Nasal manifestations of granulomatous disease

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Granulomatous disease frequently affects the head and neck region, particularly the nose and sinuses. This article describes the most common infectious and non-infectious conditions and their clinical features.

Infectious granulomatous diseases resulting from tuberculosis (TB) and leprosy have decreased in frequency in the UK in the 20th century but have returned slightly in the last 10 years (Butt, 1997). Areas with high immigrant populations will encounter these more often. Non-infectious granulomatous diseases such as Wegener's granulomatosis (WG) and sarcoidosis have been increasingly recognized. Many granulomatous diseases affect the nose and this article reviews the manifestations of these diseases. *Table 1* shows a simple classification. WG and sarcoidosis are the most common granulomatous diseases that affect the nose in the UK; however, worldwide the infective causes are more common.

SYMPTOMS AND SIGNS

Diagnosis may be difficult because the symptoms and signs are similar and non-specific. The subtle differences can be distinguished with time. Most patients present with nasal obstruction with or without a sero-sanguineous discharge. Frank bleeding may occur if the disease is particularly active. As the respiratory mucosa is destroyed, crusting becomes more of a problem and this is frequently fetid.

When the diseases go into remission, crusting, scarring and adhesions develop. Skin lesions and destruction are more common in sarcoidosis, TB and leprosy. If the nasal mucosa is destroyed on both sides of the septum, a perforation occurs since the cartilage derives its nutrition from the overlying mucosa. When the destruction is extensive, the septum collapses. Internally granulomata can be seen. They are haemorrhagic in WG and are pale and yellow in sarcoid. The nose is an ideal site for gaining samples for histology and culture. Each disease will be considered in more detail.

TABLE 1.
Classification of nasal granulomata

Non-specific	
Non-infectious	Wegener's granulomatosis
	Sarcoidosis
	Pyogenic granuloma
	Scleroma
Infectious	Tuberculosis
	Leprosy
	Syphilis
Maligancy	Lethal midline granuloma

IMAGING

Radiographic by computerized tomography (CT) and magnetic resonance imaging (MRI) may show the extent of the disease in the sinuses but often the changes are non-specific as a result of inflammation. Bone erosion, intracranial and orbital extension are well demonstrated by CT and this is the first investigation. Extensive bone erosion is more common with a T cell lymphoma (lethal midline granuloma). MRI in particular shows coincidental changes in otherwise normal sinuses and so caution is required interpreting these. Fluid or secretions may be differentiated from soft tissue swelling.

HISTOLOGY

Nasal biopsies are taken with the aid of a rigid endoscope from the septum, turbinates or any likely area including the post-nasal space. These may be done under local anaesthesia but if the sinuses are explored a general anaesthetic is preferable. The biopsy size is important and Del Buono and Flint (1991) have stated that biopsies greater than 5 mm are more helpful in

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gaining a diagnosis. Multiple biopsies have been advocated but the authors have never had a positive biopsy without macroscopic evidence of disease. The histological features may be non-specific. Acute and chronic inflammatory changes, namely macrophages, multinucleated giant cells and lymphocytic infiltration, are seen in most conditions.

Vasculitis, mucosal ulceration and necrosis are not found in all cases of WG and the biopsies need to be interpreted in the light of the clinical picture and other investigations. Sarcoid has less lymphocytic infiltration and vasculitis should be absent. Features such as Schramm bodies are calcified debris and are more common in sarcoidosis. Previously a Kveim test could be examined for comparison. Caseation is not always found in TB and is not present in sarcoidosis. Negative staining for *Mycobacterium tuberculosis* does not rule out this. Biopsies need to be deep and may require repeating. The diagnosis of leprosy is made by deep biopsies demonstrating the presence of acid-fast but not alcohol-fast bacilli. A proportion of any biopsy should be sent for culture but the form must indicate the type of organisms suspected.

Figure 1. Crusting associated with Wegener's granulomatosis.

