Intern Emerg Med (2014) 9:475–477
DOI 10.1007/s11739-013-1015-x

CE - MEDICAL ILLUSTRATION

Purple ear and retiform purpura

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Received: 6 October 2013 / Accepted: 21 October 2013 / Published online: 28 November 2013

A 40-year-old female was presented to the hospital with bluish discoloration of ears, joint pain and skin rash. The past medical history was significant for hepatitis C infection. She was enrolled in a methadone program for heroin addiction, and she reported that she had been using crack cocaine for 10 years. Physical examination revealed purplish discoloration of both right (Fig. 1a) and left ears involving the external pinnae and helixes. The tip of the nose had a prominent necrotic purpura, and the right cheek showed a tender purpuric plaque (Fig. 1b). There were multiple large painful confluent retiform purpura over the lower extremities (Fig. 1c). Multiple joint tenderness without joint effusion was noted. Significant laboratory findings included leucopenia with a WBC count of 2 300 cells/mm^3 (normal, 4 400–11 000 cells/mm^3) with a normal complete metabolic panel. Hepatitis C polymerase chain reaction (PCR) assay showed undetectable viral load and serum cryoglobulin level was normal. The antinuclear antibody (ANA), anti-Smith antibody and perinuclear anti-neutrophil cytoplasmic antibody (p-ANCA) were positive. Results of further work-up for infectious, hematologic and rheumatologic disorders were negative. Urine toxicology screening was positive for cocaine. The clinical picture was highly suggestive of levamisole-contaminated cocaine-induced cutaneous vasculitis. A punch biopsy of cutaneous purpura was performed, and showed small-vessel vasculitis with perivascular neutrophilic infiltrates (arrows) with dermal hemorrhages (asterisks), which were compatible with features of leukocytoclastic vasculitis (Fig. 1d, e). The patient was treated with systemic corticosteroids, and the leucopenia resolved and the cutaneous purpura improved significantly (Fig. 1f).

Our patient presented with the clinical, biochemical and histologic features consistent with levamisole toxicity. According to the United States Centers for Disease Control and Prevention (CDC), 70 % of cocaine supply in the United States is adulterated with levamisole, which is being cut into the cocaine before it is smuggled into the United States [1]. Levamisole is an immunomodulatory agent, and has been used for the treatment of pediatric nephrotic syndrome, rheumatoid arthritis and colon cancer [1, 2]. However, it was withdrawn from the United States due to the risk of agranulocytosis. It is currently used in the United States as an anti-helminthic medication in the veterinary field [2, 3]. The reasons for addition of levamisole to cocaine are thought to be increasing the total weight of the cocaine due to its physical similarity to cocaine, and prolonging the cocaine-induced euphoria by potentiating the nicotinic acetylcholinergic effects [1–3]. Although levamisole is a more expensive additive agent, the major attractive incentive for using levamisole as a cocaine

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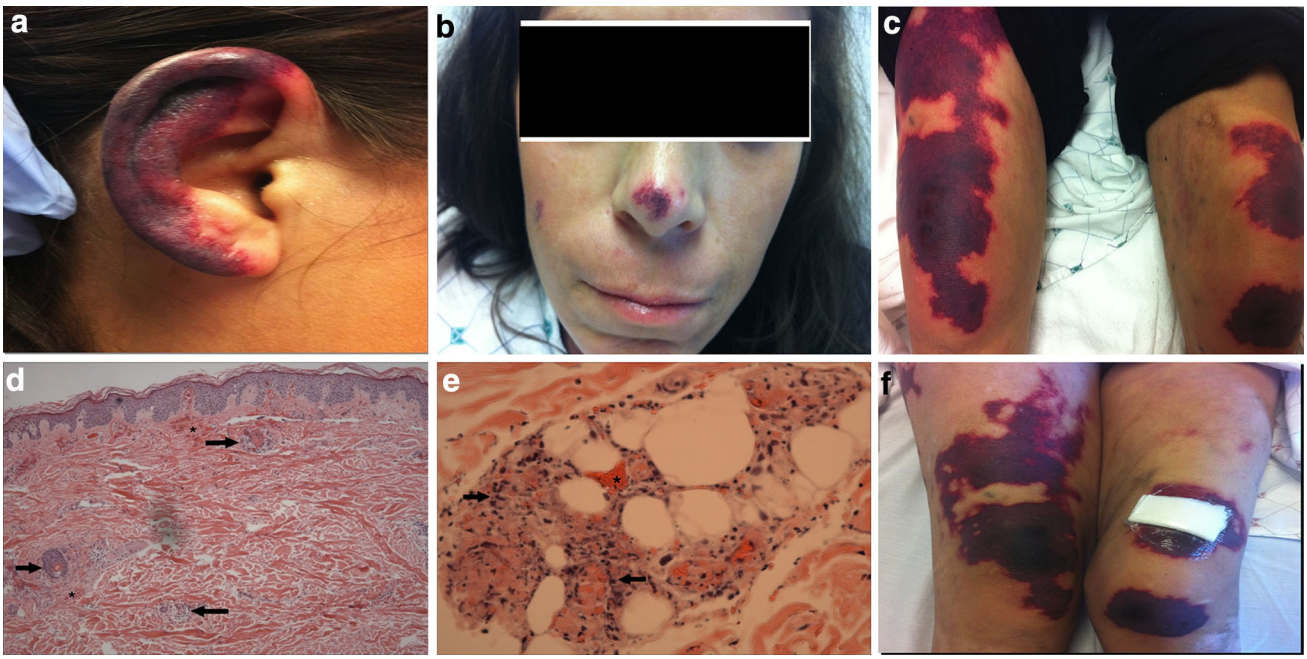

