10.5005/jp-journals-10001-1329

ORIGINAL RESEARCH

Surgery for Vasculitic Disease of the Nose and Sinuses

[1]Ivor Kwame, [2]Charles Pusey, [3]Peter Andrews

ABSTRACT

Nasal surgery in patients with granulomatosis is complex. A number of considerations are required including the risk of potential reactivation of vasculitis in the operative field after surgery, the tissue quality leading to less predictable healing, and the associated risk of postoperative infection. These are particularly relevant in nasal reconstruction and underscores the need for a multidisciplinary approach.

Management which confers stable, predictable outcomes is advantageous. In this article, we share our experience of the use of endoscopic sinus surgery (ESS) and nasal reconstruction in these difficult cases. In all cases, patients were jointly managed by a reconstructive rhinologist and a vasculitis physician.

Keywords: Antineutrophil cytoplasm antibody, Antineutrophil cytoplasm antibody-associated vasculitis, Granulomatous disease, Rhinoplasty, Vasculitis.

How to cite this article: Kwame I, Pusey C, Andrews P. Surgery for Vasculitic Disease of the Nose and Sinuses. Int J Head Neck Surg 2018;9(1):1-6.

Source of support: Vasculitis UK, Medical Research Council.

Conflict of interest: None

INTRODUCTION

Vasculitis is a rare autoimmune condition that features inflammatory infiltrates centered around blood vessels, typically with resulting necrosis. It has a slight female-to-male predominance and has an approximate incidence of 10 to 20 per million per year in populations of Northern European extraction.[1-3] Conditions most commonly associated with the nose tend to involve small- to medium-sized vessels and are often associated with an antineutrophil cytoplasm antibody (ANCA).[4-6] The ANCA may be detected in either a perinuclear or cytoplasmic pattern, targeting neutrophil proteinase-3 (PR3) or myeloperoxidase (MPO) enzymes respectively.[5-8] It is possible for the ANCA levels of patients with vasculitis to change from detectable to undetectable and vice versa, or remain entirely undetectable throughout treatment.[6-8]

While vasculitis may be limited to the nose, it is frequently part of a multisystem disorder that can have clinical features throughout the body with the nose being one of the more visible manifestations.[3-6] Life-threatening multiorgan involvement may occur which can be fatal if not appropriately managed with immunosuppressive therapy with survival still potentially conveying significant quality-of-life sequalae.[9-11]

Typical nasal features of ANCA-associated vasculitis (AAV) include inverted-V nasal deformity, septal perforation, nasal crusting, and/or bloody rhinorrhea.[9-11] These features are not diagnostic and can be seen as part of the typical array of features in patients with functional and or esthetic nasal complaints. This means it remains possible for AAV patients to be seen for surgical management without their important non-nasal features being recognized, with the risks of delayed medical treatment and resulting morbidity.[6,12]

There are three main types of AAV, namely granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with polyangiitis (EGPA), and microscopic polyangiitis (MPA).[13,14] The diagnosis is based on the typical patterns of organ involvement supported by the presence of ANCA.[12-14] Of these, GPA and EGPA tend to be more commonly associated with rhinological problems.[5,9,15] Eosinophilic granulomatosis with polyangiitis (formerly known as Churg-Strauss syndrome) typically features chronic rhinosinusitis with nasal polyps alongside pulmonary involvement.[16] The GPA (formerly known as Wegener's granulomatosis) is the most common form of AAV and may affect a number of different organs throughout the course of illness. The rhinological features tend to target the nasal architecture as well as mucosal lining.[5,9] The MPA tends to affect the kidneys and lungs but rarely affects the nose.[17] Other forms of AAV include drug-induced vasculitis, with cocaine being most commonly associated.[18-20]

[1]Registrar, [2]Professor, [3]Associate Professor and Consultant

[1]Department of Medicine and Vascular Inflammation, Imperial College London, London, United Kingdom; Department of Otolaryngology, Royal National Throat, Nose and Ear Hospital London, United Kingdom; and University College London Ear Institute, London,UK