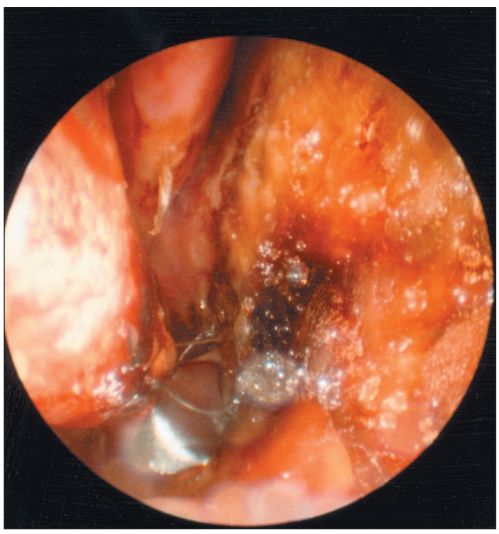
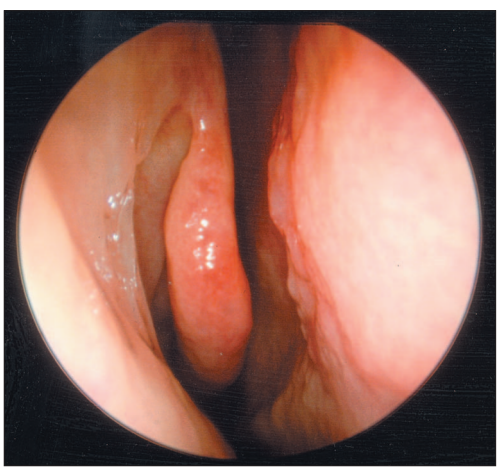


***Figure 2. Normal nose for comparison with* Figure 1.**



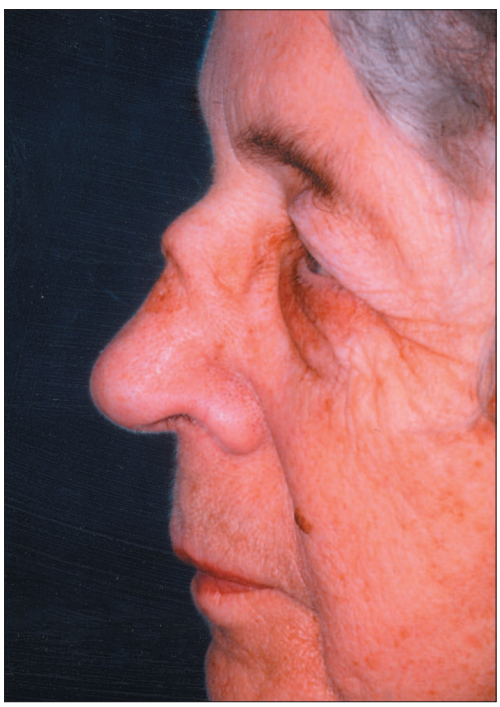
NON-INFECTIOUS CAUSES OF GRANULOMATOUS DISEASE OF THE NOSE

Wegener's granulomatosis

WG was first described in 1931 by Klinger and later in a more detailed account by Wegener (1936, 1939). The aetiology is still unknown but an immunological hypersensitivity reaction is seen as the most likely cause. Until the advent of immunosuppressive therapy, WG was frequently a fatal condition, with mortality rates greater than 90% (Fauci et al, 1983). In its generalized form, the upper and lower airways and renal systems are affected. However, the eyes, skin and nervous system may also be affected (Murty, 1990). More limited forms may affect any of the above systems.

Nasal involvement may be present in any form of the disease and gives a good clinical guide to the present disease state. Crusting, epistaxis and/or nasal swelling cause obstruction (*Figures 1* and *2*). Ulceration and septal

Figure 3. Septal collapse (saddling) as a result of Wegener's granulomatosis.



perforation are common intranasal findings. Externally there can be cosmetic changes as a result of the degree of internal destruction. Septal collapse is shown in *Figure 3*. Cutaneous involvement in WG is uncommon, but is more common with sarcoidosis. The presence of gross destruction of the skin means that an alternative diagnosis such as lymphoma should be considered (see later).

