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Eosinophilic angiocentric fibrosis affecting the nasal cavity. A mucosal variant of the skin lesion granuloma faciale

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Abstract
Eosinophilic angiocentric fibrosis (EAF) is an unusual fibrotic condition affecting the mucosa of the upper respiratory tract, of which there have been eight reported cases. The condition is thought to be associated with the rare skin disorder granuloma faciale, which is histologically identical, and was present in two cases of EAF. We report the third case where EAF and granuloma faciale occurred together, to highlight this type of intranasal fibrosis as a distinct pathological entity.

Key words: Granuloma; Eosinophilic Granuloma; Respiratory System

Introduction

Granuloma faciale is a benign disorder of the skin, that manifests as raised red-brown plaques. As the name suggest, it almost exclusively affects the skin of the face. There have been nine reports of extra-facial granuloma faciale, where the skin of the trunk and proximal extremities has been involved.[1] The overlying epithelium is smooth, and ulceration does not occur. Spontaneous involution of the plaques is rare. Treatment in the past has included surgical removal, cryotherapy, radiation therapy, systemic, topical and intralesional steroids, and the dermatological drug dapsone. Each have had only limited success. Granuloma faciale is more common in males, and in middle age. The cause is unknown.

Roberts and McCann[2] first described eosinophilic angiocentric fibrosis (EAF) in 1985. They noted a strange fibrotic condition of unknown aetiology affecting the mucosa of the nasal cavity of two patients, and the subglottic region of the larynx in a third patient. Histologically, the appearances of all three cases were very similar, and resembled the appearanes of granuloma faciale. Both conditions have a characteristic perivascular infiltrate rich in eosinophils, which progresses to a concentic 'onion-skin' fibrosis around the involved vessels. This is confined to the dermis in granuloma faciale and to the submucosa in EAF.[2]

Four more cases of intranasal fibrosis, and a further case of subglottic stenosis, all showing this characteristic pattern of fibrosis have been described to date, making a total of eight cases of EAF altogether.[2–6] Interestingly, two of these eight went on to develop granuloma faciale.[2,4] We report the ninth case of EAF, and the third to be associated with granuloma faciale, highlighting this as a rare, but well-documented cause of fibrotic narrowing of the upper respiratory tract.

Case report

A 38-year-old male presented with bilateral nasal obstruction, and external swelling of the nose. He was otherwise

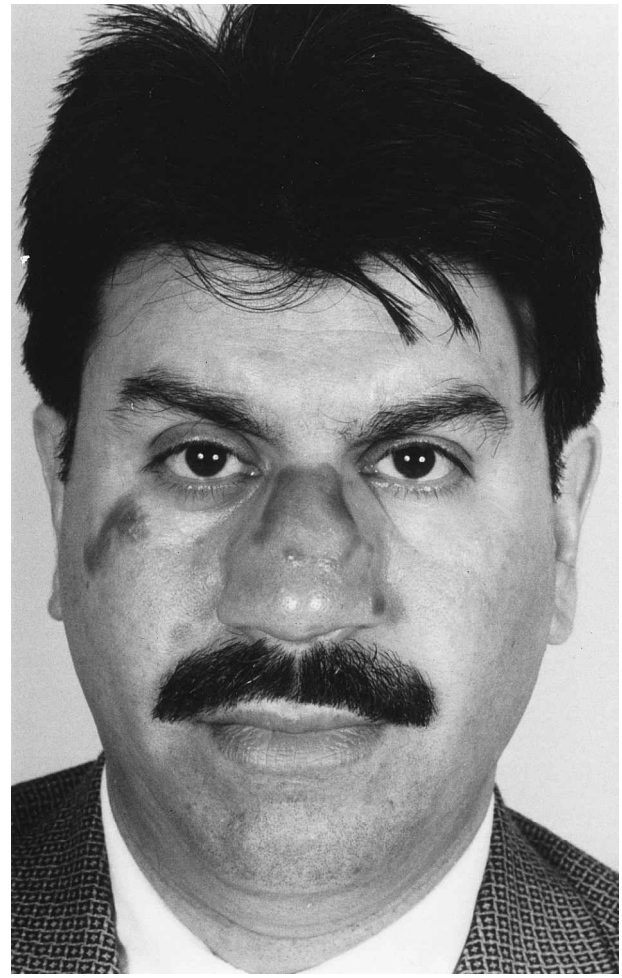

Fig. 1
Facial appearance of granuloma faciale.

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well, with no significant past history except for psoriasis. Examination under anaesthetic showed marked swelling of the nasal pyramid and septum, with a firm smooth lesion arising from the left upper lateral cartilage.