[2]Department of Medicine and Vascular Inflammation, Imperial College London, London,UK

[3]Department of Otolaryngology, Royal National Throat, Nose and Ear Hospital, London, United Kingdom; University College London Ear Institute, London,UK

Corresponding Author: Ivor Kwame, Registrar, Department of Medicine and Vascular Inflammation, Imperial College London, London, UK; Department of Otolaryngology, Royal National Throat, Nose and Ear Hospital London, UK; and University College London Ear Institute, London, UK, email: ivork1@hotmail.co.uk

Cocaine is a powerful vasoconstrictor, and intranasal use can lead to localized ischemia and necrosis. It is one of the most commonly used narcotics worldwide,[21,22] and its use may be associated with development of positive ANCA serology.[23] Septal perforation may therefore be due to ischemia secondary to direct vasoconstriction. However, as cocaine is often used with the antihelminthic adulterant levamisole, the destruction may be due to the capability of levamisole to induce ANCA and directly activate neutrophils as in other AAV. Cocaine-associated vasculitis can therefore create a difficult diagnostic problem as patients who have used intranasal cocaine and present with septal perforations and positive ANCA may have either a self-limiting nonvasculitic condition with a coincidental ANCA or may go on to develop an erosive condition with possible progress to involve other organs due to development of AAV, thus requiring immunosuppression. It may also be possible for the patient to have a primary autoimmune GPA with the history of previous cocaine use being unrelated, given the sizeable incidence of cocaine use in the general population.[21]

One of the first nasal features of AAV may be a septal perforation. Patients who present to rhinology services with an unexplained nasal perforation require a sizeable biopsy to confer sufficient information about architecture and thus increase the chances of diagnosis.[9,15,24] Nonetheless, nonspecific inflammatory features on nasal biopsies are very common, and enlarging the perforation to get a histological diagnosis may render the dimensions of the defect beyond the reasonable limits of successful surgical reconstruction. Opinions differ therefore on the need for biopsy in cases of isolated septal perforation with plausible histories of either previous nasal surgery or intranasal cocaine use. This is because both nasal surgery and intranasal cocaine carry well-established risks of septal perforation, so while nasal biopsies may help to detect features of diagnostic necrotic granulomatous inflammation, they frequently do not. Clearly, biopsies remain an important tool in helping to exclude the possibility of malignancy. Biopsies may also help in excluding other conditions which can be considered as part of the differential diagnosis in a midline destructive presentation, such as the rare eosinophilic angiocentric fibrosis, which may require similar reconstructive techniques.[25]

While there are no pathognomonic characteristics that define nasal vasculitis, features of granulomata, ulceration, bloody nasal discharge, crusting, and evidence of active sinus inflammation are accepted hallmarks of active nasal disease in patients with an established AAV diagnosis, as detailed in the Birmingham vasculitis activity score (BVAS).[13,14] The BVAS is a widely accepted multisystem scoring strategy which helps clinicians experienced in managing AAV monitor for evidence of new or persistent features of up to three months. It is a useful tool for monitoring responses to treatment and so can help guide decisions on the need for a change in treatment dose or strategy.[13,14,26]

In this article, we describe our clinical experience of managing complex AAV patients, some with histories of previous cocaine exposure being jointly managed at a tertiary reconstructive rhinology service and a tertiary vasculitis referral unit, both based in London. We outline the decision-making process and detail our novel nasal reconstruction technique to help safeguard predictable esthetic results based on our previously described principles (Fig. 1).[27,28]

MATERIALS AND METHODS

This is a prospective review of three ANCA-positive patients who underwent ESS or nasal reconstruction and were jointly managed at a tertiary vasculitis referral unit.

