

The effect of cocaine on the nasal cavity and its differential diagnoses looking at three individual cases

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Abstract

Systemic vasculitic conditions can present with sino-nasal symptoms. Due to the immunosuppressive agents used to treat such conditions it is vital that an accurate diagnosis is obtained prior to treatment commencing. We present a series of patients with significant nasal destruction and a diagnostic dilemma between a true vasculitic condition and a pseudovasculitis as a result of cocaine use. We review the investigations that can help to determine a definitive diagnosis, multidisciplinary approach needed and discuss the treatment strategies employed in our patients.

Introduction

Various systemic conditions including autoimmune, granulomatous, neoplastic, infective diseases as well as substance abuse can present with sino-nasal manifestations [1]. Due to the complexity of overlapping features, an accurate and prompt diagnosis poses a significant challenge for clinicians.

One particular area of difficulty surrounds the diagnostic uncertainty between a patient with cocaine induced midline destructive lesions (CIMDLs) and true primary systemic necrotizing vasculitis (PSNV) induced midline destruction. Amongst the subtypes of PSNV, midline lesions occur in up to 90% cases of granulomatosis with polyangiitis (GPA) [2]; up to 69% in Eosinophilic granulomatous polyangiitis (eGPA) [3] and up to 30% microscopic polyarteritis (MPA) found in [4].

Antineutrophil cytoplasmic antibodies (ANCA) play an important but cumulative role in assisting the diagnosis; along with clinical presentation, imaging, urine analysis and histology. Vasculitides can often demonstrate different patterns of ANCA positivity. GPA is associated with a positive C-ANCA pattern/PR3 antigen with MPA and EGPA being associated with P-ANCA/MPO antigen. Using the combined ANCA and associated target a sensitivity of 85.5% and specificity of 98.6% [5] can be achieved. The time to seroconvert can lead to confusion since many patients with GPA may have false negative levels for some time, despite having a significant sensitivity and specificity.

The presentation of pseudovasculitis, as a result of cocaine abuse, can be ubiquitous in both clinical findings as well as very similar serological results (positive ANCA levels) and a bewilderingly similar histological pattern. It is essential that an accurate diagnosis is made to prevent unnecessary exposure to immunosuppressants and also enable key decisions on management.

Methods

We present a series of three cases with a confirmed diagnosis of CIMDL. Data was collected from patient notes and online records. All three patients underwent the same investigative and management approach:

Step 1: Exclude systemic vasculitis

- a. Refer to rheumatology
- b. Urinalysis
- c. Bloods
- i.FBC, ESR, ANCA, Connective tissue screen, ACE, HIV, syphilis

Step 2: Determine extent of disease

- d. CT Sinus / CT Head and neck / CT thorax

Step 3: Restore some healthy nasal mucosa

- e. Saline + lubrication

Step 4: Consider associated problems

- f. Hearing aid referral
- g. Speech and swallowing: Maxillofacial surgeon assessment

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Ethical considerations

Patient confidentiality was maintained throughout the review by anonymizing data.

Results

Patient one

A 50yr old female was referred to the ENT department with nasal regurgitation; significantly hyponasal speech and a bilateral deterioration in her hearing

Oropharyngeal inspection revealed a 3cm fistula to the right of midline arising from lateral to the incisive foramen anteriorly. Anterior rhinoscopy revealed an absent cartilaginous septum and partially eroded bony septum. The floor of the nose was found to be eroded bilaterally with only a thin layer of mucosa and the lack of visible normal lateral wall architecture. Significant crusting was present, but the post nasal space mucosa was healthy.

On further questioning she admitted to a two-year history of heavy cocaine abuse; having last used cocaine 18 months previously. She also confirmed 'aggressive' picking of her nose including using cotton wool buds to remove crusts from deep within her nasal cavity.

Patient two

A 41 yr old male patient presented to the maxillofacial department with a 4-week history of oral pain and difficulty in speaking. Examination findings included a granulating septal perforation and fistula of the soft palate. On further questioning he also reported a new history of bilateral hearing loss and a 6-month history of sinusitis like symptoms with nasal obstruction and discharge; managed in the community with numerous courses of oral antibiotics. He had no significant past medical or surgical history but admitted to a four-year history of cocaine use intranasally.

