Cocaine-induced nasal/paranasal, ocular and central nervous system ANCA-associated vasculitis resolved with steroids and cocaine withdrawal

Sirs,

Cocaine consumption causes midline destruction of ear, nose, and throat (ENT) structures and vasculitis indistinguishable from granulomatosis with polyangiitis (GPA), an antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) (1-4). Sustained cocaine snorting provokes ischemic osseocartilaginous necrosis with midline destructive lesions of the nasal septum, turbinates and lateral walls, hard and soft palate, nasal columella, and upper lip. Palatal, columellar, and upper lip destruction is highly suggestive of cocaine damage since these territories are not usually affected by GPA (2, 3).

Cocaine-associated vasculitis may mimic a primary systemic vasculitis, such as GPA. Levamisole, the most frequent cocaine adulterant, is also involved in producing vasculitis and microvascular thrombotic lesions (5, 6). Both perinuclear and cytoplasmic ANCA patterns by indirect immunofluorescence, not always correlating with myeloperoxidase (MPO) and proteinase 3 (PR3) by ELISA, but often with double positivity, as well as other atypical antigens, have been detected in this secondary vasculitis. However, the presence of human neutrophil elastase (HNE) reactivity has been associated more specifically with AAV in cocaine users (1, 3, 5, 7). Neutrophil extracellular traps (NETs) formation (NETosis) is the pathway by which cocaine and levamisole have demonstrated to generate ANCA and develop vasculitis (8). NETs contain many of the ANCA-targeted autoantigens within the neutrophils, and both drugs may induce NETosis in isolated neutrophils, which in turn may secrete B cell activating factor (BAFF) with the subsequent generation of ANCA by B lymphocytes (8). The direct stimulus is proven by the fact that ANCA levels have been reported to normalise in children treated with levamisole before 2 to 14 months of discontinuing the drug (6).

Cocaine/levamisole-induced vasculitis is characterised by ENT involvement and cutaneous vasculitis, often presenting as retiform purpuric lesions due to small-vessel occlusion and skin ischaemia, mostly affecting the lower limbs, trunk, and earlobes (2, 3, 5, 6). Although less frequent, an overt systemic vasculitis with renal and pulmonary involvement may also occur (2, 3). Regarding its treatment, improvement after cocaine discontinuation has been repeatedly reported without any pharmacological therapy (3). However, glucocorticoids and additional immunosuppressive drugs are used in most patients, mainly in those able to stop cocaine use, since immunosuppression