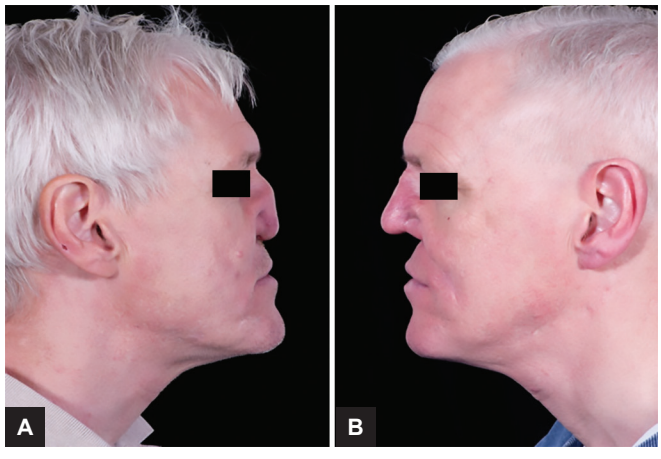
In all cases, immunosuppression was initiated first.

Patient Selection

Vasculitis patients receiving sinonasal surgery for functional and/or cosmetic complaints over a 3-year period from June 1, 2012 to May 31, 2015 were selected. Patients were selected based on having had no known cocaine exposure within a minimum of 12 months prior to surgery. They were all jointly managed by experienced surgeons and physicians with a specialist interest in vasculitis and reviewed for at least 12 months postoperatively.

Medical Intervention

Each patient was independently reviewed at a tertiary vasculitis referral center where they were investigated for multisystem involvement and started on glucocorticoids and/or other appropriate immunosuppression (such as



Figs 1A and B: Preoperative (A) and postoperative (B) images after osseocartilaginous nasal reconstruction

azathioprine or mycophenolate mofetil) based on factors which included their age, the severity of their disease manifestations, and the extent of multiorgan involvement. The patients continued to be actively monitored by the vasculitis physicians throughout the period of the study, with appropriate management of relapses or complications of medical therapy.

Surgical Technique

Endoscopic Sinus Surgery

The approach to ESS in chronic disease has been well documented. As endonasal infections are known to be associated with nasal relapse, a key aim in patients with vasculitis remain s obtaining biopsies, removing evident obstruction (e.g., uncinectomy) and necrotic tissue, while trying to avoid being too radical by leaving healthy tissue undisturbed. This is because the chronic nature of vasculitis means that patients may require further surgery at repeated points in the future.

Septal Surgery

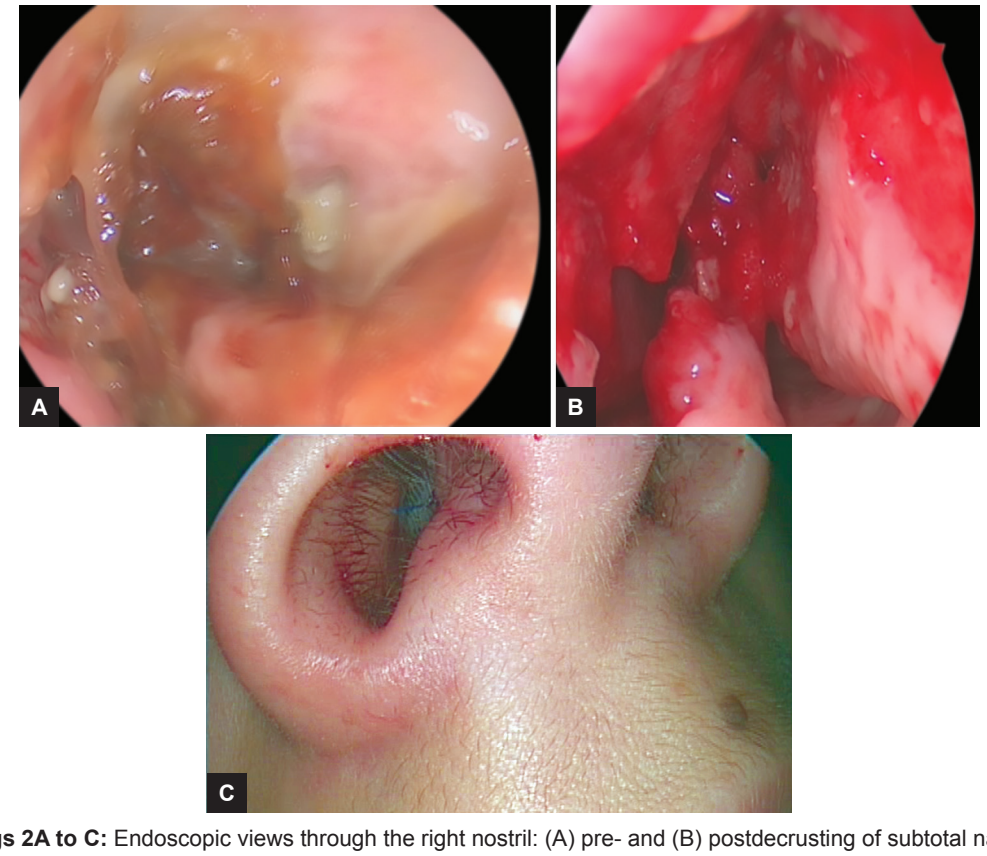
Nasal septal perforations are common in vasculitis patients and may present at any size, enlarging with time. They can induce symptomatic nasal crusting or a sense of obstruction. These symptoms are thought to be due to the perforation disrupting the natural lamina nasal airflow, with the turbulence drying nasal secretions, inducing crusts.

