Case Report

Levamisole-Contaminated Cocaine: An Emergent Cause of Vasculitis and Skin Necrosis

Osama Souied, Hassan Baydoun, Zahraa Ghandour, and Neville Mobarak

1 Department of Internal Medicine, Staten Island University Hospital, 475 Seaview Avenue, Staten Island, NY 10305, USA
2 Faculty of Medical Sciences, Lebanese University, Beirut, Lebanon
3 Department of Infectious Diseases, Staten Island University Hospital, 475 Seaview Avenue, Staten Island, NY 10305, USA

Correspondence should be addressed to Hassan Baydoun; baydounhassan@hotmail.com

Received 2 February 2014; Accepted 17 February 2014; Published 20 March 2014

Academic Editor: Jeffrey M. Weinberg

Copyright © 2014 Osama Souied et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

The prevalence of cocaine adulterated with levamisole-induced vasculitis is increasing and physicians should be aware of this unique entity. There have been many reports of cutaneous vasculitis syndrome caused by cocaine which is contaminated with levamisole. Levamisole was used as an anti-helminth drug and later was rescinded from use in humans due to adverse effects. Through this paper, we will report a 39-year-old crack cocaine user who presented with purpuric rash and skin necrosis of his ear lobes. Levamisole-induced vasculitis syndrome was suspected. A urine toxicology screen was positive for cocaine, opiates, and marijuana. Blood work revealed positive titres of ANA and p-ANCA, as well as anti-cardiolipin antibody. Biopsy taken from the left ear showed focal acute inflammation, chronic inflammation with thrombus formation, and extravasated blood cells. Treatment was primarily supportive with wound care.

1. Introduction

Levamisole, which was first developed as an anti-helminth agent in the 1960s [1], can result in toxicity from the use of adulterated cocaine. It is an increasing reported cause of agranulocytosis, vasculopathy, and skin manifestations like specific rash and skin necrosis [2]. In this report, we describe the case of a 39-year-old crack cocaine user who presents with this unique thrombotic vasculitis, purpuric lesions, and skin necrosis of the ear lobes related to levamisole toxicity.

2. Case Presentation

A 39-year-old man with past medical history of cocaine abuse, gout, attention deficit hyperactivity disorder, and hand cellulitis secondary to methicillin-resistant Staphylococcus aureus (MRSA) infection presented with painful lesions on his right hand, left foot, and bilateral ears. Onset was three days prior to presentation where he started to have a constant burning sensation, most severely on the superior aspect of his ears. He had last smoked crack cocaine one day prior to presentation and he was snorting it the day before.

On admission, the patient was afebrile, with blood pressure of 125/83 mmHg and heart rate of 110 beats per minute. On examination, the blisters on the dorsum of the right hand were new, although there was still an open wound from hand cellulitis secondary to MRSA infection 4 years ago on the dorsum of the second metacarpophalangeal joint. There was also a dry, closed, and scaly lesion on the left foot, as well as black necrotic bilateral auricular lesions with 1-2 mm blisters noted on both ears (Figure 1). The tongue had a hard nonerythematous nodule on the center, tender to touch. The rest of the physical examination was unremarkable.

Review of systems was negative for fever, chills, cough, hemoptysis, hematuria, Raynaud’s phenomenon, alopecia, and oral or nasal ulcers. The patient had a history of necrotic lesions. They started 2 years ago, while at work he noticed dark patches on his cheeks and nose that would not wash off and were painful to touch. Over the next few hours, the patches spread bilaterally over the buccal area and the lower aspect of the nose. At that time he complained of fever, chills, myalgia, and joint pain. He was hospitalized and diagnosed with having septic vasculitis secondary to MRSA and was treated with vancomycin.
spondylitis and rheumatoid arthritis as well as various can-
treatment of different autoimmune diseases like ankylosing
immunomodulatory properties, levamisole was used in the
levamisole [4]. Later on and after the recognition of its
basis. The Drug Enforcement Agency (DEA) reports that
around two million Americans who use cocaine on a regular
early intervention avoided hospitalization [3]. There are
Cocaine is the most commonly reported illicit drug in the
3. Discussion
On this admission, laboratory testing showed a white
count of 15.4 k/µL, hemoglobin of 14.9 g/dL, hematocrit of
41.9%, and platelet count of 208,000 k/µL. Basal metabolic
profile, liver function tests, and haptoglobin were normal.
Antinuclear antibody (ANA) and perinuclear-antineutrophil
cytoplasmic antibody (p-ANCA) were weakly positive at
a 1:40 titer and 11 U (normal <1U), respectively. IGM
cardiolipin antibody was positive at 19 U (normal <11 U).
Antiphospholipid antibodies, complement level, HIV anti-
bodies’ titers, hepatitis panel, cytoplasmic antineutrophil
cytoplasmic antibodies (c-ANCA), beta-2 glycoprotein, and
blood and urine cultures were all negative. A urine toxicology
screen was positive for cocaine, opiates, and marijuana.
Biopsy taken from the superior aspect of the left ear showed
focal acute inflammation of the surface epidermis, with foci
of mild perivascular acute and chronic inflammation with
thrombus formation and foci showing extravasated red blood
cells. Burn and infectious disease services were consulted
and recommended supportive wound care with bacitracin cream.
The patient improved and was discharged few days later.

