with purplish discoloration on her trunk, extremities, and ears.

History. The patient reported that the rash had started 5 days prior while she had been undergoing inpatient treatment for pneumonia at a nearby hospital. The rash had started on day 2 of her admission. She denied pain, bleeding, or pruritus associated with the lesions and denied any constitutional symptoms. Empiric intravenous antibiotics had been given for community-acquired pneumonia on her previous admission. A punch biopsy had been performed at her recent outside admission, but our attempts to obtain a report were unsuccessful. No specific treatment for her rash had yet been implemented.

The patient had left from the previous hospital against medical advice and presented to our hospital with worsening symptoms. Prior medical records, including the biopsy results and

antibiotic treatment, again were unavailable. She reported tobacco abuse and cocaine use, most recently 11 days prior. She denied intravenous drug use.

Physical examination. At presentation, the patient was nontoxic and afebrile, with stable vital signs. Skin examination revealed tender, violaceous macules and patches on the trunk, extremities, and ears (**Figures 1-3**). There were areas of retiform, stellate purpura progressing to bullae on the upper arms and lower legs. Additionally, there was a pink to erythematous maculopapular eruption on the entire back. A small eschar was present on the left medial ankle (**Figure 4**). No desquamation or mucosal involvement was noted. On the left outer arm, there was a healing, sutured punch-biopsy wound (**Figure 5**).



Figure 1.



Figure 2.



Figure 3.



Figure 4.



Figure 5.

Diagnostic tests. Laboratory test results were as follows: white blood cell count, 7020/ μ L; hemoglobin, 10.7 g/dL; platelet count, 535 \times 10³/ μ L; C-reactive protein, 2.85 mg/L; and lactate, 1.70 mg/dL. Results of a basic metabolic panel were within normal limits.

HIV test results were nonreactive, antinuclear antibody (ANA) test results were negative, and perinuclear antineutrophil cytoplasmic antibody (p-ANCA) and cytoplasmic antineutrophil cytoplasmic antibody (c-ANCA) titers were all less than 1:20.

Chest radiography and chest computed tomography angiography showed opacities in the left lower lobe and right upper lobe, along with splenomegaly and bilateral axillary lymphadenopathy.

Diagnosis. The differential diagnosis for retiform purpura included Wegener granulomatosis, cryoglobulinemia, cocaine levamisole toxicity, septic vasculitis, polyarteritis nodosa, calciphylaxis, and warfarin necrosis. Based on the patient's history and clinical presentation, a diagnosis of levamisole toxicity from adulterated cocaine was made.

Discussion. Levamisole was withdrawn from in the US market in 1999 due to serious adverse effects related to agranulocytosis, along with development of safer alternative anthelmintic agents.¹ It is still in use as an anthelmintic agent for livestock and in aquariums and thus remains available as a cutting agent in cocaine.² Approximately 70% of cocaine in the United States is contaminated with levamisole.^{3,4} It adds bulk and a purity factor due to its color, weight, and white powdery consistency. There may also be an added stimulant effect of levamisole, making it ideal for passing street tests by users and dealers.⁴

Cutaneous manifestations of levamisole toxicity can range from exanthems, urticaria, angioedema, and lichenoid eruptions to vasculitis and Stevens-Johnson syndrome.⁵ A distinguishing feature are the characteristic necrotic and purpuric skin lesions that preferentially involve the earlobes and cheeks.^{3,6}

Biopsy of a representative skin lesion reveals a leukocytoclastic vasculitis, with varying involvement of superficial and deep dermal vessels, and often vasculopathy with fibrin thrombi in vessel walls.⁷

Levamisole is not detected in routine toxicology screens, but other laboratory abnormalities can include neutropenia/agranulocytosis and positive test results for p-ANCA, lupus anticoagulant antibodies, anti-double-stranded DNA, proteinase-3, and anticardiolipin antibodies.⁸⁻¹⁰ Some laboratory test result disparities may aid in distinguishing levamisole vasculitis from idiopathic ANCA-associated vasculitis, since patients will have extremely high p-ANCA levels and low (or absent) antibodies to myeloperoxidase, the typical target of p-ANCA.^{9,10} Additionally, other types of ANCA vasculitis may show lower ANCA titers, with specific antibodies to one neutrophilic antigen rather than several.¹⁰ The various immune markers may remain positive from 2 months to up to 1 year after discontinuation.¹⁰