Surgical closure of septal perforations is commonly carried out by either an inferior turbinate turn-in flap or by nasal floor advancement flap; however, we do not advocate direct closure when the diameter of the perforation exceeds 25 mm or where the most anterior limit is within 5 mm of the nasal vestibular skin margin. Patients in this study had symptomatic perforations that were too large to be surgically closed and so were obturated with silastic splints instead. Customized silastic buttons were chosen for perforations less than 30 mm; otherwise, a pair of customized reinforced silastic nasal splints were used. The splints are secured with 4-0 polypropylene (prolene, Ethicon) sutures with the knot tied on the medial surface (i.e., away from the nasal lumen) as shown in Figure 2.

Septorhinoplasty with Osseocartilaginous Autograft

While detailed discussions about the most appropriate types of septorhinoplasty in patients with vasculitis are beyond the scope of this article, what is clear is the need for reliable techniques that yield predictable results in these difficult cases. With that in mind, costal osseocartilaginous grafts have been shown to have favorable resorption rates alongside reasonable malleability.

Nasal reconstruction was carried out via an external approach and dorsal laparotomy using costal



Figs 2A to C: Endoscopic views through the right nostril: (A) pre- and (B) postdecrusting of subtotal nasal septal perforation, and (C) after obturation of the perforation using customized reinforced silastic splints

osseocartilaginous grafts by the senior author with assistance from experienced specialist registrar surgeons. The osseocartilaginous rib graft was harvested from the free floating 10th or 11th rib, depending on length availability. This was done utilizing a standard technique of a linear 5 cm skin incision over the selected rib and subsequent dissection, respecting the contrasting directions of the external and then internal obliques, before subperiosteal harvesting of a typically 10 by 20 mm graft, which has both bony and cartilaginous components. In general, where the 10th rib did not have sufficient length, the 11th was then selected.

After graft harvest, the cartilage is contoured to create two 10 by 5 mm right triangular prisms before both are hollowed out with a drill using a 2/0 diamond. The lengths of the two grafts are then adjusted and linked together using 3/0 polydioxanone (PDS, Ethicon) to construct an L-strut, which complements the dorsal esthetic profile of the patient. The construct is then secured to the glabella and remnant maxillary spine using a titanium screw and 3/0 polypropylene (prolene, Ethicon) suture respectively as previously described (Fig. 1).[29]

Medial Epicanthal Surgery

Mucoid epiphora is a common ocular complaint in GPA patients, associated with inflammatory obstruction of the nasolacrimal duct. Its surgical management includes dacryocystorhinostomy, whether endoscopic or open, to widen the obstructed nasolacrimal duct pathway. Rarely, the epiphora may be due to discharge from an epicanthal defect and so necessitate the use of a pericranial flap via a bicoronal incision, as shown in Figure 3.