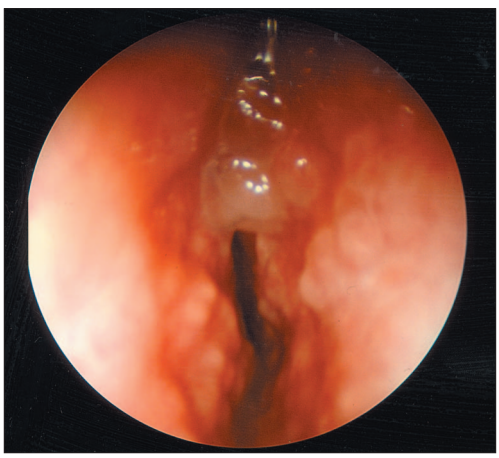
Cytoplasmic pattern anti-neutrophil cytoplasmic antibody (c-ANCA) is increasingly playing an important role in the diagnosis and monitoring of the disease process. Rao et al (1995) have shown that the sensitivity and specificity are high in acute disease (91% and 99% respectively) but this falls in inactive disease (63% and 99.5% respectively).

Sarcoidosis

Sarcoidosis is a disease characterized by non-caseating granuloma, with an unknown aetiology. Sarcoidosis is a systemic condition and can affect any tissue; but it has a predilection for lymph nodes, lung and skin. The condition was reviewed recently but excluded essentially the ear, nose and throat manifestations of the disease (Hunninghake et al, 1999). Jonathon Hutchinson described the skin manifestations first in 1877 and Caesar Boeck first described sarcoidosis in 1899, noting both nasal and skin lesions. When nasal sarcoid is present, there is a worse prognosis with the worry that the lesions will spread into the cranial cavity (Hunninghake et al, 1999). The overall mortality of the condition is 5% and this is associated with the cardiac, renal and intra-cranial spread.

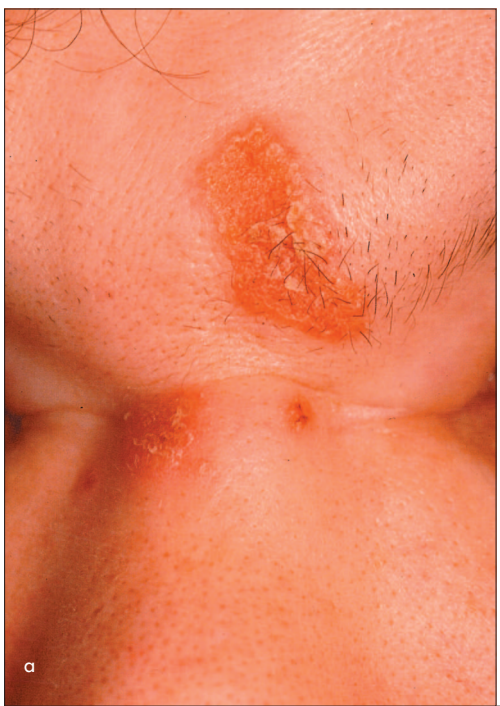
Nasal disease usually manifests its presence by nasal obstruction, epistaxis and rhinorrhoea or postnasal drip. The nasal mucosal appearance is classically 'cobble-stoned' (*Figure 4*). The granulomata are distinguished from those in WG being less haemorrhagic. Other signs include nasal polyps, crusting, perforation, adhesions, saddling and mucosal oedema. Cutaneous involvement is more common in sarcoidosis, being either the direct involvement of the skin with granulomatous disease or as 'lupus pernio' where deeper granulomas in the dermis produce red or violet skin lesions (*Figures 5a* and *b*).

Figure 4. Cobble-stone appearance of the nasal mucosa affected by sarcoidosis.



