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Case report

Early excision and grafting, an alternative approach to the surgical management of large body surface area levamisole-adulterated cocaine induced skin necrosis

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ABSTRACT

Levamisole-adulterated cocaine as a cause of retiform purpura progressing to full-thickness skin necrosis was first documented in 2003 and currently comprises over 200 reported cases [1]. Whereas, its presentation, pathophysiology, and diagnostic workup have been reasonably well-defined, only one publication has significantly detailed its surgical management. For this reason there exists a relative absence of data in comparison to its reported incidence to suggest a preferred treatment strategy. In the case mentioned, treatment emphasized delayed surgical intervention while awaiting lesion demarcation and the monitoring of autoantibodies [5]. At our institution we offer an alternative approach and present the case of a 34 year old female who presented with 49% TBSA, levamisole-induced skin necrosis managed with early surgical excision and skin grafting. The patient presented three days following cocaine exposure with painful, purpura involving the ears, nose, buttocks, and bilateral lower extremities which quickly progressed to areas of full-thickness necrosis. Lab analysis demonstrated elevated p-ANCA and c-ANCA, as well as leukopenia, decreased C4 complement, and urinalysis positive for levamisole, corroborating the diagnosis. Contrasting the most thoroughly documented case in which the patient underwent first surgical excision on hospital day 36 and underwent 18 total excisions, our patient underwent first excision on hospital day 10 and received only one primary excision prior to definitive autografting. To our knowledge, this is the largest surface area surgically treated that did not result in surgical amputation or autoamputation of limbs or appendages, respectively. We contend that early excision and grafting provides optimal surgical management of this syndrome while avoiding the morbidity seen with delayed intervention.

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1. Literature review

Levamisole is a synthetic imidazothaizole that was first marketed as an antihelminthic in human and veterinary medicine. In the 1970s, it was noted to possess immunomodulatory properties which led to its therapeutic use in rheumatoid arthritis, pediatric nephrotic syndrome, and colorectal cancer. A side effect profile notable for agranulocytosis caused the drug to be withdrawn from the U.S. market in 1999. Levamisole remains readily available as a veterinary drug and beginning in 2003 it was first detected as a new adulterating agent in cocaine [1].

Use of levamisole as a cocaine adulterant has increased dramatically over the past decade. Forensic laboratories identified levamisole in 80% of cocaine seizures analyzed by the U.S. Drug Enforcement Agency in 2011, up significantly from 10% in 2007 [2]. Data from animal models suggest levamisole's pharmacodynamics may enhance those of cocaine and propose its synergistic role as an adulterant [1]. In contrast to cocaine, which can be detected in urine for up to 3 or 4 days, levamisole, due to its minimal renal excretion and short half-life of 5.5 h, is detectable only within 48 h of last exposure [1,3,5,8]. Gas chromatography and mass spectrometry are able to detect levamisole in the cocaine itself, but such tests are not routinely available. These limitations necessitate a high index of clinical suspicion in order to initiate prompt levamisole testing within the 48-h window. In our case, early suspicion allowed for positive levamisole detection by urinalysis despite the patient's last reported usage of 72 h prior.

Immunologically, levamisole has been strongly associated with drug-induced anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). Patients with drug-induced AAV often have high ANCA titers and are usually positive against myeloperoxidase (p-ANCA) although they can develop antibodies against a number of ANCA antigens, proteinase 3 (c-ANCA) in our case [3]. ANCA-positivity, however, is non-specific and does not distinguish the cocaine-related syndrome from other vasculitides such as Wegener's Graulomatosis and polyangiitis [8]. As the prevalence of complications stemming from levamisole-adulterated cocaine has risen, research has been directed toward a means of making this distinction. Results from recent publications have suggested that antibodies against human neutrophil elastase (HNE) are a diagnostic marker specific for the cocaine-associated condition, and should be obtained in the workup of retiform purpura [1,6–8,9].

Cutaneous manifestations of levamisole exposure include lichenoid eruptions, fixed drug eruptions, nonspecific eruptions, and, very rarely, cutaneous vasculitis [4,5]. Traditionally, purpura of the ears is the most characteristic clinical feature corresponding histologically to a vasculopathic reaction pattern ranging from a leukocytoclastic and thrombotic vasculitis to a vascular occlusive disease without true vasculitis but with associated antinuclear, antiphospholipid, and anticytoplasmic antibodies [1,3–7]. In our case, the ears, nose, arms, legs, thighs, and buttocks were involved. Although lesions undergoing surgical debridement have occasionally been mentioned in the literature, to our knowledge, there have only been two previously reported cases of extensive full-thickness skin necrosis, 15% and 52% total body surface area (TBSA), undergoing excision and closure with skin grafting as present in our case [5,6] (Figs. 1–4).

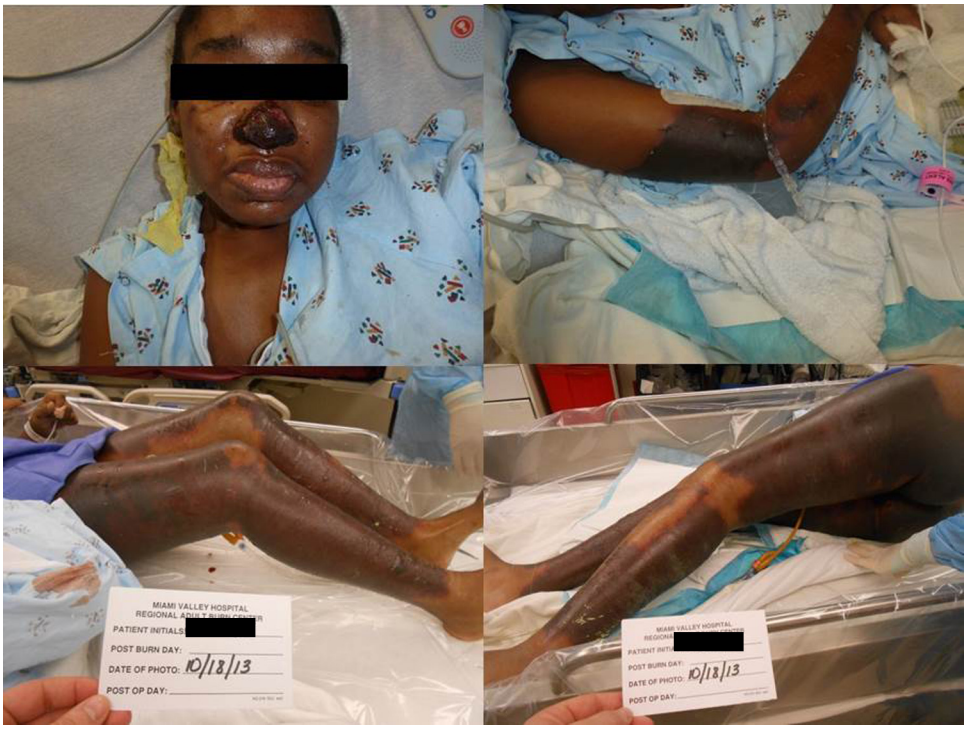

Fig. 1 – Hospital day two illustrating early cutaneous manifestation clinically consistent with deep partial and full thickness injury. Top left, nasal and facial lesions. Top right, right upper extremity. Bottom left, bilateral lower extremity lesions. Bottom right, bilateral lower extremity lesions, cont.