

# Cocaine-Induced Intermittent Purpuric Lesions of the Ear Auricle: An Increasing Entity

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## ABSTRACT

**Introduction:** A new challenge to the medical community is presented with Levamisole, an antihelminthic immunomodulatory agent, recently used in combination with cocaine to enhance its psychoactive effects. The prevalence of cocaine induced vasculopathy is increasing and physicians need to be aware of this emerging condition due to its serious possible complications.

**Methods:** We report a case of a 52 year old man with intermittent purpuric skin lesions located in the auricles in a patient with regular cocaine consumption. Histopathology of a punch biopsy, revealed diffuse presence of thrombi in the superficial and deep dermal blood vessels with a neutrophilic perivascular infiltrate with leukocytoclasia.

**Results:** There are several clinical and laboratory findings that support a diagnosis of Levamisole induced vasculitis, including ANCA positivity, specific anti-HNE antibodies and auricle involvement, that help distinguish this condition from autoimmune vasculitis and all of the results were negative.

**Conclusion:** A high index of suspicion should be kept in mind if this is considered a potential cause for purpuric intermittent lesions in cocaine abusers. To aid the diagnosis a punch biopsy associated with an extensive workup including immunologic testing is recommended. Regardless, no optimal treatment has been described, steroids have been used preventing progressive damage but complete withdrawal is indispensable.

**Keywords:** Ear auricle, Cocaine, Levamisole, Purpura, vasculopathy.

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**Conflict of Interest:** Nil.

## INTRODUCTION

Levamisole is an immunomodulatory and anti-helminthic drug, used to treat parasitic infections and inflammatory autoimmune conditions[1-3]. Recently, it has been used illegally as a cutting agent in cocaine to enhance its euphoric properties[2]. The cutaneous lesions following adulterated-cocaine consumption include a distinctive vasculopathic purpura, microvascular thrombosis and leukocytoclasia. The effects of this drug may be very severe and



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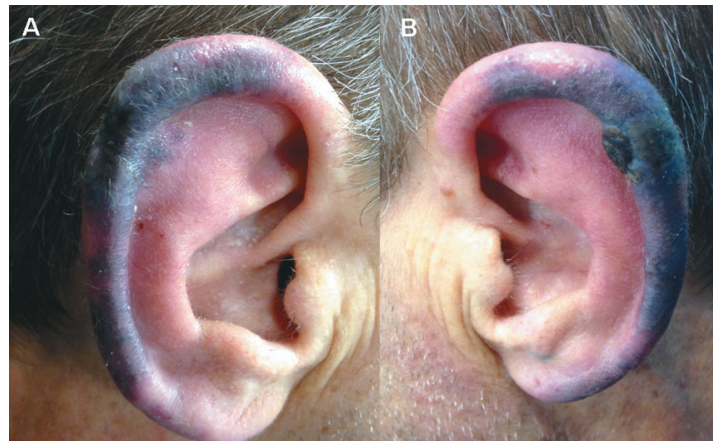
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they need a high clinical suspicion for it to be detected and avoided on time.

## MATERIAL AND METHODS

A 52 year old man with HIV (Human Immunodeficiency Virus) and Hepatitis C, presented to our OPD with a 2 year history of intermittent purpuric skin lesions in both ear auricles and a small one in his lower left limb. They occurred every time he snorted cocaine, and disappeared a couple of days later. It had worsened along the years regarding extension and recently a



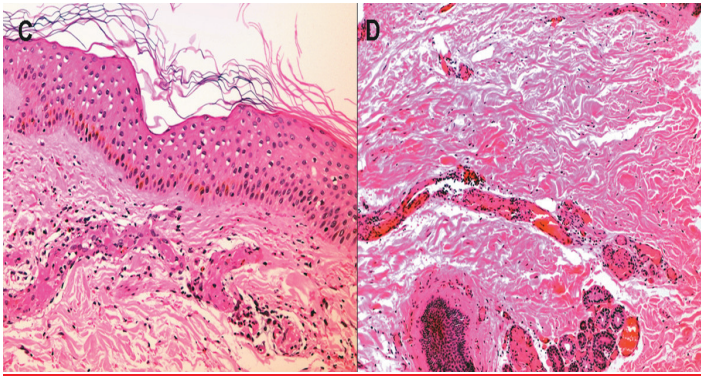
**Fig. 1: Right (A) and Left (B) auricle showing purpuric disseminated lesions. Notice the small necrotic area in the upper part of the left helix.**

small permanent ulceration in his left helix had appeared for which he consulted. (Fig. 1)

Physical examination revealed a non-toxic-appearing man with painless purpuric lesions with bilateral helical involvement, one with a small necrotic area. Besides also having a perforated nasal septum there were no other clinical findings.

Since he had consumed cocaine the day before and the lesions appeared the next day, some tests were performed immediately including urine toxicology, showing positive cocaine metabolites. Laboratories also revealed a normal hemogram and an elevated erythrocyte sedimentation rate.

## RESULTS



**Fig. 2: Thrombotic vasculopathy in a high power field sample showing intravascular eosinophilic material (occlusive thrombi) with leukocytoclasia and extravasation of erythrocytes (C). High power PAS staining field with PAS-positive occlusive thrombi (D).**

Histopathology of a punch biopsy, performed a couple of days later, revealed diffuse presence of thrombi in the superficial and deep dermal blood vessels with a neutrophilic perivascular infiltrate with leukocytoclasia and extravasation of red blood cells. No epidermal necrosis was observed (Fig. 2).

