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Case Report

Multiple mucocutaneous ulcers associated with cocaine-induced midline destructive lesions

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Abstract

Cocaine-induced midline destructive lesions (CIMDL) occur in a small subset of cocaine users, who clinically present with inflammation and necrosis of facial midline structures such as the palate, nasal septum, turbinates, and sinuses. We present a patient with CIMDL occurring concomitantly with ulcers on the cheek and upper trunk. Multiple biopsy specimens from the cutaneous and mucosal lesions consistently showed a dense dermal/submucosal infiltrate of neutrophils and plasma cells, without vasculitis or thrombosis. The ulcers resolved following cessation of cocaine use.

Keywords: Cocaine-induced midline destructive lesions, cocaine ulcers, necrosis, anti-neutrophil cytoplasmic antibodies

Introduction

A small percentage of chronic cocaine abusers develop inflammation and necrosis of midline facial structures, including the nasal septum, turbinates, sinuses, and palate, a syndrome reported as cocaine-induced midline destructive lesions (CIMDL) [1,2]. Such patients typically have positive anti-neutrophil cytoplasmic antibodies (ANCA) in a perinuclear pattern (pANCA), with specificity against human neutrophil elastase (HNE) rather than myeloperoxidase (MPO) [3]. Destructive nasal lesions have rarely been reported to extend onto the perinasal skin. We report an unusual patient with CIMDL with cutaneous involvement beyond the perinasal area.

Case synopsis

A 51-year-old man was admitted to the hospital with multiple cutaneous ulcers and a recent change in voice.



Figure 1. Ulcerated verrucous plaque of 1.5 years duration, photograph at time of admission

The largest ulcer, located on the left cheek (Figure 1), had been present for 1.5 years. Previously unsuccessful therapies included doxycycline 100 mg twice daily for 2 months, clindamycin 150 mg twice daily for 1 month, and terbinafine 250 mg daily for 2 weeks. Two prior biopsies of this lesion, taken 4 and 5 months prior to admission, had shown a dermal infiltrate of neutrophils and plasma cells (Figure 2), with no vasculitis or thrombosis. A PAS stain was negative for fungal elements. Concomitant tissue cultures showed no growth of bacteria, fungi, or mycobacteria. It is noted that the patient was taking oral clindamycin at the time of the first tissue culture, and was on no antibiotics or antifungals at the time of the second tissue culture.

