Heroin-induced nasal necrosis and septal perforation

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ABSTRACT
We present the case of a 44-year-old woman with a 28-year history of intranasal heroin use who developed severe necrosis of the nasal mucosa and septal perforation. She denied any prior insufflation of cocaine or other substances. Necrosis of the septum was recurrent and persistent despite repeated debridement. Necrosis and perforation of the nose and palate are well-described consequences of intranasal cocaine abuse, often attributed to cocaine's vasoconstrictive properties. However, there have been few reports of similar effects associated with heroin. This case and other recent reports of non-vasoconstrictive substances causing nasal and palatal necrosis suggest that vasoconstriction alone may be an incomplete explanation for the pathogenesis of cocaine induced midline destructive lesions (CIMDL). Cocaine and other recreational drugs, including heroin, may cause midline destruction through a common non-vasoconstrictive mechanism, possibly mediated by antineutrophil cytoplasmic antibodies.

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Introduction
Inflammatory injury of the nasal mucosa and underlying cartilage can result in nasal septal perforations (NSP). Necrosis and perforation of the nose and palate due to intranasal cocaine abuse have been well documented. The pathogenesis of these cocaine induced midline destructive lesions (CIMDL) [1] is commonly considered to be mediated by vasoconstriction [2,3], but this classical description may be incomplete. More recently, NSP and midline destructive lesions mimicking CIMDL have been reported as consequences of intranasal use of non-vasoconstrictive drugs such as oxycodone [4], hydrocodone [5] and acetaminophen [6]. Considering that few cocaine users ultimately develop CIMDL [1] and that non-vasoconstrictive drugs can produce clinically identical lesions, ischemic necrosis may not completely explain the pathogenesis of CIMDL.

Reports of nasal or palatal perforation associated with intranasal use of heroin and other non-vasoconstrictive substance, have been rare. Only two previous publications documenting midline destructive lesions resulting from exclusive use of heroin were identified [7,8]. We present and characterize here a case of NSP and nasal necrosis resulting from a 28-year history of intranasal heroin use. The possible non-vasoconstrictive mechanisms of drug induced midline destructive lesions are discussed and the implications of these mechanisms on the current understanding of CIMDL are outlined.

Case report
A 44-year-old woman with a 28-year history of exclusively intranasal heroin use was referred to the otolaryngology clinic for a two-week history of severe nasal congestion and crusting with accompanying necrosis of the nasal vestibules (Figure 1(A,B)). No usage of cocaine or other recreational drugs was reported. Air passage through each nasal cavity required maximal effort. Green mucoid discharge was present bilaterally. The patient reported ceasing heroin use and beginning on methadone therapy six weeks prior to symptom appearance. The patient also reported smoking half a pack of cigarettes each day but denied use of smokeless tobacco alcohol or nasal sprays, history of intranasal trauma or nasal surgery or insufflation of other substances. Medical history was significant for asthma and arthritis. Family history
included arthritis in the mother, father and sister and hearing loss in the father.

Computed Tomography (CT) scan showed opacification of the nasal cavity and nasal septal necrosis (Figure 2). Endoscopic exam confirmed CT findings and revealed a septum perforation with necrosis of circumscribing mucosa and cartilage, extending into both vestibules (Figure 1(C)). Friable tissue was noted throughout the nasal cavity, but no polyps or purulence were observed. No evidence of saddle nose

Figure 1. Gross appearance of the nasal cavity. (A) Necrosis present in both nasal cavities. (B) Necrosis of the right nasal vestibule. (C) Necrotic nasal septum after partial debridement. Large perforation is evident. (D) Nasal cavity after debridement. Remnants of the nasal septum can be seen.

Figure 2. CT scan of sinuses and facial bones with contrast demonstrating opacification of the nasal cavity (A) and nasal septal necrosis (B).
deformity was found. Intravenous antibiotics were initiated, with no response noted. Extensive debridement of necrotic mucosa and cartilage was performed in the operating room (Figure 1(D)). Biopsy showed necrosis and mixed acute and chronic inflammation, with abundant neutrophils and eosinophils (Figure 3). Fungal culture of the septal tissue was positive for Candida parapsilosis. An autoimmune panel was negative for myeloperoxidase (MPO) antineutrophil cytoplasmic antibodies (ANCA), Proteinase 3 (PR3) ANCA, rheumatoid factor and antinuclear antibodies.

