

# Cocaine-induced midline destruction lesions with positive ANCA test mimicking Wegener's granulomatosis

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## ABSTRACT

Chronic use of cocaine by inhalation may induce midline destructive lesions (CIMDL), which can sometimes be difficult to distinguish from the ear, nose and throat lesions of Wegener's Granulomatosis (WG). We describe the case of a 43-year-old female patient admitted with a two-year history of nasal obstruction and rhinorrhea. She had been diagnosed with WG for five months, being on prednisone and cyclophosphamide. On her physical examination, perforation of her nasal septum and palate was observed. Laboratory tests showed elevated acute phase proteins and a positive p-ANCA test. ELISA assays anti-proteinase 3 and myeloperoxidase were negative. The paranasal sinus computed tomography (CT) showed destruction of the nasal septum and palate, in addition to bilateral maxillary sinusitis. Chest CT was normal. Nasal mucosal biopsy revealed an inflammatory infiltrate, with neither granuloma nor vasculitis. When questioned, she admitted being a cocaine user for five years. Medical therapy and cocaine use were withdrawn. She has been followed up for six months and no other lesion or other organ symptoms occurred. Differential diagnosis in patients with midline destructive lesions can be very challenging. Evaluation should include enquiry about intranasal use of cocaine. Although ANCA testing does not clearly differentiate the ANCA found in some patients with CIMDL from those found in WG patients, the localized involvement and the biopsy findings non-characteristic of small vessel granulomatous vasculitis should be recognized as features for cocaine-induced lesions.

**Keywords:** cocaine, Wegener's granulomatosis, antineutrophilic cytoplasmic antibody, vasculitis.

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## INTRODUCTION

Perforation of the nasal septum or palate is a complication caused by cocaine chronic use.<sup>1</sup> This condition can mimic several medical conditions, including: leishmaniasis, syphilis, lymphoma, blastomycosis and Wegener's granulomatosis (WG).<sup>2</sup> WG is a systemic vasculitis characterized by inflammation and necrosis of small blood vessels which more commonly affects upper and lower airway (lung parenchyma and bronchi), as well as kidneys, causing a glomerulonephritis that can evolve to renal failure.<sup>3</sup>

Cocaine is an alkaloid that increases the activity of monoamine neurotransmitters in the central and peripheral nervous system by blocking reuptake pumps (transporters) of dopamine, norepinephrine and serotonin. This substance can be used orally, intranasally (inhalation), by intravenous or subcutaneous injections, or via genital mucosa, and it also can be smoked (crack). Each one of the routes of administration presents differences in the severity and quality of the effects and risks of complications associated with its use. Inhaled cocaine can cause inflammation and ulceration of the nasal mucosa with perforation of the septum (cocaine-induced

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midline destructive lesions – CIMDL). The mechanism of nasal inflammation and necrosis is multifactorial and includes local ischemic vasoconstrictor effect, local trauma, irritation of the mucosa due to other mixed substances, deficit in mucociliary transport and, rarely, secondary bacterial infection.<sup>4</sup> Frequent and prolonged inhalation can cause osteocartilaginous necrosis which can extend to cornets and maxillary sinus. In rare circumstances, the bones of the palate suffer necrosis and perforate.<sup>5</sup>

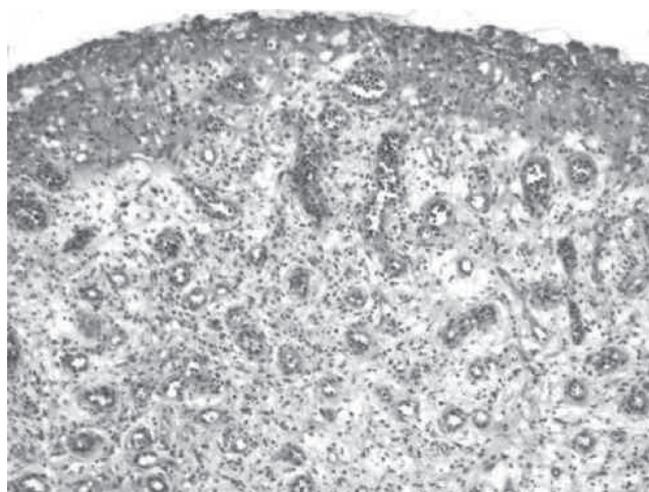
Here we describe the case of a patient who presented with cocaine-induced nasal/palate perforation and also with a positive perinuclear antineutrophil cytoplasmic autoantibody (p-ANCA) test. We further discuss the diagnosis work-up and differential diagnosis with limited WG.