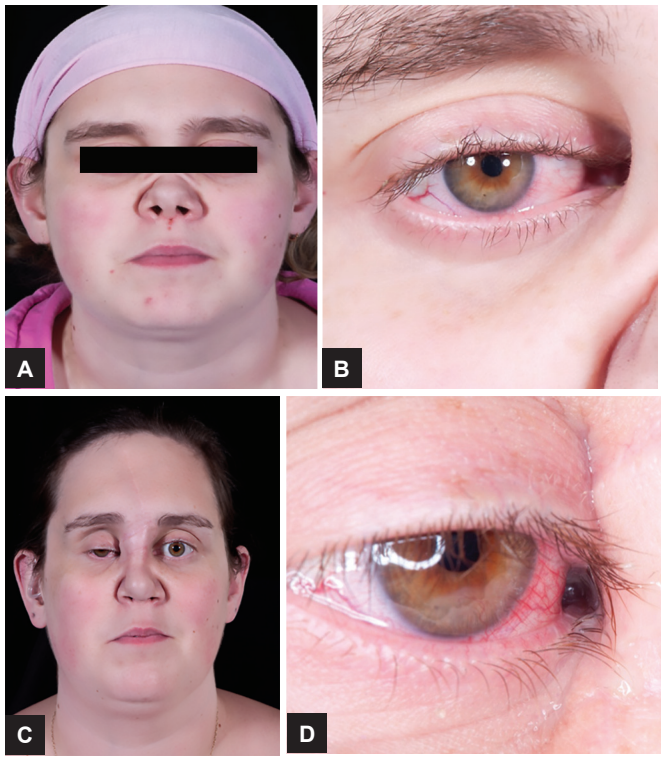
RESULTS

Three patients underwent sinonasal surgery and were regularly reviewed independently by vasculitis physicians and the nasal reconstructive surgeons for at least 12 months. Surgery was undertaken after established relapse with immunosuppression.

Patient 1

- *Diagnosis:* Drug-induced, PR3-positive vasculitis.
- *Systems affected at time of surgical intervention:* Nose.
- *Medical treatment:* Azathioprine (100 mg) and prednisolone (20 mg).
- *Complications:* Postoperative infection of columella with skin loss requiring composite graft repair.

A 62-year-old male with ear, nose, and throat (ENT)-limited nasal deformity secondary to drug-induced vasculitis underwent osseocartilaginous septorhinoplasty. Patient did experience postoperative infection of his columella, which required prolonged antibiotics. Within the 12 months of follow-up, he did not require revision rhinoplasty surgery. He did not go on to develop multiorgan AAV involvement nor experienced relapse of his vasculitis.



Figs 3A to D: Preoperative (A, B) and postoperative (C, D) images after pericranial flap reconstruction of a right medial epicanthal fistulation, with close-up images B and D showing the preoperative absence and then postoperative presence of epicanthal mucosa

Patient 2

- *Diagnosis:* Drug-induced, PR3-positive vasculitis.
  Systems affected at the time of surgical intervention: Nose.
- *Medication: Azathioprine 100 mg, prednisolone (20 mg).*
- *Complications:* Nil.

A 25-year-old female with ENT-limited drug-induced (cocaine) vasculitis underwent ESS featuring standard bilateral uncinectomy and anterior ethmoidectomy for painful, turbid anterior rhinorrhea with significant crusting and nasal obstruction. She also had obturation of her subtotal perforation with customized silastic splints. Her nasal crusting and sense of obstruction improved postoperatively (Fig. 2).

Patient 3

- *Diagnosis:* GPA, PR3-positive vasculitis.
  Systems affected at the time of surgical intervention: Nose, eye.
- *Medical therapy:* Mycofenalate (2 gm) and prednisolone (7.5 mg).
- *Complications:* Nil.

A 28-year-old female with PR3-positive GPA underwent a pericranial flap reconstruction of a chronically discharging right medial epicanthal fistulation into the nose. The procedure enabled the insertion of a vascularized mucosal layer into the field in the form as well as larger than normal glabella flap, which will set in over time but importantly will allow for further revision in the future if required. She had an uncomplicated recovery with clear evidence of remucosalization of the epicanthal defect at 6 months postoperatively. The patient did experience relapse of her ocular vasculitis postoperatively which was successfully managed with immunosuppression (Fig. 3).