Immunology showed positive anti-cardiolipin, P-ANCA and ANAs. His viral load and CD4+ T-cell counts were stable compared with previous. Internists that evaluated him excluded systemic involvement.

Treatment involved a complete withdrawal, which at this time during follow-up was not accomplished by our patient.

## DISCUSSION

Levamisole-adulterated cocaine induced vasculitis is a condition with increasing prevalence in the last decade due to its illegal use as a cutting agent [1, 4-6]. Cocaine is the illicit drug most frequently reported in the emergency department of the United States of America. It is believed that the percentage of levamisole adulterated cocaine has risen to approximately 82% in the USA and Europe [3,4,7]. Because of its physical properties it blends easily with cocaine.

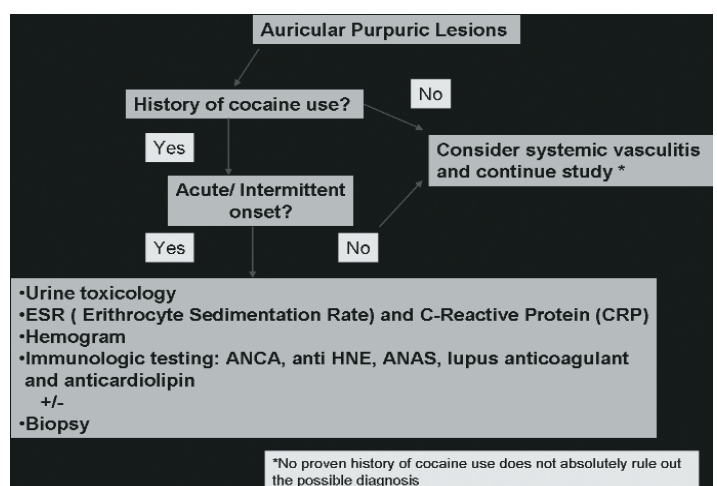
Studies have suggested that the enhancing of stimulating, addictive and euphoric properties of cocaine is due to its effect on dopamine release [3-5]. Negative testing does not rule out the presence of levamisole or its causative role in the signs of this type of vasculitis, due to its short half life as happens with out patient, who has negative laboratory findings [4, 8, 9].

Cases have been described in the 70's when this drug was used, due to its immunomodulatory properties, to treat cancer, rheumatoid arthritis and nephrotic syndrome[4, 6, 9], in which purpuric lesions appeared beginning the treatment and disappeared with withdrawal. With re-exposure, progression and wors-

ening of the lesions was observed. If consumption is not withdrawn on time, skin ulceration and extensive necrosis may result being exceedingly painful and requiring hospital admission with special wound care [1-3]. The small necrotic area in the left helix described in our case was still painless. Surgical interventions are similar to the ones used in burn lesions. In some cases wound care is not enough and serial debridement and skin grafts may be required [8, 10]. Bilateral helix involvement is seen in numerous cases, being the most "pathognomonic" site, but if this condition is not known, suspicion of this possible etiology may pass unnoticed [3,7]. Our patient referred cocaine consumption during his interrogatory. Systemic vasculitis rarely involves the ears [10]. Some characteristics of the clinical syndrome may easily be confused with true vasculitic diseases such as Churg-Strauss syndrome, cutaneous polyarteritis nodosa (PAN) and Wegener syndrome. Systemic involvement was ruled out in our case.

The pathogenesis of this condition is unclear. Cocaine by itself causes intense vasoconstriction which enhances platelet aggregation decreases fibrinolytic activity and activates immunologic mechanisms with consequent vasculopathic effects [7, 10]. Histopathological features of LIVEN (Levamisole-induced vasculopathy) are occlusive thrombotic vasculopathy with or without leukocytoclastic vasculitis and fibrinoid necrosis [2, 4, 6]. Thrombotic vasculopathy features are characterized by eosinophilic PAS positive deposits in the luminal vessels as can be observed in our Figure.2 [7]. Lesions are characterized by being retiform and purpuric with occasional necrotic patches with perivascular lymphocytic infiltrates and ANCA positivity [5, 7, 9]. Characteristic histologic patterns make biopsy very useful in narrowing diagnostic possibilities [9].

This condition has a strong association with P-ANCA (HNE-ANCA: Human Neutrophil Elastase-ANCA specific for autoimmunity induced by cocaine) anticardiolipin and lupus anticoagulant antibodies (Fig.3)[1, 2, 5-8, 10]. In a literature review per-



**Fig. 3: We present a diagnostic algorithm for Auricular Purpuric lesions including: Urine toxicology, ESR (Erythrocyte Sedimentation Rate) and C - Reactive Protein (CRP), Hemogram, Immunologic Testing: ANCA, Anti HNE, ANAS, Lupus AntiCoagulant and Anticardiolipin, and Biopsy.**

formed by Pearson et al. HNE-ANCA showed positive results in 100% of the cases analyzed [7]. After exposure to levamisole, antibodies normalize within 2-14 months after discontinuation. This entity is usually also accompanied by neutropenia and agranulocytosis [3, 4, 10]. Steroids have shown unclear benefits. They are usually indicated in extensive lesions to prevent complications such as necrosis [4, 5]. But there is no firm evidence that systemic steroids are indicated [10]. Immunosupresors are used sometimes to maintain remission but in our patient due to his medical history (HIV and Hepatitis C) this was not considered. The only effective treatment is withdrawal [2].

## CONCLUSION

The increasing number of cases of vasculitis induced by levamisole-contaminated cocaine represents a diagnosis that must be known by every physician. Serious possible consequences, should aware clinicians to be able to recognize the characteristic features usually involving ears, face and lower limbs associated to this condition.

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