Six months prior to presentation a skin lesion had been excised from the right malar prominence. This was reported as granuloma faciale. The lesion recurred, and a new lesion appeared over the right alar of the nose, both of which were excised, confirming granuloma faciale. Again, these lesions reappeared after excision, along with new lesions over the bridge of the nose, and left and right temporal areas (Figure 1).

Biopsies, and partial debulking of the lateral nasal lesion were performed a total of three times, but each time the fibrotic nasal masses recurred. Histology reported these as fibrosis and chronic inflammation with no specific features.

Stains for fungi, tubercle and lepra bacilli were negative. Anti-neutrophil cytoplasmic antibodies (ANCA) were not present. A chest X-ray was reported as normal. A computed tomography (CT) scan confirmed soft tissue swelling of the septum and lateral nasal walls, with no evidence of bony erosion.

Plenty of histological material was available but no firm diagnosis could be made. The specimens were sent to an expert histopathologist who diagnosed the recently described condition, EAF. To confirm this diagnosis, and to aid in the further understanding of this condition, we also contacted P.F. Roberts, the histopathologist who originally described EAF in his paper in 1985.[2] Specimens were sent, and both granuloma faciale and EAF were confirmed.

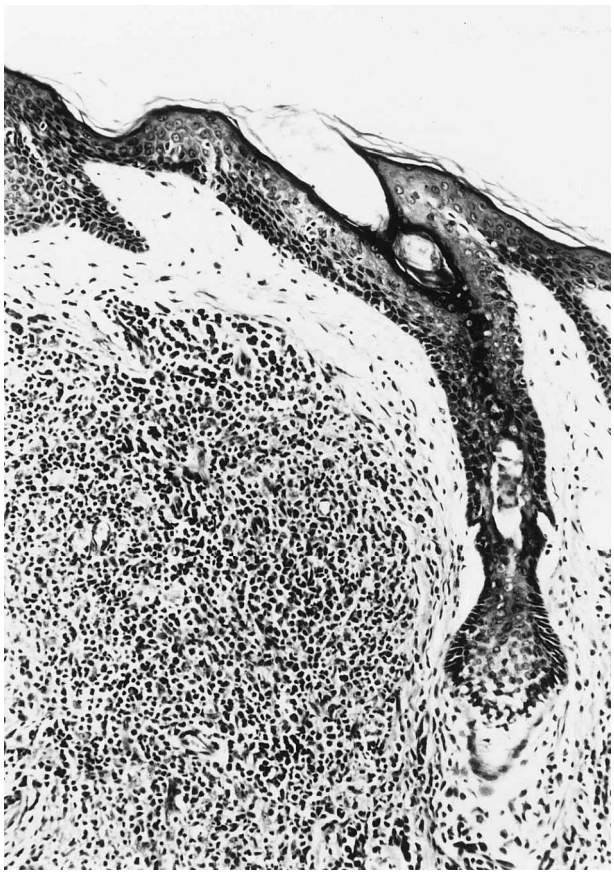

FIG. 2

Facial skin biopsy showing Grenz zone between inflammatory infiltrate and epidermis (H & E; ×120).

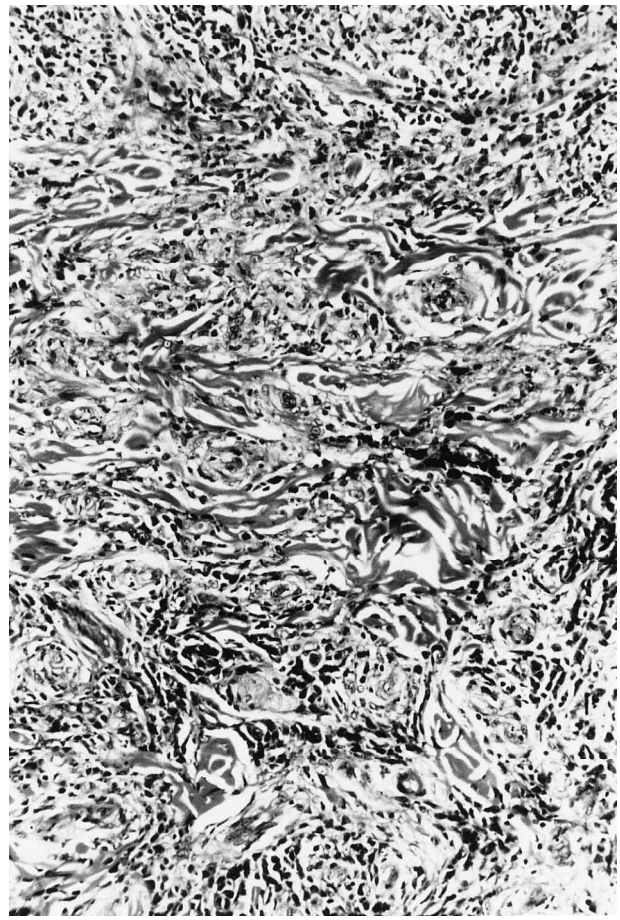

FIG. 3

Deeper part of skin biopsy showing fibrosis replacing the inflammatory infiltrate and exhibiting and early 'onion-skin' pattern (H & E; ×120).