3. Discussion
Cocaine is the most commonly reported illicit drug in the
emergency department in the United States [3]. There are
around two million Americans who use cocaine on a regular
basis. The Drug Enforcement Agency (DEA) reports that
69% of cocaine in the United States is contaminated with
tobacco [4]. Later on and after the recognition of its
immunomodulatory properties, levamisole was used in the
treatment of different autoimmune diseases like ankylosing
spondylitis and rheumatoid arthritis as well as various can-
cers [1, 5, 6]. It was withdrawn for use in humans in the
United States in 1999 [2] due to its adverse side effects of
agranulocytosis and vasculopathy [7].

Levamisole was first identified as a cocaine adulterant
in the USA in 2003 and now it is found in around 70%
of the cocaine seized in the United States as an adulterant
[8]. The reason why levamisole is added intentionally during
the manufacturing process of the cocaine is to potentiate the
psychoaffective effects mainly by its stimulant activity
due to dopamine release and also because of the similar
appearance. It is usually detected by gas chromatography
mass spectroscopy technique in urine specimens [9]. The
first cases of levamisole-associated vasculitis and agranu-
locytosis among cocaine users were reported in 2008 in
the southwestern United States [8]. Since that time, the
number of cases continues to increase with more than 200
reported cases of levamisole related toxicity [4] which causes
cutaneous, hematological, and neurological manifestations.
The cutaneous involvement includes development of skin
rash as purpuric papules, ecchymosis, and skin necrosis
often having a “retiform,” “reticular,” or “stellate” pattern
leading to ulceration and secondary infection and associated
with leukopenia and autoantibody production [10]. Bilateral
ear involvement, especially helical margins, is seen also
in the majority of patients [11]. It was also described in
some pediatric cases related to the use of levamisole in
nephritic syndrome where the pathological examination revealed
a mixed leukocytoclastic and thrombotic vasculitis, or a purely
thrombotic vasculopathy [12].

Although cocaine contaminated with levamisole was
previously reported to be associated with neutropenia or
agranulocytosis [13, 14], our patient did not have these
findings.

Another characteristic of the vasculitis related to lev-
amisole is the association of autoantibodies production
especially ANCA, antiphospholipid antibodies, and lupus anticoagulant
antibodies [15]. Previous reports showed also that cocaine
by itself can be associated with an ANCA positive vasculitis
and pseudovasculitis with specific specificity for human neu-
trophil elastase (HNE-ANCA) in cocaine-induced midline
destructive lesions, as well as antiphospholipid antibody pro-
duction [16–18]. It is not known for the moment if these anti-
bodies, which are associated with cocaine and levamisole use,
are pathogenic or bystanders produced by general immune
reaction. After exposure to levamisole, these antibodies
normalize within 2–14 months after discontinued the
drug [10]. Our patient showed weakly positive titers of ANA
and p-ANCA as well as positivity for antiphospholipid antibody.

The diagnosis of cocaine/levamisole-induced cutaneous
vasculitis relies on the history, clinical findings and a positive
urine toxicology test with a 2-3-day window as well as the
detection of levamisole both serum and urine using gas
chromatography and mass spectrometry with a short half-life
of 5.6 hours [19].