Fig. 1 Cutaneous manifestations of levamisole-induced vasculitis: **a** purplish purpura of the right ear; **b** purpuric lesions over the right cheek and tip of her nose; **c** classic large confluent dusky palpable retiform purpura on both thighs. **d, e** Histopathological examination of skin biopsy showed evidence of leukocytoclastic vaculitis with perivascular nuclear neutrophil infiltrates (*arrows*) and dermal hemorrhages (*asterisks*). **f** The retifom purpura over the thighs was improved after 3 days of systemic corticosteroid therapy (a dressing applied over the skin biopsy site on the left lower thigh)

adulterant is reported that levamisole-tainted cocaine passes the street test (known as "bleach test"), which is used to detect impurities in the cocaine. It retains the iridescent fish-scale sheen of pure cocaine when testing with the "bleach test" whereas other cutting agents (such as sugar, baking powder, lidocaine, procaine, etc.) fail to pass the test [4].

Levamisole causes a serious idiosyncratic reaction such as bone-marrow suppression, resulting in leucopenia, neutropenia, or agranulocytosis [1–3]. Typical cutaneous manifestations of levamisole toxicity are painful palpable purpura and hemorrhagic bullae [2, 3], reportedly developing within 24 h of the last cocaine use [5]. The external ears including ear lobes, cheeks and nasal tips are commonly affected sites. Confluent palpable purpuric cutaneous patches with or without retiform formation are frequently seen and involve the extremities, chest and abdomen [3]. Common laboratory findings include leukopenia, neutropenia, agranulocytosis, and positive ANA, anti-double-stranded DNA, lupus anticoagulants and ANCA antibodies [1–3]. One of the ANCA antibodies directed against human neutrophil elastase (HNE) is proposed to be used as a diagnostic marker due to its high sensitivity and specificity for levamisole-induced vasculitis, and the test can distinguish this disease from classic ANCA-associated vasculitis [3, 5]. Detection of levamisole in urine or blood by using advanced gas chromatography/mass spectrometry can be performed within 48 h of last use (the half-life of levamisole is 5.6 h), but the test is expensive and not widely available [3]. In a patient known to have used cocaine presenting with classic cutaneous lesions, detection of levamisole, however, is not required to make the diagnosis of this syndrome [5]. Histopathologic examination of the skin lesions typically shows distinctive features ranging from immune complex-mediated leukocytoclastic and thrombotic vasculitis to vascular occlusive disease without true vasculitis [2, 3]. Treatment is usually supportive, cessation of cocaine use and a short course of corticosteroids.

In conclusion, given that the worldwide high prevalence of illicit cocaine abuse, the practicing clinicians should suspect an exposure to cocaine contaminated with levamisole in patients presenting with a pentad of necrotic skin lesions with a preponderance of ears and nose, retiform purpura, leukopenia/neutropenia, a positive ANCA test and evidence of cutaneous vasculitis on histopathologic examination.

Conflict of interest None.

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