Case Report

Necrotizing Granulomatous Vasculitis Associated with Cocaine Use

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ABSTRACT. Cocaine abuse may be associated with a destructive nasal and pharyngeal process felt to be due to ischemia secondary to vasoconstriction. This report is the first to document a necrotizing granulomatous vasculitis associated with nasal destruction and an oronasal fistula in a chronic cocaine user. Cocaine is an environmental insult that may play a role in triggering cerebral and non-cerebral vasculitis including a necrotizing granulomatous vasculitis of the respiratory tract. (J Rheumatol 2002;29:1795–7)

Key Indexing Terms:
NECROTIZING GRANULOMATOUS VASCULITIS COCAINE

Cocaine abuse is associated with numerous medical complications through various mechanisms including arterial constriction, platelet aggregation, and a procoagulant effect. Nasal and pharyngeal destruction associated with heavy cocaine use is well documented and thought to be due to ischemia from vasoconstriction. We describe a destructive upper respiratory tract process leading to necrosis of sinus and nasal turbinates, and development of an oronasal fistula in a patient with a 30 year history of cocaine use. A necrotizing granulomatous vasculitis was seen on pathological examination.

CASE REPORT

A 53-year-old Caucasian male presented to the hospital with an oronasal fistula. He first developed a sensation of fullness in his sinuses in the mid 1970s which was attributed to allergies. He underwent rigid fixation in 1985 after a traumatic fracture of the ramus of his mandible. Soon thereafter he began having episodes of swelling of the mandible that would occasionally drain a foul tasting material into his mouth. One year prior to admission he noticed increasing pain and drainage from the left jaw, a sensation of fullness in his ears and drainage from his nose. Two months prior to admission he blew his nose and subsequently noted a large oronasal fistula in his palate. He was unable to eat or drink as the food would enter into his nose and he lost 24 lbs. Review of systems was otherwise totally unremarkable for inflammatory collagen vascular disease including any symptoms associated with the vasculitides. He had a history of alcohol abuse and a 60 pack/yr smoking history. There was no family history of arthritis or vasculitis. On examination he had no temporal artery tenderness, iritis, or conjunctivitis. Pain was present over the sinuses. A large oronasal fistula was present (Figure 1). There were otherwise no oral ulcerations. Swelling was noted over the left mandible and there was asymmetry of the lower jaw line on the left. The remainder of the physical examination was unremarkable.

Chest radiograph was unremarkable. Laboratory studies revealed urinalysis with no proteinuria or active sediment, erythrocyte sedimentation rate 60 mm/h, serum creatinine 0.8 mg/dl, and normal white blood count with differential. Computerized tomographic (CT) scan revealed complete opacification of most of the sinuses, partial absence of the medial walls of the maxillary sinuses, and absence of the nasal turbinates. A defect was seen in the hard palate. Magnetic resonance imaging (MRI) of the paranasal sinuses revealed extensive mucoperiosteal thickening throughout. Testing for antineutrophil cytoplasmic antibodies (ANCA) revealed negative c-ANCA but positive p-ANCA. Antimyeloperoxidase antibodies were negative. CT of chest revealed no pulmonary nodules or infiltrates.

Serological studies included an antinuclear antibody of 1:40. Anti-dsDNA, anti-Sm, anti-RNP, anti-Ro and La, anti-Scl 70, anticentromere, antichromatin, and anticardiolipin antibodies were all negative. Complement levels were normal and HIV testing was negative.

The patient underwent functional endoscopic sinus surgery with bilateral maxillary antrostomies and debridement of tissue in both nasal cavities. He also had debridement of the gingival mucosa. At surgery the majority of the patient's turbinates as well as most of his nasal septum were found to have been eroded (Figure 2). A large amount of necrotic tissue was debrided from both nasal cavities. Biopsies of the bilateral nasal contents and pharynx revealed necrotizing granulomatous vasculitis. Stains for fungus and acid fast bacilli were negative.

After multiple visits to the hospital the patient admitted to cocaine use of 30 years' duration. He used to be a heavy cocaine user (up to 2 to 3 g/wk). He always snorted cocaine, but never used intravenous (IV) preparations. His sinus symptoms had started a few years after he began using cocaine.

Given the evidence of necrotizing granulomatous vasculitis on biopsy and the absence of vasculitis clinically or serologically elsewhere, it was felt that this localized vasculitis might be related to his cocaine use. He was counseled to abstain from cocaine. Because of ongoing inflammation and the destructive nature of the lesions he received oral prednisone at 1 mg/kg/day for 2 weeks, which was then tapered. He also received a 6 month course of IV cyclophosphamide therapy. A palatal obturator was fashioned for his oronasal fistula. He tolerated the medication well and showed no evidence of systemic disease throughout the course. Repeat otolaryngology examination showed no recurrence of inflammation or necrotic debris. His jaw healed well with no further drainage. His c-ANCA