Stellate purpura in the setting of recent cocaine use is becoming a recognizable clinical syndrome.⁷ Our patient's recent hospitalization for pneumonia with intravenous antibiotic treatment widened the differential to a possible drug reaction. Such clinical findings also require consideration of autoimmune and inflammatory vasculopathic conditions.¹⁰ Levamisole can cause extracutaneous disease secondary to vasculitis involving any organ system—most notably pulmonary vasculopathy, glomerulonephritis, coronary vasculitis, ischemic colitis, ulcers, and

rarely pancreatitis.^{1,11} Renal and pulmonary disease occur more commonly in idiopathic ANCA-associated vasculitis; reports suggest that it is commonly overlooked in levamisole toxicity cases.^{9,10} Early recognition of levamisole as the offending agent is paramount in avoiding unnecessary aggressive treatments associated with the misdiagnosis of an autoimmune cause of vasculitis.¹⁰

Management. Treatment is primarily supportive following strict abstinence from cocaine. Necrotic plaques may require debridement and prevention of secondary infection.¹² Corticosteroids, hyperbaric oxygen, and methotrexate have led to improvement in case reports; however, no evidence-based studies have demonstrated benefit over a conservative approach.^{3,8} Skin grafting may be necessary; some studies recommend early graft intervention with large body surface area involvement.¹²

References

1. Lee KC, Ladizinski B, Nutan FNU. Systemic complications of levamisole toxicity. *J Am Acad Dermatol.* 2012;67(4):791-792.
2. Drug Enforcement Administration, Office of Diversion Control, Drug & Chemical Evaluation Section. Levamisole (Ergamisol®). https://www.deadiversion.usdoj.gov/drug_chem_info/levamisole.pdf. April 2013. Accessed November 27, 2018.
3. Bradford M, Rosenberg B, Moreno J, Dumyati G. Bilateral necrosis of earlobes and cheeks: another complication of cocaine contaminated with levamisole. *Ann Intern Med.* 2010;152(11):758-759.
4. Mallette JR, Casale JF, Jones LM. The separation of cocaine and phenyltetrahydroimidazothiazole mixtures. *Microgram J.* 2013;10(2):12-16.
5. Bologna JL, Jorizzo JL, Schaffer JV, eds. *Dermatology.* Vol 2. 3rd ed. Philadelphia, PA: Elsevier Saunders; 2014:1402-1403.
6. Chung C, Tumei PC, Bimbaum MD, et al. Characteristic purpura of the ears, vasculitis, and neutropenia—a potential public health epidemic associated with levamisole adulterated cocaine. *J Am Acad Dermatol.* 2011;65(4):722-725.
7. Nolan AL, Jen K-Y. Pathologic manifestations of levamisole-adulterated cocaine exposure. *Diagn Pathol.* 2015;10:48.
8. Belfonte CD, Shanmugam VK, Kieffer N, Coker S, Boucree A, Kerr G. Levamisole-induced occlusive necrotizing vasculitis in cocaine abusers: an unusual cause of skin necrosis and neutropenia. *Int Wound J.* 2013;10(5):590-596.
9. Álvarez Díaz H, Mariño Callejo AI, García Rodríguez JF, Rodríguez Pazos L, Gómez Buena I, Bermejo Barrera AM. ANCA-positive vasculitis induced by levamisole-adulterated cocaine and nephrotic syndrome. *Am J Case Rep.* 2013;14:557-561.
10. Strazzula L, Brown KK, Brieva JC, et al. Levamisole toxicity mimicking autoimmune disease. *J Am Acad Dermatol.* 2013;69(6):954-959.
11. Pearson T, Bremmer M, Cohen J, Driscoll M. Vasculopathy related to cocaine adulterated levamisole: a review of the literature. *Dermatol Online J.* 2012;18(7):1

levamisole: a review of the literature. *Dermatol Online J.* 2012;18(7):1.

12. Miner J, Gruber P, Perry TL. Early excision and grafting, an alternative approach to surgical management of large body surface area levamisole-adulterated cocaine induced skin necrosis. *Burns.* 2015;41(3):e34-e40.

[HMP Education](#) [HMP Omnimedia](#) [HMP Europe](#)

© 2024 HMP Global. All Rights Reserved. [Cookie Policy](#) [Privacy Policy](#) [Term of Use](#)