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CASE REPORT

# Sino-nasal bony and cartilaginous destruction associated with cocaine abuse, *S. aureus* and antineutrophil cytoplasmic antibodies

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## ABSTRACT

**Three male patients aged 29, 30 and 34 years and a 36-year-old female are reported with nasal septum perforation and a history of cocaine abuse. Two of the patients also had a perforation of the hard palate. In all four, antineutrophil cytoplasmic antibodies (ANCA) were found. One had a cytoplasmic immunofluorescence-staining pattern (c-ANCA), the other three showed a perinuclear staining pattern (p-ANCA). Furthermore, all patients were found to be nasal carriers of *S. aureus*. We hypothesise that tissue damage to the nasal and palatal area in patients using cocaine may partly be mediated by the presence of ANCA antibodies. Furthermore, we speculate that *S. aureus* facilitates the development of these ANCA antibodies.**

## KEYWORDS

ANCA, cocaine, *S. aureus*, sino-nasal destruction

## INTRODUCTION

Cocaine, derived from the leaves of the coca plant (*Erythroxylon coca*), has central stimulatory as well as anaesthetic effects through the release of dopamine, norepinephrine and/or serotonin. It is bedrock knowledge that cocaine can cause tissue damage to the nasal area, lungs, cardiac conduction system, and the brain. Septum perforation of the nose alone or together with a hard palate defect are recognised as local complications of nasal cocaine abuse.[1-12]

Antineutrophil cytoplasmic antibodies (ANCA) were first described in 1982 by Davies *et al.*, who found these antibodies in patients with glomerulonephritis.[13] Later, ANCA was found to be associated with Wegener's granulomatosis. In addition to the classical cytoplasmic immunofluorescence-staining pattern (c-ANCA), a perinuclear pattern (p-ANCA) was recognised. In the majority of cases, the c-ANCA is directed against proteinase 3 (PR3), and the p-ANCA is directed against myeloperoxidase (MPO). In addition to Wegener's granulomatosis, the ANCAs are important in other systemic vasculitis syndromes as well, including Churg-Strauss syndrome, microscopic polyangiitis, idiopathic pauci-immune necrotising crescentic glomerulonephritis and in some cases Goodpasture's disease.[14,15] The diagnosis of Wegener's granulomatosis is based clinically on the presence of nose bleeds, nephritis (crescentic glomerulonephritis with necrosis) and pulmonary involvement. More than 70% of patients with Wegener's granulomatosis have PR3-ANCA, whereas in 10 to 30% of the cases MPO-ANCA is present. Although c-ANCA (PR3-ANCA) is predominately associated with Wegener's granulomatosis, and p-ANCA (MPO-ANCA) with microscopic polyangiitis, idiopathic pauci-immune necrotising crescentic glomerulonephritis and Churg-Strauss syndrome, there is not an absolute specificity.

Positive ANCA titres have been described in drug-induced vasculitides as well, especially in association with propylthiouracil treatment for hypothyroidism.[16]

We report four patients suffering from sino-nasal destruction caused by cocaine abuse. Two of the patients also had destructive perforation of the hard palate. ANCAs were found in all four patients. Furthermore, all patients were *S. aureus* carriers. We speculate that production of ANCA, combined with the presence of *S. aureus*, contributes to this local toxic effect of cocaine.

## CASE REPORT

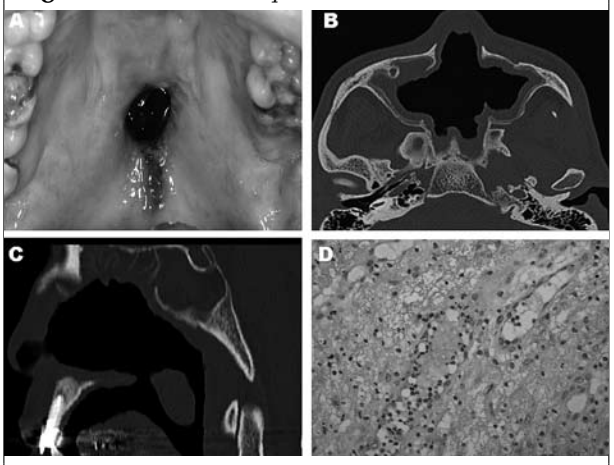
A 34-year-old male was seen at the ENT outpatient clinic because of persistent nose blockage for one year. His medical history was unremarkable. He was a semi-professional boxer and admitted to having used cocaine frequently. Examination showed a saddle nose deformity, crusts in the nasal cavity, and a subtotal septum perforation.