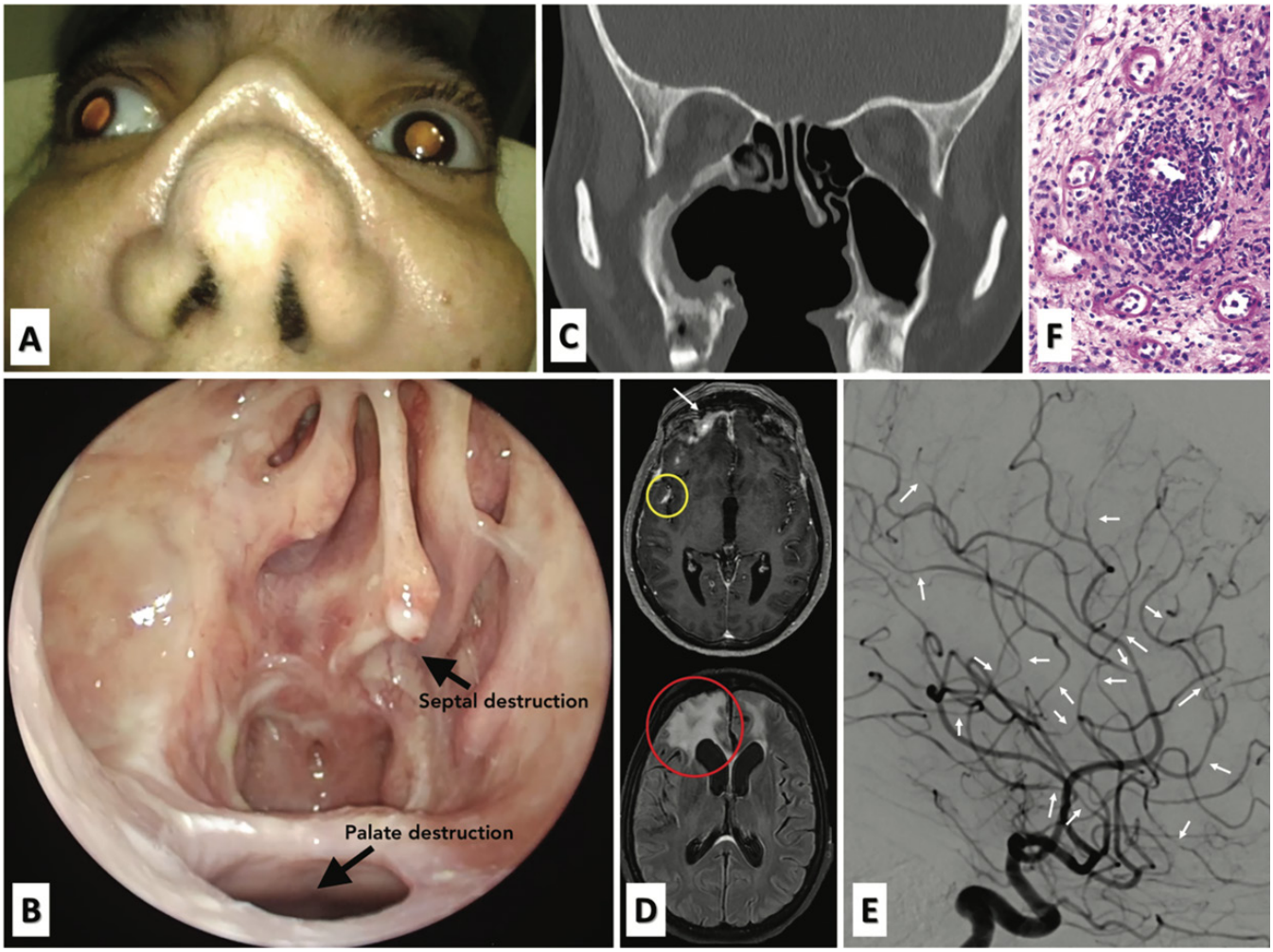

Fig. 1. **A**) Marked saddle nose due to an extensive destruction of nasal osteocartilaginous septum. **B**) Massive palate and septal destructive lesions by nasal endoscopy. **C**) CT showing complete midfacial bone/cartilage and right maxillary sinus destruction. **D**) (Upper) post-contrast axial T1-weighted image showing frontal pachymeningeal thickening and enhancement (arrow) associated with leptomeningeal enhancement in the Sylvian fissure (yellow circle), and (Down) axial fluid-attenuated inversion recovery (FLAIR) image showing frontal acute/subacute ischaemic areas (red circle). **E**) Right internal carotid artery digital subtraction angiography (DSA) showing multiple stenoses predominantly in medium vessels from the right anterior and middle cerebral arteries (arrows). **F**) Nasal biopsy disclosing perivascular and transmural lympho-monocytic inflammation of a small nasal artery with vessel wall necrosis and chronic inflammation of the nasal tissue.

has been shown to be ineffective in patients on active cocaine consumption and also increases the baseline high risk of infection in these patients (3).

Herein, we report the case of a chronic cocaine user presenting with cocaine-induced midline destructive lesions, and severe ocular and central nervous system (CNS) AAV treated with glucocorticoids and cocaine cessation.

A 36-year-old woman with 17 years background of cocaine snorting (up to 2 grams/day) was transferred to our centre because of behavioural changes, bradypsychia, confusion, and asthenia during the last three weeks, with the addition of left upper extremity abnormal movements, headache, and progressive bilateral vision loss. The nose was collapsed (Fig. 1A) and nasal endoscopy demonstrated total septal and hard palate destruction (Fig. 1B). Eye examination showed bilateral papilledema with peripapillary haemorrhages suggestive of vasculitic anterior ischaemic optic neuropathy. A craniofacial CT scan revealed complete midfacial bone, hard palate necrosis, and right maxillary sinus destruction (Fig. 1C). A brain MRI showed diffuse vasogenic oedema mainly in the right frontal and temporal lobes, frontal acute and subacute ischaemic lesions, and adjacent pachy- and leptomeningitis (Fig. 1D). A cerebral angiography revealed multiple stenoses in the territory of both the anterior and middle cerebral arteries (Fig. 1E). A PET/CT scan disclosed no pulmonary lesions or signs of large and medium-vessel vasculitis in other territories. Remarkable laboratory results included increased acute-phase reactant levels and normocytic anaemia. Renal function and urinalysis were normal. Urine toxicology screening was negative for cocaine (intake was stopped 6 weeks before). Among autoimmune markers, raised levels of PR3-ANCA (74.7 U/mL; normal <20 U/mL) with cytoplasmic pattern by indirect immunofluorescence were detected. MPO and other ANCA-related antigenic specificities (HNE, lactoferrin, cathepsin-G, azurocidin, lysozyme, and bactericidal/permeability-increasing protein) were negative. Palate and nasal biopsies depicted chronic inflammation with necrotising vasculitis in a small vessel (Fig. 1F).

A diagnosis of cocaine-induced midline destructive lesions and cocaine-induced PR3-ANCA-associated vasculitis with nasal/paranasal, ocular, and CNS involvement was established. Intravenous 250 mg methylprednisolone pulses for 3 days followed by 1 mg/kg/day were initiated with neurological improvement, except for blindness. Posterior prednisone tapering was the only therapy administered together with sustained cocaine withdrawal. Four months later, ANCA became and persisted negative. Prednisone was discontinued after 20 months, and the patient remained in remission at the 28-month follow-up.

To the best of our knowledge, this is the first case published in the literature of a histologically and angiographically proven AAV secondary to cocaine consumption with ENT, ocular, and CNS involvement, with clinical and immunological resolution after (only) glucocorticoids and sustained cocaine withdrawal. Therefore, this case opens a window of opportunity to treat severe forms of cocaine/levamisole-induced vasculitis only with glucocorticoids and cocaine cessation, which at the same time will avoid more aggressive immunosuppressive strategies in these already immunocompromised patients.

Acknowledgments

We would like to thank the patient and her family for their confidence and participation in this study.

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Competing interests: none declared.

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