DISCUSSION

In this article, we have demonstrated that surgical management of AAV patients can be successful when complemented with coordinated medical management of their vasculitis with immunosuppression.

We have discussed the known limitations of relying on ANCA screens and/or septal perforation biopsies alone in excluding this important condition,[5-7,9,24,30] which may present to the rhinologist first and have outlined how delayed diagnosis may lead to reduced quality of life,[10,11] and increased rates of morbidity and mortality. As the kidneys are commonly affected in AAV, urinalysis and a renal function blood test may also aid detection, but ultimately, our recommendations remain consideration of referral to experienced vasculitis clinicians if doubt remains of unexplained ongoing nasal inflammation, before attempting surgical intervention.

We have also highlighted the complexities of managing cocaine-associated (drug-induced) AAV patients, including the difficulty in establishing a clear diagnosis and outlined key principles for deciding on the need for immunosuppression or not.

Finally, we have also shared our experience on the use of a range of surgical techniques for managing some of the nasal features of vasculitis and have shown how the use of reliable techniques, which convey predictable outcomes, is vital in these hugely challenging cases.

REFERENCES

1. Watts RA, Lane SE, Bentham G, Scott DG. Epidemiology of systemic vasculitis. Arthritis Rheum 2000 Feb;43(2): 414-419.
2. Ntatsaki E, Watts RA, Scott DG. Epidemiology of ANCA-associated vasculitis. Rheum Dis Clin North Am 2010 Aug;36(3):447-461.
3. Kwame, I. Inflammatory disorders of the larynx. In: Costello D, Sandhu G, editors. Practical laryngology. London: CRC Press; 2015. p. 149.
4. Kotanko P, Pusey C D, Levy JB. Recurrent glomerulonephritis following renal transplantation. Transplantation 1997 Apr;63(8):1045-1192.
5. Kwame I, Kariyawasam H. The relationship between the upper and lower airway—an ENT perspective. J ENT Masterclass 2014;7(1):65-69.
6. De'Oliviera I, Gaskin I, Dash A, Rees A, Pusey C. Relationship between disease activity and anti-neutrophil cytoplasmic antibody concentration in long-term management of systemic vasculitis. Am J Kidney Dis 1995 Mar;25(3):380-389.
7. Jayne DR, Gaskin G, Pusey CD, Lockwood CM. ANCA and predicting relapse in systemic vasculitis. QJM 1995 Feb;88(2):127-133.
8. Booth AD, Almond MK, Burns A, Ellis P, Gaskin G, Neild GH, Plaisance M, Pusey CD, Jayne DR; Pan-Thames Renal Research Group. Outcome of ANCA-associated renal vasculitis: a 5-year retrospective study. Am J Kidney Dis 2003 Apr;41(4):776-784.
9. Srouji IA, Andrews P, Edwards C, Lund VJ. Patterns of presentation and diagnosis of patients with Wegener's granulomatosis: ENT aspects. J Laryngol Otol 2007 Jul;121(7):653-658.
10. Srouji IA, Andrews P, Edwards C, Lund VJ. General and rhinosinusitis-related quality of life in patients with Wegener's granulomatosis. Laryngoscope 2006 Sep;116(9):1621-1625.
11. Srouji I, Lund V, Andrews P, Edwards C. Rhinologic symptoms and quality of life in patients with Churg-Straus Syndrome vasculitis. Am J Rhinol 2008 Jul-Aug;22(4)406-409.
12. Flossmann O, Berden A, de Groot K, Hagen C, Harper L, Heijl C, Höglund P, Jayne D, Luqmani R, Mahr A, et al. Long-term patient survival in ANCA-associated vasculitis. Ann Rheum Dis 2011 Mar;70(3):488-494.
13. Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, Flores-Suarez LF, Gross WL, Guillevin L, Hagen EC, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. Arthritis Rheum 2013 Jan;65(1):1-11.
14. Lionaki S, Blyth ER, Hogan SL, Hu Y, Senior BA, Jennette CE, Nachman PH, Jennette JC, Falk RJ. Classification of antineutrophil cytoplasmic autoantibody vasculitides: the role of antineutrophil cytoplasmic autoantibody specificity for myeloperoxidase or proteinase 3 in disease recognition and prognosis. Arthritis Rheum 2012 Oct;64(10):3452-3462.
15. Hoffman GS, Kerr GS, Leavitt RY, Hallahan CW, Lebovics RS, Travis WD, Rottem M, Fauci AS. Wegener granulomatosis: an analysis of 158 patients. Ann Intern Med 1992 Mar;116(6): 488-498.
16. Lanham JG, Elkon KB, Pusey CD, Hughes GR. Systemic vasculitis with asthma and eosinophilia: a clinical approach to the Churg-Strauss syndrome. Medicine (Baltimore) 1984 Mar;63(2):65-81.
17. Chung SA, Seo P. Microscopic polyangiitis. Rheum Dis Clin North Am 2010 Aug;36(3):545-558.
18. Rachapalli SM, Kiely PD. Cocaine-induced midline destructive lesions mimicking ENT-limited Wegener's granulomatosis. Scand J Rheumatol 2008 Nov-Dec;37(6):477-480.
19. Lancaster J, Belloso A, Wilson CA, McCormick M. Rare case of naso-oral fistula with extensive osteocartilaginous necrosis secondary to cocaine abuse: review of otorhinolaryngological presentations in cocaine addicts. J Laryngol Otol 2000 Aug;114(8):630-633.
20. Goodger NM, Wang J, Pogrel MA. Palatal and nasal necrosis resulting from cocaine misuse. Br Dent J 2005 Mar;198(6): 333-334.
21. Prinzleve M, Haasen C, Zurhold H, Matali JL, Bruguera E, Gerevich J, Bácskai E, Ryder N, Butler S, Manning V,