The approach to treat these patients differs between the
reported cases. Steroids were used in some cases with unclear
benefit. However, most of the cases were treated supportively
with a self-limited course. Cocaine/levamisole should be
withdrawn from all the patients. Extensive skin involvement
and necrosis will need treatment in special burn unit as well
as debridement, skin grafts, and reconstructive procedures.

4. Conclusion
The number of cases of cocaine contaminated with
levamisole-induced vasculitis is increased rapidly. This
diagnosis should be suspected in any patient who presents
with purpuric rash or skin necrosis and associated

Figure 1: Tender and purpuric lesions with mild skin necrosis on
the helical rim of the right ear.
neutropenia, agranulocytosis, or positive ANCA or anticyclophilin antibody.

**Conflict of Interests**

The authors declare that there is no conflict of interests regarding the publication of this paper.

**References**

[1] W. K. P. Amery and J. P. J. M. Bruynseels, "Levamisole, the story and the lessons," *International Journal of Immunopharmacology*, vol. 14, no. 3, pp. 481–486, 1992.

[2] A. Chang, J. Osterloh, and J. Thomas, "Levamisole: a dangerous new cocaine adulterant," *Clinical Pharmacology and Therapeutics*, vol. 88, no. 3, pp. 408–411, 2010.

[3] K. R. Merikangas and V. L. McClair, "Epidemiology of substance use disorders," *Human Genetics*, vol. 131, no. 6, pp. 779–789, 2012.

[4] O. Metwally, M. Hamidi, L. Townsend, H. Abualula, A. Zaitoun, and T. Lall, "The cocaine trail: levamisole-induced leukocytoclastic vasculitis in a cocaine user," *Substance Abuse*, vol. 34, no. 1, pp. 75–77, 2013.

[5] L. A. Runge, R. S. Pinals, S. H. Lourage, and R. H. Tomar, "Treatment of rheumatoid arthritis with levamisole. A controlled trial," *Arthritis and Rheumatism*, vol. 20, no. 8, pp. 1445–1448, 1977.

[6] K. D. Christensen, "Treatment of seronegative spondylarthritides with levamisole: a double-blind placebo-controlled study," *International Journal of Immunopharmacology*, vol. 1, no. 2, pp. 147–150, 1979.

[7] D. R. Czuchlewski, M. Brackney, C. Ewers et al., "Clinicopathologic features of agranulocytosis in the setting of levamisole-tainted cocaine," *American Journal of Clinical Pathology*, vol. 133, no. 3, pp. 466–472, 2010.

[8] "Agranulocytosis associated with cocaine use—four States, March 2008–November 2009," *Morbidity and Mortality Weekly Report*, vol. 58, no. 49, pp. 1381–1385, 2009.

[9] M. L. Trehy, D. J. Brown, J. T. Woodruff et al., "Determination of levamisole in urine by gas chromatography-mass spectrometry," *Journal of Analytical Toxicology*, vol. 35, no. 8, pp. 545–550, 2011.

[10] S. R. Jacob, J. Brucker, A. Bahce-Altuntas et al., "A novel cutaneous vasculitis syndrome induced by levamisole-contaminated cocaine," *Clinical Rheumatology*, vol. 30, no. 10, pp. 1385–1392, 2011.

[11] R. S. Jacob, C. Y. Silva, J. G. Powers et al., "Levamisole-induced vasculopathy: a report of 2 cases and a novel histopathologic finding," *American Journal of Dermatopathology*, vol. 34, no. 2, pp. 208–213, 2012.

[12] S. Menni, G. Pistritto, R. Gianotti, L. Ghio, and A. Edefonti, "Ear lobe bilateral necrosis by levamisole-induced occlusive vasculitis in a pediatric patient," *Pediatric Dermatology*, vol. 14, no. 6, pp. 477–479, 1997.

[13] N. Y. Zhu, D. F. Legatt, and A. R. Turner, "Agranulocytosis after consumption of cocaine adulterated with levamisole," *Annals of Internal Medicine*, vol. 150, no. 4, pp. 287–289, 2009.

[14] J. A. Buchanan, R. J. Oyer, N. R. Patel et al., "A confirmed case of agranulocytosis after use of cocaine contaminated with levamisole," *Journal of Medical Toxicology*, vol. 6, no. 2, pp. 160–164, 2010.