

# Chronic levamisole-induced vasculitis: A case report

After exposure to cocaine adulterated with the immunomodulator levasimole, a 48-year-old patient developed acute inflammation and ulcers that were expected to require long-term home nursing care.

**ABSTRACT:** In the case reported here, cocaine abuse led to levasimole-induced vasculitis and chronic ulcers. Levamisole is an old immunomodulator that is no longer approved for human use in North America, but is used to dilute or “cut” cocaine. Studies report that 46% of cocaine in circulation in Canada contains levamisole. Although the role of levamisole as a cutting agent is unclear, its adverse effect is apparent. Many case reports describe vasculitis and neutropenia, both of which are transient and often resolve spontaneously once exposure to the substance ends. This case and others reviewed suggest that early recognition of levasimole-induced vasculitis is needed to prevent ulcers from developing and becoming chronic.

## Case data

A 48-year-old female presented with a 2-day history of severe pain. Examination revealed redness and heat on her left thigh, with multiple new bullous formations and ulcerations. The patient reported inhaling cocaine before symptom onset. Central necrotic tissues were present in some of the ulcers examined (Figure 1). Purpura in the pinna and the lobes of the ears were also noted. Chronic ulcers in the anterior tibial area were also noted (Figure 2). Her history included multiple previous admissions over the years with the same symptoms. Since her most recent previous admission, the patient had been taking a maintenance dose of prednisone. She was also taking part in a methadone maintenance program for past heroin addiction and current cocaine abuse.

Because of the overt signs of inflammation, vasculitis and bacterial super-infection were suspected. The patient was started on piperacillin and tazobactam and soon switched to vancomycin and ceftazidime because of an allergic reaction. Clinical diagnosis of levamisole-induced vasculitis was made and antibiotics were discontinued. Acute inflammatory lesions improved over the next 24 hours.

Records from past admissions indicated that her lesions had initially

presented as purpuric macules that coalesced into patches on the right hip, then rapidly spread distally and bilaterally, evolving into painful bullae and necrotic plaques. With subsequent episodes of cocaine abuse, these lesions recurred and progressed to become chronic ulcers.

In the immediately preceding admission, wound culture had shown Methicillin-resistant *Staphylococcus aureus* (MRSA) and pseudomonas, and skin biopsy confirmed vasculitis with immune deposits of IgM, IgG, and C3. Pathology did not indicate thrombosis. The urine test was positive for levamisole. At this time, an attempt to perform a skin graft was made by plastic surgery and failed due to graft tissue infection and possible necrosis, as well as because of impaired wound healing secondary to cocaine use.

The patient's condition during the admission described in this case report was further complicated by development of mild leukopenia. The immune

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workup included testing for levels of C-reactive protein, antineutrophil cytoplasmic antibody (ANCA), and antinuclear antibody (ANA). Test results revealed the following: normal CRP of 8.7, equivocal levels of ANCA (myeloperoxidase of 39.3 and proteinase 3 of 30.2) with atypical perinuclear pattern, ANA of 1:80, normal complements levels, and no cryoglobulins.

By day 4 of admission, the patient had improved clinically. Her only treatment at that time was prophylactic subcutaneous heparin for deep vein thrombosis. Subsequently, a trial of IV heparin was initiated and found to provide no additional improvement. The acute inflammation was resolved, but her chronic ulcers were expected to cause further debilitating pain and require long-term home nursing care.

## Discussion

Cocaine abuse is common in North America, with an estimated 2 million people identified as current (past month) users.<sup>1</sup> Levamisole has been

isolated in 30% to 71% of cocaine samples circulating in the US<sup>2,3</sup> and up to 46% of cocaine samples in Canada.<sup>4</sup> It is thought that levamisole is a preferred adulterant because it enhances the cocaine effect.<sup>5</sup> Levamisole was used in the past as an immunomodulator, a steroid-sparing agent for conditions such as nephritic syndrome.<sup>6</sup> Since the 1970s it has fallen out of favor because of numerous reports of vasculitis and agranulocytosis/neutropenia, and because other safe agents are now available. Current use is limited to veterinary practice, where levamisole serves as an anthelmintic.<sup>3</sup>

Despite increasing recognition of levamisole-induced adverse effects, no effective treatment has been delineated. Anticoagulation is suggested, but the effectiveness of this is uncertain. Recent case series by Han and colleagues describe a patient with recurrent levamisole-related purpura despite a trial of warfarin within therapeutic INR levels and a trial of dalteparin anticoagulation.<sup>7</sup> While prednisone showed promise in many case

reports,<sup>7</sup> and while high doses helped our patient's acute inflammatory symptoms, prednisone was ineffective in resolving her more chronic, ulcerated lesions.

All other levamisole-related case reports we reviewed described rapidly resolving lesions as the patients avoided further cocaine exposure.<sup>7-9</sup> As in these cases, our patient presented with familiar symptoms of levamisole-related vasculitis with ear-lobe<sup>8</sup> and leg involvement, as well as neutropenia.<sup>4,10,11</sup> Where our case differed from others was in the chronicity of the patient's ulcers. Although the acute inflammation of levamisole-induced vasculitis improves once cocaine use ends, the lesions can progress to a chronic state and may not be as readily reversible. This poses a notable impact on public health given the prevalence of cocaine abuse.

## Summary

In the case reported here, the patient's cocaine abuse led to levamisole-induced vasculitis and chronic leg



Figure 1. Central necrotic tissues on patient's thigh.



Figure 2. Chronic ulcers in anterior tibial area.

ulcers. This case and others suggest that early recognition of vasculitis is needed to prevent chronic ulcers. Clinicians should note that patients presenting with levamisole-induced vasculitis may appear to have cellulitis and that IV antibiotics will often have been initiated in the ER. It is important to make the correct diagnosis and discontinue unnecessary antibiotics. Clinicians should inquire about recent cocaine use and the route of administration, as well as previous similar reactions.

It is reasonable to suspect a reaction to levamisole in the following clinical situations:

- New-onset vasculitis in patients suspected of using cocaine.
- Vasculitis involving the earlobes.
- Recurrent vasculitis that rapidly resolves spontaneously.
- Vasculitis that persists despite treatment.
- Unexplained leukopenia in patients suspected of using cocaine.

An initial diagnosis can be confirmed by urine levamisole screening and a skin biopsy.

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#### Competing interests

None declared.

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#### References

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