Pyogenic granuloma

Pyogenic granuloma (lobular capillary haemangioma) often present as an alarming, rapidly enlarging unilateral nasal mass causing epistaxis



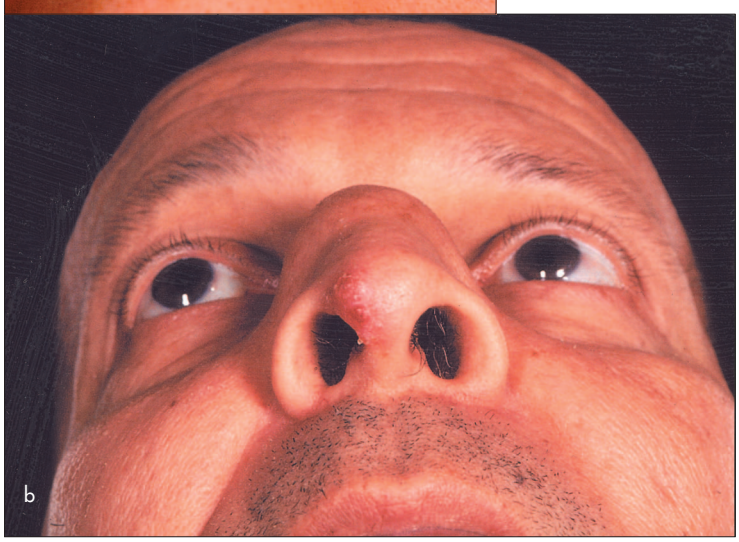


Figure 5a and b. Skin manifestations of sarcoidosis.

and nasal blockage. This problem is uncommon but occurs through the age ranges and is seen in children. A history of trauma is not always given but is almost always the cause and treatment is surgical excision. Recurrence is uncommon (el-Sayed and al-Serhani, 1997).

Scleroma

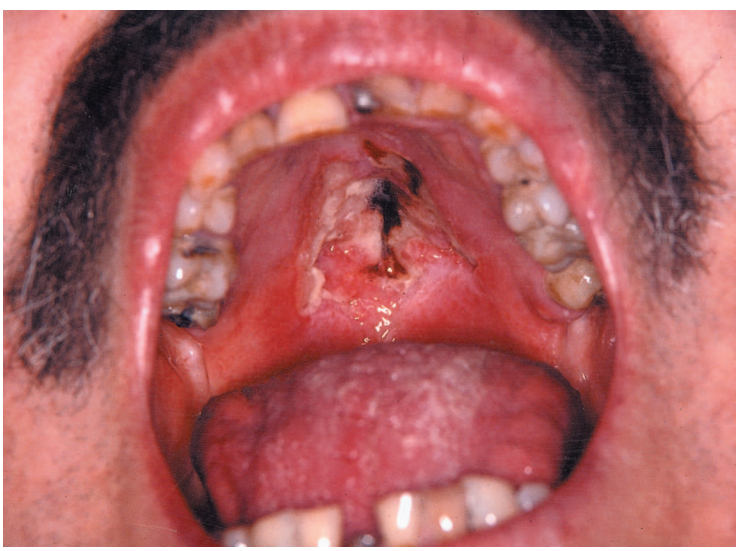
Scleroma is a chronic granulomatous condition, which is slowly progessive. Typically the disease is present initally in the nose but then extends into the nasopharynx, oropharynx and larynx. This condition is very rare in the UK. It is more common in the subtropics and the Middle East. The causative organism is *Klesbiella rhinoscleroma*. Three clinical stages have been described: catarrhal rhinitis, inflammatory granulomatous and cicatricial deformative. The first stage gives symptoms similar to a cold, the second nasal blockage, ulceration and foul discharge, the third produces disfigurement.

INFECTIOUS CAUSES OF GRANULOMATOUS DISEASES OF THE NOSE

Tuberculosis

Classically there are two forms of TB of the nose; lupus vulgaris and granulomatous TB. It is a rare condition, with only 35 cases being reported in the English language medical literature in the last 95 years (Butt, 1997), although clearly the disease is more common in the non-English speaking world. Lupus vulgaris is a destructive skin lesion, which may involve the nasal vestibule; granulomatous TB involves the anterior nasal septum rather than the skin, producing nasal obstruction and foul-smelling discharge. The bony septum is not involved and cosmetically unappealing scarring may occur after the initial ulceration. Atrophic rhinitis is a frequent sequel. There is confusion regarding whether nasal TB is strongly associated with pulmonary TB.

