HCA South Atlantic

# The Dramatic Effects of Cutting Cocaine with Levamisole

Kalpesh Mistry, MD, PGY3 Family Medicine; Robert Quick, MD, PGY3 Family Medicine;
William Cantrell, MD, PGY2 Family Medicine; Sonya Chelliah, MD, PGY2 Family Medicine;
Susan Brickle, MD Family Medicine

## Abstract

Cocaine use in the United States remains an ongoing burden and is associated with a host of well-studied and commonly understood medical consequences. Users of cocaine purchase a product which has been 'cut' or diluted by sellers to increase its volume.

Levamisole, an antihelminthic and antineoplastic agent previously banned in the US, was found to be a common cutting agent and was present in approximately 80 percent of cocaine tested in the US. Reports recently began to surface indicating a trend in cocaine users presenting with a similar constellation of findings which could not be directly attributed cocaine and its known effects. Most notably was the consistent appearance of an atypical vasculitis. Investigation into the cause of this condition revealed a direct link between the ingestion of levamisole-adulterated cocaine and the development of vasculitis.

Although this link has been established and its presentation better recognized among physicians, its existence, diagnosis, and management have not been intensively studied or widely disseminated.
Furthermore, there are currently no definitive recommendations for diagnostic criteria or management of patients affected by levamisole-adulterated cocaine.

The information contained herein is based upon review of multiple cases published within and outside of the US.

## Objective

- Review the basic mechanism resulting in this condition
- Information to aid in clinical suspicion diagnostic approaches
- Highlight differential diagnoses and associated complications
- Review treatments which have been applied in documented cases.

## Clinical Presentation

- **Symptoms**: fever, malaise, sore throat, arthralgias, myalgias, night sweats, rhinorrhea, lymphadenopathy
- **Painful Purpuric/ Necrotic Lesions**: ears, cheeks, mouth
- **Labs**: Agranulocytosis, End-organ damage, elevated creatinine

## Differential Diagnoses

- **ANCA associated vasculitides (AAV)**
- **Drug-Induced AAVs** (causes include: Hydralazine, Propylthiouracil, and Minocycline)
  - unlikely in presence of both PR3 & Anti-MPO positive
- **Granulomatosis with Polyangiitis**
  - unlikely with findings of vasculitis involving the ears
- **Malignancy**

## Initial Evaluation

- **Thorough patient history (Drug usage)**
- **At presentation:**
  - CBC, CMP, ESR, CRP, UDS w/ cocaine use w/in 48 hours
- **Subsequent Testing:**
  - P-ANCA, PR3, IgM Anticardiolipin antibodies, serum/urine levamisole or gas chromatography, MPO antibodies, Antihuman neutrophil elastase (Anti-HNE)

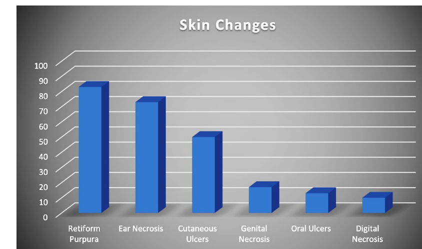
## Making the Diagnosis

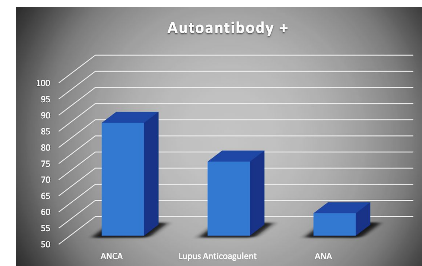
Elevated ESR/CRP

- **High suspicion with combination findings of:**
  - Fever, Leukopenia/agranulocytosis + retiform purpura + positive cocaine/levamisole screen
  - Positive ANCA + PR3 + Anti-MPO, Anti-HNE
- **Studies also consistently revealed:**
  - Reduced granulocyte proliferation on BM Biopsy
  - Positive HLA B27, ANA, Lupus Anticoagulant

## Illustration

## Figures




## Associated Complications

- Retiform Purpura with or without Bullae affecting the Extremities
- Skin Necrosis, Ulcers, Skin Abscesses
- Neutropenia, Thrombocytopenia
- Severe Sepsis
- Glomerulonephritis, Pulmonary Hemorrhage
- Seizures

## Initial Management

- **Withdrawal from offending agent**: Cocaine/Levamisole
- If **Glomerulonephritis**: short course of immunosuppressive agents
- If **Pulmonary Hemorrhage**: plasmapheresis + immunosuppressives
  - Immunosuppressive eg: prednisone and cyclophosphamide. Some cases included infusion with rituximab and maintenance with azathioprine.
  - Durable responses, partial remission and interval improvement in kidney function, in particular, can be achieved with short course of aggressive steroids even with continued exposure to Levamisole
- **Grafting** and/or **amputation**

## Long Term Management

- First and foremost, patients must be counseled to abstain from further cocaine use and subsequent re-exposures to levamisole.
- Drug rehabilitation should be considered in patients who are unable to abstain from drug use.
- In patients that relapse and are re-exposed to levamisole, supportive/wound care and short courses of immunosuppressive therapy have been associated with resolution of skin lesions and improvement in renal function.
- Long-term dialysis may be required in patients with advanced renal disease.
- More data is needed to determine the optimal long-term management goals and prognosis of the disease.

## Bibliography

- Arora, N., Jain, T., Bhanot, R. and Natesan, S. (2012). Levamisole-induced leukocytoclastic vasculitis and neutropenia in a patient with cocaine use: An extensive case with necrosis of skin, soft tissue, and cartilage. *Addiction Science & Clinical Practice*, 7(1).
- Carlson,A.(2014)Pauci-Immune Glomerulonephritis in Individuals With Disease Associated With Levamisole-Adulterated Cocaine. Medicine, 93 (17), 290-297. doi: 10.1097/MD.0000000000000090im
- Dherange PA,Beatty N, Al-Khashman A.Levamisole-adulterated cocaine: a case of retiform purpura, cutaneous necrosis and neutropenia. BMJ Case Rep Published online: 10.27.2019. doi:10.1136/bcr-2015-211768
- HAHN, E. and BOGOCH, I. (2015). *Levamisole-induced Vasculitis in a Cocaine User*. [online] The Journal of Rheumatology. http://www.jrheum.org/content/42/10/1924 [Accessed 31 Oct. 2019].
- Lee, K., Ladizinski, B. and Federman, D. (2012). Complications Associated With Use of Levamisole-Contaminated Cocaine: An Emerging Public Health Challenge. *Mayo Clinic Proceedings*, 87(6), pp.581-586.
- Lui, Y. Mutnuri, S. Levamisole-Adulterated Cocaine Nephrotoxicity. Am J Clin Pathol May 2016;145:720-726 DOI: 10.1093/AJCP/AQW029
- Morris,G.Levamisole-Adulterated Cocaine: A Case Series JABFM July–August 2012 (25)14.doi: 10.3122/jabfm.2012.04.110287
- Muñoz-Vahos, C., Herrera-Uribe, S., Arbeláez-Cortés, Á., Jaramillo-Arroyave, D., González-Naranjo, L., Vásquez-Duque, G., Restrepo-Escobar, M., Correa-Londoño, L., Arias-Restrepo, L. and Vanegas-García, A. (2019). Clinical Profile of Levamisole-Adulterated Cocaine-Induced Vasculitis/Vasculopathy. *JCR: Journal of Clinical Rheumatology*, 25(3), pp.e16-e26.