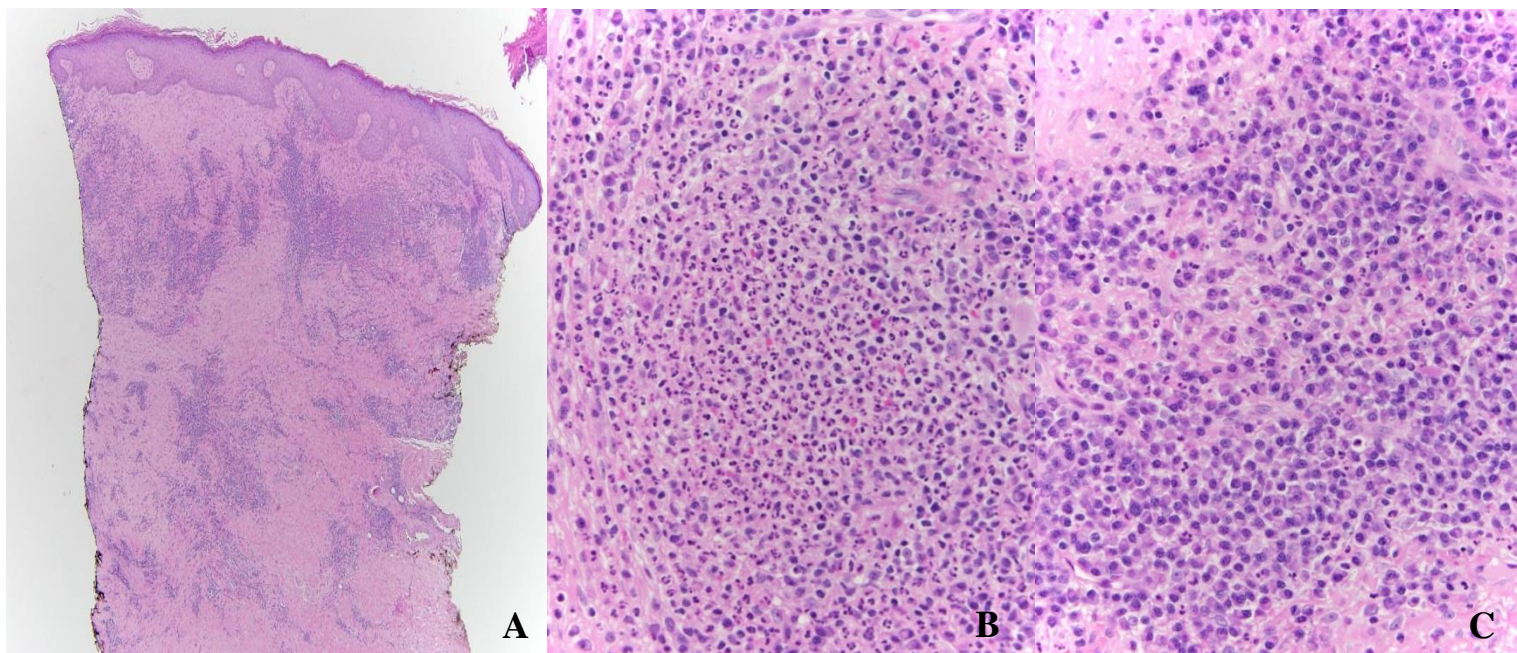


Figure 2. Punch biopsy from right cheek lesion, performed 4 months prior to admission, showing dermal fibrosis with patchy dermal infiltrate (A, x40) composed of a mixture of neutrophils (B, x400) and plasma cells (C, x400)

In the 2 months prior to admission, he developed new ulcers on the right flank and right shoulder (Figure 3), and during the preceding 3 weeks, he had noticed a change in his voice, as well as dysphagia.



Figure 3. New ulcers on the right flank (A) and right shoulder (B)



Figure 4. Defect in hard palate

Physical examination showed a perforated nasal septum and a defect in the hard palate (Figure 4). A computed tomography scan additionally showed thickening of the walls of the maxillary and sphenoid sinuses.

Laboratory evaluation showed negative/normal values for a complete blood count, comprehensive metabolic profile, antinuclear antibody, rheumatoid factor, hepatitis panel, rapid plasma reagin, fluorescent treponemal antibody absorption, and HIV test. He had a positive ANCA (1:320) with an atypical pattern (neither pANCA nor cANCA), and was negative for antibodies against myeloperoxidase (MPO) and proteinase 3 (PR3).

Following admission, biopsies were taken from the skin adjacent to the ulcers on the right shoulder and left cheek, as well as from the nasal septum and palate. These showed a dermal/submucosal infiltrate with aggregates of neutrophils and plasma cells (Figure 5), entirely similar to those in the prior biopsies from the left cheek lesion. Gram, Ziehl-Neelsen, and GMS stains did not reveal pathogenic microorganisms. Tissue cultures from the left cheek and right flank were negative for growth of bacteria, mycobacteria, and fungi. The patient had received one dose of intravenous vancomycin approximately 18 hours prior to the collection of the tissue cultures, which may have decreased culture sensitivity. A superficial swab culture taken from the left

cheek wound prior to administration of any antibiotics showed light growth of diphtheroids and coagulase negative staphylococci, consistent with normal skin flora.

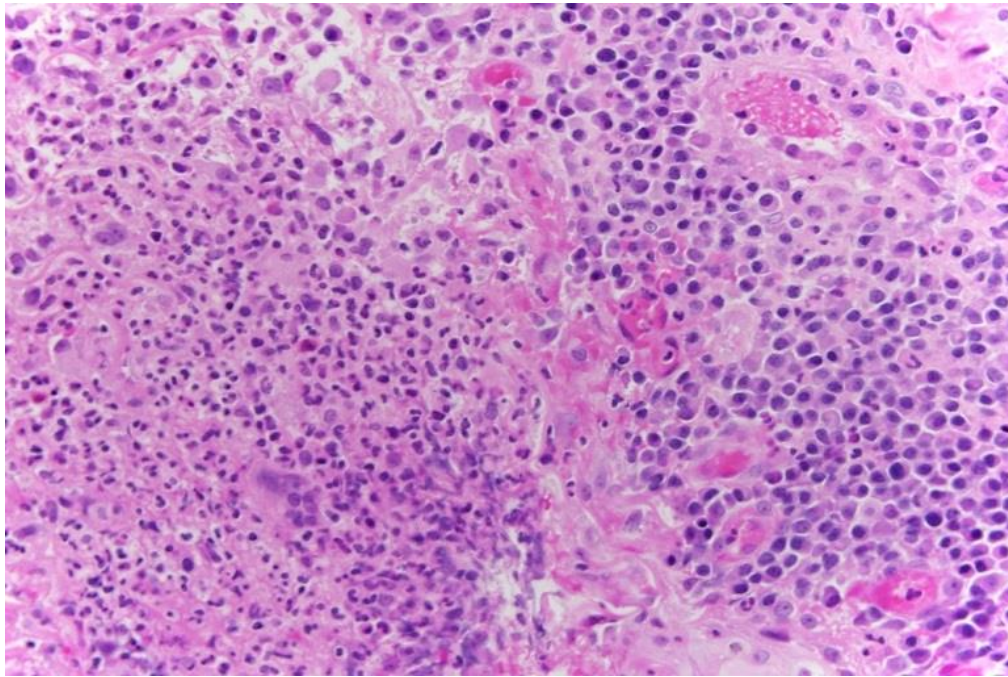


Figure 5. Punch biopsy from intact skin adjacent to right shoulder ulcer, showing a dense dermal infiltrate composed of neutrophils and plasma cells (x400)

Following discovery of the nasal septal perforation, a urine toxicology screen was performed, and was positive for cocaine. The patient then admitted to a long history of cocaine abuse that had continued until the time of admission.