The initial diagnosis was septum perforation caused by cocaine abuse and repeated facial trauma. Local therapy (Sofradex® drops and nasal lavage) was started and he was strongly advised to stop using cocaine. Follow-up examination several months later revealed a perforation of the hard palate (*figure 1A*). Computer tomography showed destruction of the entire nasal septum and medial borders of the maxillary sinus and ethmoids (*figures 1B* and *C*). Microscopy of the nasal mucosa showed a chronic active, partly necrotising inflammation without a clearly granulomatous aspect (*figure 1D*). Microbiological culture of the nose revealed *S. aureus*. Because Wegener's granulomatosis was considered an alternative diagnosis, serological investigation was performed (*table 1*).

The serological findings led to the diagnosis of septum and hard palate perforation due to the combination of trauma, cocaine abuse and limited Wegener's granulomatosis (normal kidney function, normal urinalysis, and normal computer tomography of the lungs). Treatment initially consisted of sulphametoxazole and trimetroprim, followed by the addition of oral corticosteroids. The patient's symptoms improved dramatically. In six months' time, the c-ANCA titre had decreased significantly to 1:40. In addition, anti-PR3 antibodies were no longer detected. Local treatment was continued, and an obturator was placed in the palatal defect. Despite clinical and biochemical improvement, the patient still periodically requires local treatment, possibly due to persisting abuse of cocaine, confirmed by detecting cocaine in urine samples.

For the clinical, serological, microbiological and therapy data of the other three patients, see *table 1* and *figure 2*.

**Figure 1.** *The oral cavity*

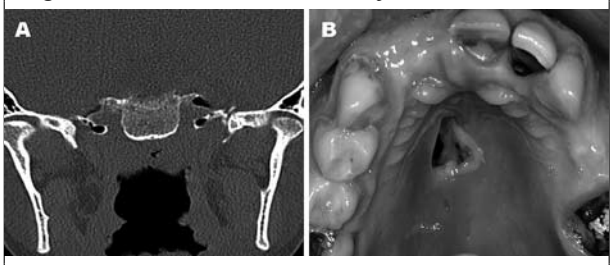



**A. Defect of the palate. B. Sagital CT scan of the nasal cavity, demonstrating the absence of the nasal septum. C. Coronal CT scan of the nasal cavity, showing the absence of the nasal septum as well as the palate defect. D. A representative section of a nasal mucosa biopsy showing an aspecific inflammation, without evident signs of vasculitis.**

## DISCUSSION

In this paper we present four patients with local destructive changes in the nasal and palatal area, associated with cocaine abuse and the presence of ANCAs. This combination of findings caused difficulties in the diagnostic

**Figure 2.** *A transversal CT scan of the head*




**A. Absence of the nasal septum on CT scan. B. Oral cavity with hard palate defect.**

**Table 1.** *The patient characteristics*

| Patient | Sex/age | Clinical manifestation | ANCA type (titre) | ANCA specificity | *S. aureus* | Treatment |
|---|---|---|---|---|---|---|
| A | M/34 | Septum perforation<br>Hard palate perforation | c-type<br>(1 :320) | Anti-PR3 | + | SMX/TMP<br>Steroids |
| B | F/36 | Septum perforation<br>Saddle-nose deformity | p-type<br>(1 :80) | Anti-PR3 | + | SMX/TMP<br>Steroids<br>Mtx |
| C | M/29 | Septum perforation<br>Necrotising crescentic glomerulonephritis | p-type<br>(1 :1280) | Anti-PR3 | + | Steroids<br>Cy |
| D | M/30 | Septum perforation<br>Hard palate fistula | p-type<br>(1:320) | none | + | SMX/TMP |