## CASE REPORT

A 43-year-old female patient was admitted in our hospital with a two year history of nasal obstruction, nasal voice and rhinorrhea. She reported a WG diagnosis five months before admission and had been on oral prednisone 60 mg/day and cyclophosphamide 100 mg/day since then. Her physical examination revealed a nasal septum and palate perforation with 1.5 cm of extension (Figure 1). Laboratory tests showed hematocrit 30.2%, hemoglobin 9.9 g/dL, mean cell volume (MCV) 63.7 fL, leukocytes 8,500 cells/mm<sup>3</sup>, platelets 521,000/mm<sup>3</sup>, erythrocyte sedimentation rate (ESR) 120 mm/h, C-reactive protein (CRP) 31.2 mg/L, and creatinine 0.6 mg/dL. Tests for ANA, rheumatoid factor, hepatitis C virus, HIV virus, hepatitis B virus, venereal disease research laboratory (VDRL) and FTA-ABS were all negative. Purified protein derivative (PPD) test was not reactor. Leishmaniasis and blastomycosis serology were both negative. The ANCA test (indirect immunofluorescence – IIF) was positive (1:360 dilution) with a p-ANCA pattern. Enzyme-linked immunosorbent assays (ELISA) for antigen-specific ANCA directed against proteinase 3 (PR3) and myeloperoxidase (MPO) were negative. The nasal paranasal computed tomography (CT) showed destruction of nasal septum and palate, as well as bilateral maxillary sinusitis. Chest CT was normal. A nasal mucosal biopsy revealed an inflammatory infiltrate, without granuloma or vasculitis (Figure 2). When questioned, she admitted to be a cocaine user (nasal inhalation) for at least five years. Prednisone and cyclophosphamide were suspended and a causal relationship between cocaine and the destructive lesions was established. The patient no longer used the drug. She has been followed-up for six months and no other lesion or other organ symptoms occurred.



**Figure 1**  
Palatal defect with extensive ulceration.



**Figure 2**  
Biopsy material shows acute and chronic inflammation with granulation tissue. There is no evidence of vasculitis or granuloma formation.

## DISCUSSION

Cocaine use can cause destructive facial injuries that mimics the clinical picture of other diseases associated with necrotizing midfacial lesions. This is an important clinical scenario that is likely to become more common as worldwide use of cocaine increases.

ANCA directed against PR3 or MPO are sensitive and specific markers for the idiopathic small vessel vasculitis including WG. It is generally believed that the presence of a positive ANCA test with either of the two antigen specificities

facilitates the differential diagnosis of vasculitis. The sensitivity of c-ANCA for WG diagnosis ranges from 34%–92%, depending on the extension of the compromise of disease, and the specificity ranges from 88%–100%.<sup>6</sup> The p-ANCA pattern which usually corresponds to the presence of anti-MPO antibodies (in patients with vasculitis) occurs in only 5% of WG patients. When the antigenic target is not the MPO, as occurred in our patient, a multitude of other targets have been reported including cathepsin G, lactoferrin, elastase and lysozyme. The International Consensus Statement on testing and reporting of ANCA states that ANCA are most readily demonstrated by using a combination of IIF of normal peripheral blood neutrophils and ELISAs that detect ANCA specific for PR3 or MPO.<sup>7</sup> According to this consensus, a p-ANCA positive-MPO-ANCA negative result may occur in treated, inactive, or relapsing microscopic polyangiitis (MPA) (and its renal-limited variant), WG and Churg-Strauss syndrome. This result also is common in inflammatory bowel disease and other autoimmune diseases where its clinical significance is unclear.<sup>7</sup>

Instances of positive ANCA test results have also been reported in patients with lesions attributed to cocaine abuse.<sup>2,8</sup> Trimarchi et al.<sup>9</sup> evaluated 25 patients with sinus and nasal necrosis secondary to cocaine and showed that 14 (56%) of this patients were ANCA positive, being nine with p-ANCA and five with c-ANCA pattern, some of them with reactivity against PR3. In another study, Wiesner et al.<sup>10</sup> evaluated human neutrophil elastase (HNE) ANCA in CIMDL, WG and MPA patients and healthy volunteers. The authors found that 19 patients (76%) with destruction of nasal septum secondary to cocaine had ANCA positive (in most cases p-ANCA) and 12 (57%) had positive reactivity against PR3. Among patients with CIMDL, HNE ANCA were detectable in 84%. Fifty-seven percent of HNE ANCA-positive CIMDL sera were also PR3 ANCA-positive. Sera obtained from patients with WG or MPA were universally HNE ANCA-negative, as were sera obtained from healthy controls. They concluded that HNE ANCA may discriminate between CIMDL and WG, whereas a positive test result for PR3 ANCA may not.<sup>10</sup> Unfortunately we could not test for the HNE ANCA in our patient, since until now it is available only for experimental purposes.