Figure 6. Left cheek lesion with significant improvement at 3 week follow up, after cessation of cocaine use

During his one week hospitalization, no new lesions developed, and the existing lesions were stable. He received one week of intravenous vancomycin and piperacillin-tazobactam, and antibiotic therapy was then discontinued owing to negative cultures and the impression of a non-infectious etiology. He was discharged with instructions to abstain from cocaine use. Wound care involved erythromycin ointment and non-adherent dressing pads, changed daily. No other treatment was prescribed. At the three-week follow up, the left cheek lesion had significantly improved (Figure 6), and the right shoulder and right flank lesions had completely healed (Figure 7).



Figure 7. Right shoulder ulcer completely healed at 3 week follow up

He denied any further cocaine use since discharge, and a repeat urine toxicology screen was negative. He subsequently had reconstructive surgery for the palatal defect, with good functional results. At one year after discharge, he had experienced no recurrent skin lesions.

Discussion

Common findings in CIMDL include nasal obstruction, epistaxis, nasal crusting, facial pain, and septal perforation. More severe cases eventuate to necrosis and ulceration involving the palate, turbinates, and sinuses [2]. Reported histologic features are nonspecific and include fibrosis, mixed inflammation, and necrosis. A minority (24.1%) of cases show leukocytoclastic vasculitis [1]. In our patient, it is notable that biopsies from multiple cutaneous ulcers and nasal septum showed a consistent histologic pattern, with a brisk dermal/submucosal infiltrate of neutrophils and plasma cells, even in areas not immediately adjacent to the ulcer edge.

The clinical differential diagnosis of CIMDL includes granulomatosis with polyangiitis (GPA), extranodal NK/T cell lymphoma, deep fungal infection, rhinosporidiosis, rhinoscleroma, tuberculosis, and syphilis (Table 1). Although histologic distinction between GPA and CIMDL is sometimes not possible, serologic evaluation can be useful. The majority of CIMDL patients are positive for pANCA, with most having reactivity against HNE. About half are reactive against PR3 and most are not reactive against MPO. In GPA, the typical profile is positivity for ANCA in a cytoplasmic pattern (cANCA) with specificity against PR3. Microscopic polyangiitis (MPA) most often shows pANCA with MPO reactivity. Notably, unlike CIMDL, both GPA and MPA are negative for anti-HNE reactivity [3], although the utility of this distinction is limited by the inconsistent availability of HNE testing. ANCA positivity can also be observed in levamisole-associated vasculopathy. However, this condition differs from CIMDL by virtue of its presentation with cutaneous purpura. Additionally, in our patient, the multiple biopsy specimens did not show the vasculitis or thrombosis most often observed in levamisole-associated vasculopathy [4, 5]. We consider it unlikely that our patient's ulcers were caused by a cutaneous infection, given that he had not responded to multiple courses of oral antibiotics as an outpatient. In addition, punch biopsies submitted for tissue culture were negative on three separate occasions, including one occasion during which no antimicrobials were being administered.

The pathogenesis of CIMDL is poorly understood. It appears to affect only a very small fraction of cocaine abusers, presumably owing to variability in host susceptibility. Whereas the majority of patients have ANCA with HNE reactivity, the mechanistic role of these antibodies is uncertain. Since the lesions are not limited to areas of cocaine contact with the mucosa, a purely direct vasoconstrictive/ischemic effect seems unlikely.

The management of CIMDL consists primarily of abstinence from cocaine. Immunosuppressive therapy is not advocated [2]. After sustained abstinence from cocaine abuse and clinical stabilization of lesions, surgical repair of palatal and septal defects may be considered.

Table 1. Differentiation of cocaine-induced midline destructive lesions (CIMDL), granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and levamisole-associated vasculopathy (LAV)

Disease	Clinical Presentation	Histopathology (Skin)	Predominant ANCA pattern	HNE	PR3	MPO
CIMDL	Nasal obstruction, facial pain, headache, epistaxis, necrosis/ulceration of palate, nasal septum, turbinates, and sinuses; possible cutaneous ulceration	Ulceration, necrosis, fibrosis, mixed inflammation; minority with LCV	pANCA	+	+/-	-
GPA	Palpable purpura, mucosal and cutaneous ulcers, fever, epistaxis, cough, hemoptysis, pulmonary infiltrates, azotemia, hematuria, proteinuria	LCV, neutrophilic and granulomatous dermatitis	cANCA	-	+	-
MPA	Palpable purpura, ulcers, fever, myalgia, weight loss, dyspnea, pulmonary infiltrates, hematuria, proteinuria	LCV	pANCA	-	-	+
LAV	Retiform purpura and necrosis, often involving ears and face; neutropenia	LCV and/or thrombosis	cANCA or pANCA	+/-	+/-	+/-

Conclusion

Although rare, persistent cutaneous ulceration may occur in the setting of CIMDL. When evaluating refractory cutaneous ulcers, especially involving the face, it is pertinent to look for nasal septal defects and other midline facial abnormalities, and to assess for cocaine abuse. When CIMDL is identified and other etiologies excluded, abstinence from cocaine is the critical step in management of mucosal and cutaneous lesions.

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