et al. Cocaine use in Europe—a multi-centre study: patterns of use in different groups. Eur Addict Res 2004 Sep;10(4): 147-155.
22. Ehleringer JR, Casale JF, Lott MJ, Ford VL. Tracing the geographical origin of cocaine. Nature 2000 Nov;408(6810):311-312.
23. Pieterse E, van der Vlag J. Cracking the pathogenesis of cocaine-induced vasculitis. Rheumatology (Oxford) 2017 Apr;56(4):503-505.
24. D'Cruz D P, Baguley E, Asherson RA, Hughes GR. Ear, nose, and throat symptoms in subacute Wegener's granulomatosis. BMJ 1989 Aug;299(6696):419-422.
25. Rimmer J, Andrews P, Lund VJ. Eosinophilic angiocentric fibrosis of the nose and sinuses. J Laryngol Otol 2014 Dec;128(12):1071-1077.
26. Weiner M, Goh SM, Mohammad AJ, Hruskova Z, Tanna A, Bruchfeld A, Selga D, Chocova Z, Westman K, Eriksson P, et al. Outcome and treatment of elderly patients with ANCA-associated vasculitis. Clin J Am Soc Nephrol 2015 Jul;10(7):1128-1135.
27. Poirrier AL, Ahluwalia S, Kwame I, Chau H, Bentley M, Andrews P. External nasal valve collapse: validation of novel outcome measurement tool. Rhinology 2014 Jun;52(2): 127-132.
28. East C, Kwame I, Hannan SA. Revision rhinoplasty: what can we learn from error patterns? An analysis of revision surgery. Facial Plast Surg 2016 Aug;32(4):409-415.
29. Christophel J, Hilger PA. Osseocartilaginous rib graft rhinoplasty: a stable, predictable technique for major dorsal reconstruction. Arch Facial Plast Surg 2011 Mar-Apr;13(2):78-83.
30. Diamantopoulos II, Jones NS. The investigation of nasal septal perforations and ulcers. J Laryngol Otol 2001 Jul;115(7):541-544.