**SMX/TMP = Sulphametoxazole and trimetroprim; Mtx = methotrexate; Cy = cyclophosphamide**

process, because cocaine-induced toxicity may mimic the lesions resulting from (limited) Wegener's granulomatosis, especially in those cases when patients deny the use of cocaine.[1,8] With the recent report that ANCAs reacting with human neutrophil elastase (HNE) may be used as a diagnostic marker for cocaine-induced destructive lesions in the nasal and palatal area, this difficulty may be circumvented.[17] It may be easy to distinguish patients with cocaine-induced midline destructive lesions (CIMDL) from those with Wegener's granulomatosis. In their paper, Wiesner *et al*. characterised the reactivity of HNE-ANCA in 25 patients with CIMDL and compared this with a control group of 604 consecutive patients, including 64 patients with Wegener's granulomatosis, 14 patients with microscopic polyangiitis and 526 patients with other vasculitis together with 45 healthy volunteers.[17] Using three different assays (indirect immunofluorescence, capture ELISA and direct ELISA), HNE-ANCAs were detectable in 84% of the patients with CIMDL. No HNE-ANCAs were detected in patients with Wegener's granulomatosis or microscopic polyangiitis. Among the three assays, the capture ELISA was the most sensitive method, detecting HNE-ANCAs in 76% of the patients with CIMDL. In 13 of the 25 patients with CIMDL, PR3-ANCAs could be detected. Unfortunately, this paper appeared after we had seen and treated our patients. Therefore, we were not able to test our patients for HNE-ANCA positivity. Nevertheless, our study provides the literature with four patients with sino-nasal bony and cartilaginous destruction during/after use of cocaine and the association with *S. aureus* and ANCAs.

Positive ANCA has previously been reported in cases of nasal septum perforation attributed to cocaine abuse, but this usually involved lower titres than in the patients described in this study.[8,10,11] In only one of the four patients in our study was a c-ANCA pattern found with a higher titre than in the previously reported cases (*table 1*).

Thirteen cases have been reported before describing extensive palatal destruction attributed to cocaine abuse.[2-12] The c-ANCA serology was only reported in five of these cases.[2,8,10-12] This usually involved lower titres of c-ANCA, except in two cases.[2,12] This major lesion was found in two of our patients, one with c-ANCA (patient A) and one with p-ANCA pattern (patient D). Although in patient A specificity for the c-ANCA could be detected, in patient D the p-ANCA lacked any specificity. One possibility is that at the time of determination of the specificity in patient D the disease activity might have been low. Another possibility could be that other aetiological agents are more important in the destruction of the oronasal mucosa (*S. aureus*).

The exact mechanism behind the presence of p- or c-ANCA (in cocaine abusers) is not known. Several studies have demonstrated the pathogenetic role of ANCA. However, environmental factors, such as infection (particularly *S. aureus*) or drugs, are required for the production and/or activation of ANCAs.[15,18,19] It has been shown that (chronic) nasal carriage of *S. aureus* is associated with higher relapse rates in Wegener's granulomatosis.[20] It is remarkable that all our patients were carriers of *S. aureus* (*table 1*). A possible pathogenetic mechanism for the lesions in the oronasal region may be that due to the repetitive local vasoconstrictive effects of cocaine on the nasal mucosa when sniffing, ischaemia may occur. Subsequently, the damage to the mucosa causes the infiltration of *S. aureus*. This in turn is followed by the formation of ANCAs. Together with the direct toxicity of cocaine, the infection/infiltration/inflammation with *S. aureus* and the destructive effects of ANCAs, microscopic as well as macroscopic lesions occur. Thus ANCAs can develop upon exposure to 1) environmental factors, such as medication (hydralazine, propylthiouracil), toxic effects of silicon or cocaine; 2) infection, including *S. aureus* and 3) a certain susceptibility due to genetic factors, such as polymorphisms, the genes encoding Fcγ receptors, α1-antitrypsin, PR3 and MPO. These environmental and inherited factors together may break through the immunological barriers of self-tolerance, thus causing autoimmunity. We believe that ANCA should be measured in cocaine users presenting with nasal septum/palate perforation, particularly when signs of local inflammatory activity predominate. It has not yet been determined what the optimal therapy is for the cocaine-induced destructive lesions in the nasal and palatal area, but a short course of immunosuppressive therapy should be considered in patients with extensive disease or in patients who do not improve on cessation of cocaine use.

In conclusion, the association between cocaine (ab)use, nasal septum perforation, and positive ANCA serology is described. Cocaine use and the presence/production of ANCA may not be coincidental. We hypothesise that cocaine may trigger p- or c-ANCA production via *S. aureus* as an intermediate, which may partially explain the ischaemic necrosis seen in cocaine-associated lesions. Moreover, the presence of genetic factors (Fcγ receptor polymorphisms) may explain the susceptibility for the toxic effects of micro-organisms and drugs, leading to the formation of ANCAs.

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