Figure 6. Palatal destruction as a result of a lymphoma.



Leprosy

Leprosy produces a wide range of clinical features dependent upon the host immunological reaction to the intracellular *Mycobacterium leprae*. The lepromatous form produces large quantities of mycobacterium as opposed to the tuberculoid leprosy where the numbers of organisms may be very small. Nasal discharge is a potent method by which leprosy is spread. Skin involvement is very frequent in leprosy and the nose is often the first site involved. Clinical features are granulomatous nodules, perforation and ulceration on the septum and turbinates. These tend to heal producing atrophic rhinitis. There has been one documented case presenting to an ear, nose and throat department in Birmingham in the last 10 years and as expected it occurred in an immigrant.

Syphilis

Syphilis has decreased in frequency with increasing antibiotic usage, but should always be considered in a case of granulomatous nasal disease. Transmission is either congenital or acquired. Recently there has been an increase in the reported prevalence, particularly epidemics occurring in Russia and within the male homosexual community (Borisenko et al, 1999). In congenital syphilis, the nose is always involved and causes discharge that may be present at birth. The erythematous patches of secondary syphilis tend to develop within the next 3–6 months. This chronic discharge is thick, yellow and blood stained. Tertiary syphilis causes nasal deformity, collapse of the bridge of the nose, perforation of the hard palate and septum and ulceration of the nasal skin.

Acquired syphilis first gives a primary chancre of the nose, usually of the vestibule or anterior part of the septum. Cervical lymphadenopathy is not uncommon. Secondary syphilis then develops and is similar to the ulceration seen in the other orifices such as the mouth. Tertiary syphilis develops to give the characteristic saddle deformity (as a result of nasal bone destruction, not septal perforation), and granulomatous lesions in the nose with ulceration. A posterior septal perforation is associated with syphilis, whereas an anterior perforation is not caused by syphilis. The

destruction by tertiary syphilis may be very expensive and cause bone necrosis.

TB, leprosy and syphilis are the commonest infectious causes of granulomatous disease but there are other rare causes, including Yaws, actinomycosis, nocardiosis, some fungal infections especially aspergillosis, leishmaniasis and Churg–Strauss disease (allergic granulomatosis). All are rare but should be considered in the differential diagnosis.

Lethal midline granuloma (Stewart's granuloma)

Lethal midline granuloma is a misnomer; the condition is a nasal T cell lymphoma (*Figure 6*). This is an extremely destructive lesion of the mid-face and requires a biopsy for diagnosis; these may require repeating. The treatment is radiotherapy but cure is not guaranteed. Previously 'midline destructive lesions' of the sinonasal tract had a variety of terms including midfacial destructive lesion, Stewart's granuloma, midline malignant reticulosis but probably represent the lymphoma described previously (Harrison, 1987). However, recent studies have again suggested that 'idiopathic midline destructive disease' is still a valid description/diagnosis for a few patients where other diagnoses have been excluded (Barker and Hosni, 1998).

CONCLUSIONS

The nose is part of the respiratory tract and may be involved in any systemic disease that affects any part of it. WG has a predilection for presenting with nasal symptoms. While in the UK, the causes are usually WG or sarcoidosis, worldwide infection remains the commonest cause. The role of the ear, nose and throat surgeon is to help make the diagnosis and monitor the progress of the condition and therapy is best left to those who specialize in medical treatment. HM

Conflict of interest: none.

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KEY POINTS

- Granulomatous disease may present with nasal symptoms in the absence of more generalized symptoms.
- Nasal features are classically epistaxis, discharge, crusting and ulceration.
- The interpretation of histology is often difficult and requires repeated biopsies. The findings must be interpreted in the light of the clinical picture.
- The nasal mucosa is a good guide to the activity of the disease but the medical management of these patients is best left to specialized units.

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