Clinical examination revealed a large septal perforation with a single nasal cavity. Significant crusting was identified within the nasal cavity with ulceration involving destruction of the turbinates.

Patient three

A 24yr old male presented to the respiratory physicians with a 3-year history of increasing shortness of breath and a single episode of haemoptysis. Further questioning revealed a long-standing history of nasal congestion, epistaxis and frontal headaches as well as a history of cocaine abuse having stopped 2 years previously.

Clinical examination revealed a saddle shaped deformity of the nasal bridge with a large septal perforation but a relatively healthy mucosal lining.

Investigation results

Table 1 summarizes the key laboratory investigative findings for the three patients. Importantly, all patients were found to have a mildly raised ANCA with PR3 positive, but no evidence of systemic vasculitis was identified. Follow-up investigations (Table 2) revealed no evidence of systemic involvement with normal renal function and urinalysis. Table 3 demonstrates that significant destruction was seen in 2/3 of the patients CT imaging.

Discussion

Key findings

A diagnostic dilemma arises when a patient with known substance abuse presents to clinic with significant nasal destruction and the clinician has to be able to exclude a systemic vasculitic condition the unfortunate sequelae being that a multisystem disease can go undiagnosed. Early diagnosis of such conditions is key as advanced disease limits the potential benefit of therapy [6].

Cocaine itself is well recognized for its vasoconstrictive properties resulting in localized necrosis of tissues. The vasculitic response seen in CIMDLs is hypothesized to be a response from the cocaine but increasing evidence has identified levamisole adulterated cocaine to be more toxic in this way and is the main trigger to the vasculitic process. Crew identified that 50% of UK cocaine is cut with levamisole [7] - a synthetic imidazothiazole with immunomodulatory properties. When used in sufficient quantities, it can result in the localized tissue destruction seen with CIMDLs and also systemic vasculitis and agranulocytosis [8].

Our three cases aid in identifying key differences in presentation, serology and imaging which can help to differentiate CIMDLs from true vasculitides. Table 4 provides a comparison between the vasculitic processes that can help with this diagnostic uncertainty looking at histology, serology and systemic involvement.

A key aspect of this is the requirement for histology. In 2016, the European League Against Rheumatism produced consensus statements providing guidance on the management of AAV patients [11] including discussions over the role of performing biopsies. In this study, they explain that a positive biopsy is strongly supportive of a diagnosis and biopsies are recommended to assist in establishing a new diagnosis. The important element to consider is the location from which they are taken. In GPA patients with renal involvement, diagnostic yield from renal biopsy can be as high as 91.5% and biopsies of nasal mucosa may be positive for inflammatory changes in 68.4%. A large study looking at diagnostic yield from ENT biopsies revealed that they are often positive for non-specific chronic inflammation and it is significantly less common to find granulomas and vasculitis when compared to lung and kidney biopsies [12].

Table 1. Blood test results

Blood tests	Case one	Case two	Case three	Normal ranges
FBC	Hb 124	Hb 95	Hb 164	115-165
ESR	29	68	3	0-27
ANCA (IU/ml)	MPO < 0.2 PR3 3.8	MPO < 0.4 PR3 4.5	MPO 0.9 PR3 11	< 0.9 < 0.9
DsDNA, Centromere B, SS-A, SS-B, Sm, SmRNP, SCL-70, Jo-1, Ribosomal P, Chromatin	Negative	Negative	Negative	
RF	Negative	Negative		
ACE	Negative	Negative		
TPHA	Negative	Negative		
HIV	Negative	Negative		

Table 2. Follow up investigations

Follow-up investigations	Case one	Case two	Case three
URINAYSIS	Normal	Normal	Normal
U+E	Normal	Normal	Normal
Biopsy	Not performed	Nonspecific changes consistent with vasculitis	Bronchial washings performed: No granulomas or overt necrotic material seen