Necrosis of the septum, vestibule, floor and lateral wall of both nasal cavities recurred rapidly after initial debridement. Necrosis of the anterior nasal floor and inflammation of posterior tissue was seen through endoscopy. A second debridement was performed in the operating room three weeks after the initial surgery. Biopsies taken during this procedure showed mixed inflammation similar to that seen previously, with no fungal elements.

Nasal congestion progressively worsened for two weeks after the second debridement. Rigid nasal endoscopy revealed another recurrence of necrosis. The left nasal cavity featured crusting, purulence and no discernible airway while the right nasal cavity featured crusting, scab formation, and a 1mm airway. A third debridement was performed, including a posterior septectomy and partial endoscopic medial maxillectomy. Xeroform gauze was placed after completion.

Follow-up saw eventual cessation of the spreading necrosis, which continues to heal to date. The patient continues on a methadone regimen and was referred to a pain specialist and a primary physician for further care. Diagnosis was noted as heroin-induced midline necrosis.

Discussion

Destructive lesions due to intranasal cocaine use (CIMDL) has been extensively documented in the literature. CIMDL is commonly considered to be a consequence of chronic ischemia. Contaminants in cocaine such as talcum powder, mannitol and amphetamines may also contribute to the pathogenesis by causing irritation and inflammation [9].

Reports of midline destructive lesions and septal perforations due to heroin or other substances are unique as they produce the same necrotic lesions as cocaine but do not share its vasoconstrictive
properties [4,6,8]. Although their adulterants share irritating and inflammatory properties, heroin and cocaine are prepared differently. Heroin contaminants and diluents are distinct from those in cocaine both in frequency and identity, suggesting that the adulterants in both substances may contribute to but do not fully account for the similarity of noted midline destructive lesions [10]. Variance among the likelihood of cocaine users who develop CIMDL corroborates this conclusion. As Trimarchi et al.’s noted, vasoconstriction and mechanical irritation should affect all cocaine users similarly, but only 4.8% of regular intranasal cocaine users develop NSP [1]. The low frequency of CIMDL among cocaine users also suggests that an additional unidentified or overlooked factor may contribute to the pathogenesis of these lesions.

Recent research has suggested a role of antineutrophil cytoplasmic antibodies (ANCA) in CIMDL. Wiesner et al. detected human neutrophil elastase (HNE) ANCA in 84% and proteinase 3 (PR3) ANCA in around half of CIMDL patients, but ANCA positivity was not present in cocaine users who did not have CIMDL [11]. The similar histopathology and midline destruction found both in CIMDL and in ANCA-positive autoimmune diseases such as granulomatosis with polyangiitis (GPA) further supports this conclusion [1].

Based on this evidence, we hypothesize that pathogenesis of CIMDL may occur through two distinct mechanisms. One follows the traditional model of chronic vasoconstriction progressing to CIMDL. The other involves ANCA-mediated autoimmunity. The existence of two distinct mechanisms of pathogenesis may explain why not all patients with CIMDL have ANCA positivity and why midline destructive lesions caused by non-vasoconstrictive substances resemble CIMDL. CIMDL, therefore, may fall under a broader category of drug-induced midline destructive lesions, all of which may be mediated by ANCA.

The negative PR3 and MPO ANCA results for our patient, although is somewhat discouraging, but does not rule out the possibility of an ANCA-mediated heroin induced midline destructive lesion. Only about half of CIMDL patients are positive for PR3 ANCA and none seem to be positive for MPO ANCA [11,12]. Heroin, like cocaine, could be associated with the presence of HNE ANCA rather than PR3 or MPO ANCA. Unfortunately, we did not obtain HNE ANCA levels in our case. To our knowledge, there are no other reported measurements of ANCA in cases of heroin or other non-cocaine drug associated midline destruction.

The possibility of false negative results and laboratory error should also be given consideration in the diagnostic evaluation of autoimmune-mediated pathologies. Several cases of autoimmune diagnoses have tested positive upon repeat testing.

Future study of the prevalence and mechanism of ANCA activity in cases of both heroin and cocaine associated nasal and palatal necrosis will help elucidate the pathogenesis of drug-induced midline destructive lesions. Heroin abuse should be considered along with cocaine abuse in the differential diagnosis of NSP.

Disclosure statement

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