As some patients, especially with limited WG, might have a p-ANCA positive-MPO-negative result and drug use history provided by patients is notoriously unreliable, differentiation of cocaine-induced lesions from necrotizing granulomatous

inflammation of the upper respiratory tract associated with WG may be very challenging. In addition, specifically in our case, the patient presented with anemia and elevated ESR and CRP which could represent other factors for confusion. We cannot be sure about the reason for these findings but anemia with low VCM is extremely common in fertile women and the inflammatory tests are very unspecific. The mechanism of nasal inflammation and necrosis is multifactorial and also includes secondary bacterial infection. Thus, it is possible that elevated inflammatory tests could be ascertained just for the local inflammation and necrosis. Fortunately, although nasal and sinus biopsies have less than a 30% chance of showing granulomatous inflammation due to the small size of the specimens obtained, certain non-characteristic biopsy findings may alert towards one diagnosis or the other.

Trimarchi et al.<sup>8</sup> evaluated histopathologic examination of 18 cocaine abusers with midline destructive lesions in comparison to 21 WG patients. In summary, biopsies with nonspecific changes were more frequent in CIMDL (44%) than in WG patients (24%), but the difference was not statistically significant. Microabscesses in the vascular wall and perivulinitis were observed with similar frequencies in both groups. Leukocytoclastic vasculitis and fibrinoid necrosis appeared to be more frequent in WG ( $P = 0.02$ ). However, when the data analysis was based on the occurrence of the lesion in individual patients rather than individual biopsies, no difference was detectable: it occurred in six of 18 CIMDL and in nine of 21 WG patients ( $P = 0.11$ ). In contrast, extravascular changes consisting of stromal granulomas with giant cells, microabscesses, and deeply located necrosis were features exclusively found in WG ( $P = 0.001$ ).<sup>8</sup>

In summary, whereas routine ANCA testing does not clearly differentiate the ANCA found in some CIMDL patients from those of WG patients, more detailed investigations suggest interesting differences between the ANCA of the two patient populations. Vascular abnormalities mimicking vasculitis are frequently found in biopsy specimens of CIMDL patients and are not helpful in the differential diagnosis. However, extravascular necrosis, microabscesses, granulomas, and giant cells are differentiating histopathologic hallmarks of WG. A complete evaluation of patients with nasal septum and/or palate perforation should always include an investigation about the use of cocaine, ANCA, and histopathologic examination in order to avoid diagnostic mistakes and possibly harmful treatments.

## REFERENCES

### REFERÊNCIAS

1. Simsek S, de Vries XH, Jol JA, Spoelstra-de Man AM, Nanayakkara PW, Smulders YM *et al*. Sino-nasal bony and cartilaginous destruction associated with cocaine abuse, *S. aureus* and antineutrophil cytoplasmic antibodies. *Neth J Med* 2006; 64(7):248–51.
2. Armstrong M Jr, Shikani AH. Nasal septal necrosis mimicking Wegener's granulomatosis in a cocaine abuser. *Ear Nose Throat J* 1996; 75(9):623–6.
3. Al Maini M, Carette S. Diagnosis of Wegener's granulomatosis in the ANCA era. *Journal Rheumatol* 2006; 33(10):1923–5.
4. Rachapalli SM, Kiely PD. Cocaine-induced midline destructive lesions mimicking ENT-limited Wegener's granulomatosis. *Scand J Rheumatol* 2008; 37(6):477–80.
5. Seyer BA, Grist W, Muller S. Aggressive destructive midfacial lesion from cocaine abuse. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2002; 94(4):465–70.
6. Schönemarck U, Lamprecht P, Csernok E, Gross, WL. Prevalence and spectrum of rheumatic diseases associated with proteinase 3-antineutrophil cytoplasmic antibodies (ANCA) and myeloperoxidase-ANCA. *Rheumatology (Oxford)* 2001; 40(2):178–84.
7. Savige J, Dimech W, Fritzler M, Goeken J, Hagen EC, Jenette JC *et al*. Addendum to the International Consensus Statement on testing and reporting of antineutrophil cytoplasmic antibodies. Quality control guidelines, comments, and recommendations for testing in other autoimmune diseases. *Am J Clin Pathol* 2003; 120(3):312–8.
8. Trimarchi M, Gregorini G, Fachetti F, Morassi ML, Manfredini C, Maroldi R *et al*. Cocaine-induced midline destructive lesions: clinical, radiographic, histopathologic, and serologic features and their differentiation from Wegener granulomatosis. *Medicine (Baltimore)* 2001; 80(6):391–404.
9. Trimarchi M, Nicolai P, Lombardi D, Facchetti F, Morassi ML, Maroldi R *et al*. Sinonasal osteocartilaginous necrosis in cocaine abusers: experience in 25 patients. *Am J Rhinol* 2003; 17(1):33–43.
10. Wiesner O, Russell KA, Lee AS, Jenne DE, Trimarchi M, Gregorini G *et al*. Antineutrophil cytoplasmic antibodies reacting with human neutrophil elastase as a diagnostic marker for cocaine-induced midline destructive lesions but not autoimmune vasculitis. *Arthritis Rheum* 2004; 50(9):2954–65.