

Cocaine-induced Pseudo-GPA

Irish Rhinology Society Guidelines

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Summary

The United Nations Office on Drugs and Crime reports a continuing rise in cocaine use, especially over the past decade. Widespread adulteration of cocaine and higher purities are producing more extensive local destruction and increasing systemic complications beyond the simple nasal perforations historically seen.

These guidelines reflect the Irish Rhinologic Society's recognition of the increasing prevalence of cocaine-related disease, but also the expanding associated clinical complexity and demonstrating our commitment to improving its timely recognition and accurate diagnosis.

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Background

Cocaine, often adulterated with levamisole, can trigger a destructive, localised vasculitis-like process within the sinonasal cavity. Levamisole, a synthetic anti-helminthic drug originally developed for veterinary use, is frequently mixed with cocaine and can trigger an ANCA-associated vasculitis, characterised by neutropenia, with widespread cutaneous and systemic vascular injury. It remains unclear whether cocaine or levamisole is the primary cause of the pathology.

Cocaine induced midline destructive lesions (CIMDL) describe the local tissue necrosis caused by intranasal use but, when it includes autoimmune features such as ANCA positivity and vasculitis, it is sometimes referred to as cocaine-induced pseudo-granulomatosis with polyangiitis (CIE-pGPA). (1-3). A growing body of literature acknowledges the similarities with GPA but that the underlying cause is a drug-induced vasculitis rather than primary autoimmune disease. (4–6).

Diagnosis

1. Clinical features: Cocaine-related disease of the nose and midface spans a spectrum from mucosal inflammation, with irritation, crusting and recurrent nosebleeds, to progressive ischaemic damage that erodes cartilage and bone. Septal perforation can be associated with crusting and nasal obstruction but can progress to external deformities including saddle deformities of the nasal dorsum and loss of tip support. Severe necrosis can extend to the lateral nasal walls and hard palate, presenting as severe crusting and palatal perforation (a distinguishing feature from true GPA). Cutaneous manifestations, particularly with levamisole adulterated cocaine exposure, include purpuric necrotic or ulcerated lesions on the face or extremities, sometimes with columella loss or soft tissue loss of the nasal region. Patients with CIE-pGPA tend to be younger than those presenting with GPA. They can experience severe pain and are prone to secondary bacterial and fungal infections.
2. Laboratory: Up to 70% of cases of CIE-pGPA demonstrate pANCA positivity, most commonly directed against proteinase-3 (PR3), but atypical or dual ANCA patterns are frequent (5,6). The divergent ANCA staining pattern (pANCA + anti-PR3 antibodies) usually arises because of the presence of anti-neutrophil elastase antibodies. Anti-MPO or dual-ANCA positivity is more indicative of levamisole exposure.

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3. Histology: Usually demonstrates non-specific chronic inflammation; granulomas are rarely seen (unlike GPA). Neoplasia and invasive fungal disease must be excluded.

4. Imaging: CT scanning is recommended to map necrosis and destruction, which often begins at the septum but may extend to palate, lateral wall, orbit, or skull base (2).

5. Exclusion: True GPA, invasive fungal disease and malignancy must be ruled out (8). True GPA should be suspected in the presence of a c-ANCA staining pattern, granulomatous lung lesions and/or evidence of glomerulonephritis.



Cocaine Screening

1. Clinical history and examination.
2. Urine toxicology detects use for 3–14 days and is most useful early in the week following weekend consumption. While not necessary for all cases it can be particularly valuable where considerable nasal destruction exists and / or the diagnosis relating to clinical presentation remains unclear when usage is denied, or when confirming abstinence when planning surgical treatment. Access to toxicology can vary nationwide so please discuss availability with local laboratories.
3. Hair testing can demonstrate exposure months to years after use and is increasingly available (9). It can be valuable where diagnosis is challenged by patient denial of use and negative urinalysis.

NB: Patients often deny cocaine use; confidentiality and a supportive approach are critical to avoid misdiagnosis and inappropriate immunosuppression.

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Investigations

1. Urine toxicology at each clinic visit, if available/required for clinical reasons.
2. Urinalysis for blood and protein
3. Bloods: ANCA indirect immunofluorescence with testing for anti-PR3 and anti-MPO antibodies, FBC, U&E, ESR CRP. Consider measurement of anti-elastase antibodies.
4. CT sinuses for disease extent.
5. EUA and biopsy before immunosuppressive therapy, to exclude GPA, neoplasia, or fungal disease.
6. Chest imaging



Management

1. Absolute cocaine cessation is the cornerstone of therapy (4,5), with compliance monitored regularly with urine.
2. Supportive care: saline irrigation, topical emollients, analgesia, and treatment of bacterial colonisation (particularly *Staphylococcus aureus*) or secondary bacterial infections if suspected.
3. Topical $\pm$ systemic corticosteroids: May reduce inflammation, although responses are variable (7) and very likely to be transient if cocaine use continues.
4. Immunotherapy: Reserved for patients with progressive disease despite abstinence, or with systemic involvement. Corticosteroids, cyclophosphamide or rituximab have all been used, but evidence remains case-based (7,8).
5. Addiction services referral is vital. Patients refusing urine monitoring or continuing to use cocaine should be redirected to GP and community rehabilitation pathways.

Patients with suspected drug-induced vasculitis should be referred to a Specialist Vasculitis team if active or extensive destructive disease is present, there is diagnostic uncertainty (e.g.



urinalysis is negative, cocaine denied)and/ or investigations demonstrate evidence of potential systemic involvement (renal, neurological or pulmonary).

Surgical Considerations

1. Avoid surgery during active disease. Early debridement or sinus surgery risks worsening destruction and may facilitate ongoing cocaine use (9).
2. Definitive reconstruction (septal, palatal, or nasal framework repair) should only be considered when:
 - a) At least 12–18 months of abstinence and inflammatory quiescence are demonstrated, and
 - b) Multidisciplinary consensus (ENT, vasculitis, reconstructive, and addiction teams) agrees on safety (8).
3. Patients must be warned that relapse into cocaine use may reactivate inflammation and cause reconstructive failure.

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Key Messages for Irish Practice

1. Cocaine related disease is increasingly encountered in Irish ENT clinics.
2. Urine toxicology should be used to evaluate for cocaine use in patients who deny substance abuse, where the clinical presentation requires clarification and can also be used to ensure patients are abstinent prior to offering surgical intervention.
3. Misdiagnosis as GPA can lead to inappropriate immunosuppression — always exclude cocaine use.
4. Multidisciplinary approach to care - ENT, Nephrology/Rheumatology/Vasculitis and Addiction services are essential.
5. Surgery should be deferred until sustained abstinence and disease quiescence are confirmed.

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Role of the General Practitioner

1. Clarify cocaine use via history and/or toxicology. Screen haematologically for systemic toxicity. Chest imaging if antibody positivity. Counsel patient, encourage immediate cessation of cocaine and, if needed, refer for community rehabilitation.
2. Referral to ENT Specialist if abstinent: Nasendoscopy, biopsy and CT imaging.
3. Referral to Rheumatology/Nephrology: Systemic involvement or active destruction evident, or where diagnosis uncertain or GPA suspected/ confirmed (Fig 1).



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