Table 3. CT sinus reports

Case one CT SINUS	Absence of hard palate with evidence of fistula between oropharynx and nasal cavity. Absent right middle turbinate and nasal septum. Erosion of medial pterygoid plate. Maxillary and ethmoid sinus mucosal thickening.
Case two CT SINUS	Extensive destruction in the paranasal sinuses with destruction of the hard palate on the left and fluid in bilateral mastoid air cells / middle ear clefts with dilatation of the left ICA in the cavernous sinus.
Case Three CT Head and neck CT Thorax	No overt signs of systemic vasculitis seen (No CT sinus performed)

Table 4. Diagnostic features of ANCA associated vasculitides

	MPA Microscopic polyangitis	GPA Granulomatosis with polyangitis	eGPA Eosinophilic granulomatosis with polangitis	Cocaine induced vasculitis
Vessel size	Predominantly small vessel	Predominately small vessel	Predominatly small to medium vessels	Small vessel
Serology	P-ANCA/MPO antigen	C-ANCA pattern/PR3 antigen	P-ANCA/MPO antigen	C-ANCA pattern/PR3 antigen (50% cases) P-ANCA/MPO antigen (almost 100%) [9]
Histology findings [10]	Necrotizing arteritis, glomerulonephritis and capillaritis common. Granulomatous inflammation absent.	Necrotizing granulomatous inflammation of upper and lower respiratory tract. Necrotizing glomerulonephritis, pulmonary hemorrhage and ocular vasculitis	Necrotizing granulomatous inflammation – eosinophil rich	Leukocytoclastic vasculitis
Systemic involvement	Common	Common	Asthma	Rare

The implication of such a low diagnostic yield has led to our conclusion that nasal biopsies should not be part of routine practice (as demonstrated within our cases series). The exception to this is in the presence of very abnormal looking mucosa where other differential diagnoses are being considered such as lymphoma.

Treatment strategies

All three patients were managed by the same rheumatology, maxillofacial and ENT teams with short term oral steroids and abstinence from cocaine use.

Though the literature search is limited, we have found that a moderate dose of steroids normally 60-80 mg on a reducing regime over 3 to 6 months works well as an immunomodulator to halt the vasculitic process. Very few patients, as described above, need steroid sparing agents (such as Azathiaprine). However, if a systemic vasculitic process has been identified, this would have been the next management step. Case one and two had significant palatal destruction requiring temporary management with an obturator and are both planed for reconstructive surgery with a radial forearm free flap when the mucosa is more healthy.

Clinical applicability

In summary we have identified that there are certain features that can aid in confirming a diagnosis of CIMDLs over other causes:

- CT scans often demonstrate soft tissue thickening of nasopharynx, soft palate and oropharynx with bony destruction of palate, lateral nasal wall, turbinates, septum and ethmoid sinuses [13].
- Biopsy should only be done to exclude malignancy where abnormal mucosa is seen.

- Serological markers can improve diagnostic yield with up to 56% c-ANCA positive with CIMDL [14] and more often very high titres of MPO ANCA antibodies [15].
- Once the diagnosis is confirmed, such patients must be managed by a multidisciplinary team:
- ENT surgeons are required to consider the potential of a systemic vasculitic condition, manage the nasal mucosa and aid in performing biopsies when needed.
- Rheumatologists can help with the diagnostic dilemma and also given advice on the management of such localized vasculitis as well as manage any associated systemic involvement.
- Maxillofacial teams can facilitate both temporary and long-term management of the extensive destruction that may occur.

Key points

- CIMDLs to this extent are rare but it is important that we make an accurate diagnosis since the differential diagnosis is PSNV which needs an aggressive management plan.
- Patients with confirmed vasculitis should be managed by specialist teams in a multidisciplinary approach with CIMDLs requiring input from ENT, Maxillofacial, rheumatology as well as allied teams such as audiology.
- The diagnosis can be difficult, but clinicians should always enquire about cocaine use in the patient history. Diagnostic features that help to confirm a CIMDL rather than primary vasculitis include characterized destructive changes on CT, but clinicians must be aware of the overlap in serology and histological features.

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