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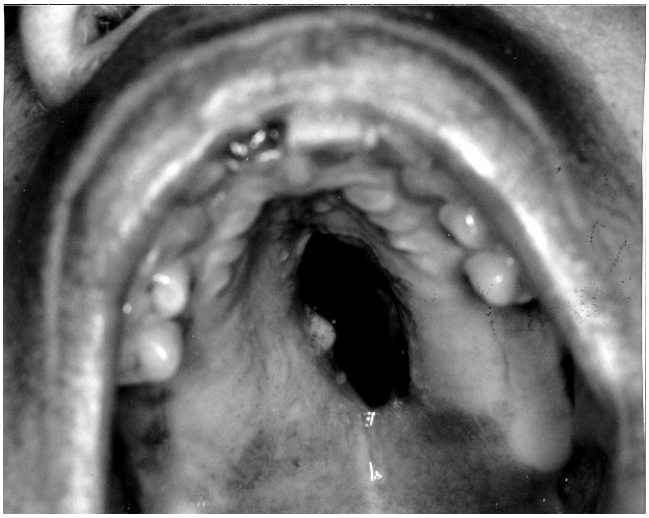

Figure 1. Large oronasal fistula in palate.

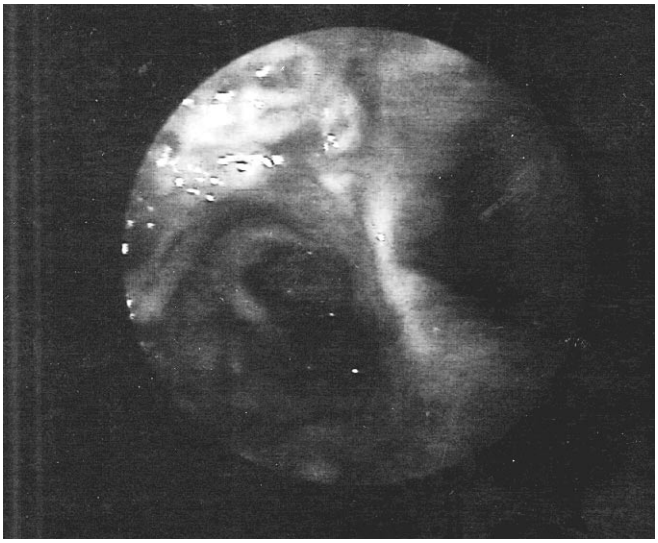

Figure 2. Endoscopic view of the choanae with a completely eroded nasal septum.

remained negative throughout the course. The p-ANCA remained positive but antimyeloperoxidase antibody was always negative.

DISCUSSION

Cerebral and non-cerebral systemic vasculitis has occasionally been described with cocaine use. Eight cases of central nervous system vasculitis associated with various forms of cocaine administration (nasal inhalation, lung inhalation, and IV use) were reviewed by Merkel, *et al*[1]. Pathological specimens showed acute and chronic small vessel inflammation with lymphocytic or polymorphonuclear cell infiltration. Non-cerebral vasculitis including Schoenlein-Henoch purpura[2], leukocytoclastic vasculitis[3], Churg-Strauss vasculitis[4], a focal periaortitis[5], and possible conjunctival vasculitis[6] has also been reported.

While nasal and pharyngeal disease is described with prolonged cocaine use, this appears to be the first description of a destructive necrotizing granulomatous vasculitis involving the sinuses, nose, and the palate. Previous descriptions of severe upper respiratory tract disease noted necrosis without evidence of vasculitis or granuloma formation[7-9].

Since these destructive processes may be associated with vasculitis, does ANCA aid in the diagnosis? In the cases reported to date, ANCA have usually been negative, although positive results have been noted even in the absence of pathologic evidence of vasculitis[10,11]. On repeat testing 1-2 years later, ANCA, however, was negative. In the current case, c-ANCA was consistently negative, p-ANCA consistently positive, and antimyeloperoxidose antibodies negative.

Vascular inflammation and occlusion leading to tissue ischemia is a hallmark of Wegener's granulomatosis. Although strong evidence indicates that such blood vessel damage is immunologically mediated, the mechanisms that initiate this process are largely unknown. Specific infectious agents or environmental irritants may play a role in triggering the disease[12]. Perhaps exposure to an environmental insult such as infection and/or autoantigens induces an excessive macrophage Interleukin 12 response, leading to an unbalanced production of Th1 cytokines. Aberrant production of tumor necrosis factor-α and interferon-ß could initiate and perpetuate the granulomatous inflammatory vascular lesion that characterizes Wegener's granulomatosis[13]. It is therefore interesting to note that cocaine injection to cocaine dependent subjects tipped the balance of cytokine secretion by mononuclear cells to Th1 type[14].

In summary, a destructive nasal and pharyngeal process associated with prolonged cocaine abuse can occur. A granulomatous necrotizing vasculitis may be seen on pathological examination, or vasculitis may be absent. Vasculitis may also be found in other organ systems secondary to cocaine use. Abstinence from cocaine is essential, but optimal therapy when vasculitis is found remains to be determined. Treatment should be individualized: while some patients may need cytotoxic therapy, other patients may likely be managed conservatively with avoidance of cocaine.

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