Recognizing Granulomatosis with Polyangiitis in the Setting of Intranasal Cocaine Use with a Multidisciplinary Approach

Elise Peyroux[1] (epeyro@lsuhsc.edu) LSUHSC SOM New Orleans
Hanna Almoaswes M.D.[2] (halmoa@lsuhsc.edu) LSUHSC Department of Medicine
Keisha Patel[1] (kpat19@lsuhsc.edu) LSUHSC SOM New Orleans
Nadjel Opamen M.D.[2] (nopame@lsuhsc.edu) LSUHSC Department of Medicine
Sanjay Kamboj M.D.[2] (skambo@lsuhsc.edu) LSUHSC Department of Medicine

Case Presentation:

50-year-old woman with a history of hypertension and hyperlipidemia, and a social history notable for intranasal cocaine use for over a decade, presented to an otolaryngology clinic with progressive nasal obstruction, anosmia, rhinorrhea, facial pressure, and postnasal drip that had worsened over several years. Several years prior, she had undergone endoscopic sinus surgery for nasal polyps, with symptomatic improvement lasting only a few months. After discontinuing topical steroid therapy and being lost to follow-up, her symptoms gradually returned and progressed. At the time of presentation to otolaryngology, diagnostic nasal endoscopy demonstrated severe grade 4 bilateral nasal polyposis, diffuse mucosal edema with boggy turbinates and thick mucopurulent secretions, with a Lund–Kennedy score of 12, consistent with severe inflammatory disease. During this evaluation, a large nasal septal perforation was identified. In the context of her history, this finding was initially attributed to cocaine-induced midline destructive lesions (CIMDL). At this time, she was referred to Allergy/Immunology to manage chronic rhinitis for further evaluation. She was initiated on topical therapies, including corticosteroid nasal rinses.

Computed tomography of the Maxillofacial area with contrast was ordered and later revealed chronic sinusitis with probable pharyngeal polyposis and postsurgical changes from bilateral antrostomy. Histopathologic evaluation of sinonasal tissue showed necrotic inflammatory debris and granulation tissue, without evidence of fungal infection. Lab evaluation revealed elevated anti-proteinase 3 (PR3) antibody level (>8.0), with negative myeloperoxidase (MPO) antibodies and initially negative c-ANCA and p-ANCA by immunofluorescence. Though the immunofluorescence pattern was negative, the positive antigen specific immunoassay result of PR3-ANCA was of concern for an ANCA-associated vasculitis, so the patient was referred to Rheumatology for evaluation of possible systemic inflammatory disease in the upcoming months.

Over the ensuing weeks, serial ENT follow-up demonstrated objective improvement in endoscopic findings, with resolution of visible polyposis but persistent mucosal edema and secretions. Her Lund–Kennedy scores improved from 12 to 8 and subsequently to 6, reflecting decreasing but ongoing inflammatory activity. Despite improvement in sinonasal findings, she developed new lower respiratory symptoms, including intermittent dyspnea and chronic cough requiring bronchodilator use, along with a single episode of mild hemoptysis. At rheumatologic evaluation, repeat laboratory testing demonstrated persistent high-titer PR3 antibody elevation, with new development of positive p-ANCA, while MPO antibodies remained negative. There was no associated eosinophilia, and infectious workup was still negative. These evolving serologic findings further increased suspicion for ANCA-associated vasculitis, yet still not showing signs of renal involvement.

Through a coordinated multidisciplinary approach involving otolaryngology, allergy/immunology, and rheumatology, and the combination of chronic refractory sinonasal disease, nasal septal perforation, persistent PR3 elevation, new pulmonary symptoms, and evolving p-ANCA serologies, the likelihood for limited granulomatosis with polyangiitis was high. The decision was made to initiate methotrexate with folic acid supplementation. Over subsequent weeks, the patient reported improvement in respiratory symptoms and overall clinical stability, and she continues to undergo close follow-up across specialties with plans for ongoing monitoring of symptoms and serologic markers.

Discussion:

This case highlights the diagnostic challenge of distinguishing granulomatosis with polyangiitis (GPA) from cocaine-induced midline destructive lesions (CIMDL). The patient's 10-year history of intranasal cocaine use and presence of nasal septal perforation initially supported cocaine-induced disease, a known cause of sinonasal destruction due to vasoconstriction and ischemic injury. Additionally, cocaine exposure has been associated with ANCA positivity, including PR3, further complicating interpretation.

Emerging evidence suggests that cocaine may not only mimic vasculitis but may also trigger or unmask ANCA-associated vasculitis in susceptible individuals. Proposed mechanisms include chronic mucosal injury leading to antigen exposure, immune dysregulation, and neutrophil activation with autoantibody formation. This may result in persistent or evolving ANCA positivity rather than the transient patterns more typically seen in isolated drug-induced disease.

However, several features raised concern for an underlying vasculitis process. The patient demonstrated persistently elevated PR3 antibodies, rather than transient serologic findings, along with progression of symptoms despite cessation of cocaine use prior to the initial ENT visit. She also developed new respiratory symptoms, including dyspnea and a single episode of hemoptysis, suggesting evolving systemic involvement. Notably, she lacked renal manifestations, but this does not exclude GPA, as limited disease may initially spare the kidneys.

This case demonstrates the risk of premature diagnostic anchoring in patients with known cocaine use. A key clinical takeaway is that cocaine use does not exclude ANCA-associated vasculitis. Instead, diagnosis should rely on longitudinal assessment, integrating clinical progression, repeat serologies, and multidisciplinary evaluation. Early recognition is critical, as delayed treatment of GPA can lead to irreversible organ damage, whereas cocaine-induced disease is managed with cessation alone.

Granulomatosis with polyangiitis (GPA) remains a critical do-not-miss diagnosis, particularly when presenting with destructive sinonasal disease. This case emphasizes that even in patients with a clear alternative explanation, such as intranasal cocaine use, clinicians must keep their differential diagnosis broad until disease pathophysiology is truly confirmed.