The skin biopsy shows the typical appearances of granuloma faciale with a dense perivascular infiltrate of eosinophils, neutrophils and plasma cells with characteristic sparing of the superficial and perifollicular collagen (Grenz zone, Figure 2). The deeper dermis shows progressive fibrosis developing into an 'onion-skin' (Figure 3). Biopsies from the lateral nasal swellings showed an almost identical pattern of 'onion-skinning' with very few residual eosinophils – a later stage in the evolution of the histological process (Figure 4).

As the nasal lesions recurred following debulking, treatment was started with intra-lesional injection of steroids, and later with a one-month course of prednisolone orally, with little benefit. The facial lesions were being treated by the dermatologists at the same time. Dapsone, which has been reported to have some effect in granuloma faciale,[7,8] was used for three years. There was little, if any, beneficial effect. Treatment with Yag laser (532 nm i.e. green) was tried on the largest facial lesion, again with little benefit.

Both the facial and nasal lesions developed fully over a two-year period. Nasal obstruction continues, and the facial lesions are fluctuant between firm red masses, and soft paler plaques, but there has been no further progression of the disease over the subsequent six years.

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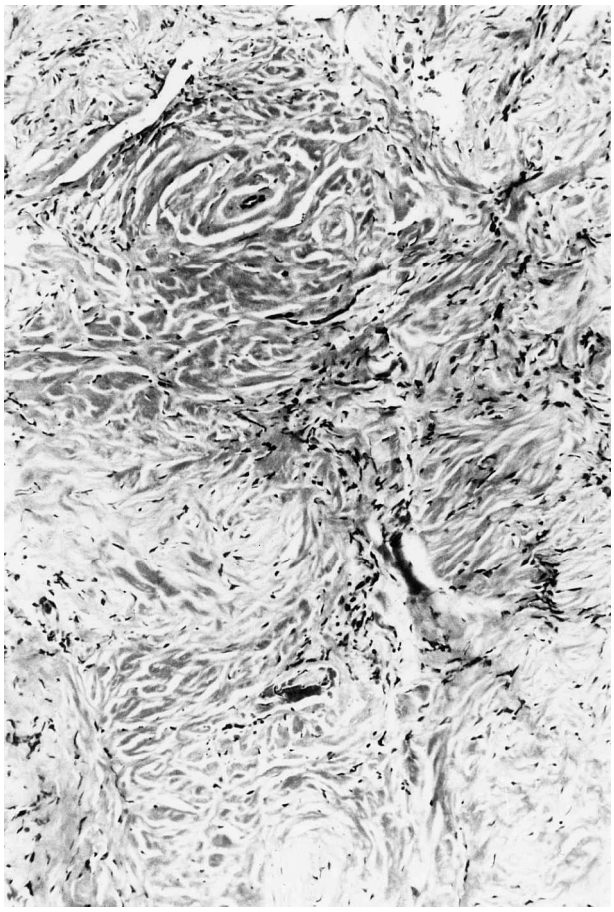

FIG. 4

Third biopsy from thickened lateral wall of nasal cavity showing typical late stage 'onion-skin' fibrosis (H & E; ×120).

Discussion

The characteristic features of specific types of inflammation, e.g. necrotizing vasculitis, intravascular thrombosis, fibrinoid necrosis of the blood vessel wall or granuloma formation, which are seen in Wegener's granulomatosis, sarcoidosis or tuberculosis, are absent in EAF.[2] It is this lack of specific features that results in a report of fibrosis by the pathologist. The characteristic concentric perivascular pattern of this fibrosis has not previously been associated with any diagnostic significance.

Holmes and Panje[4] gave the first description of an intranasal mass showing this pattern, occurring in a 49-year-old male. This was excised, and reported as the first intranasal occurrence of granuloma faciale. The patient went on to develop multiple granuloma faciale lesions on the face a few months later. In 1985 Roberts and McCann[2] described three patients, two with intranasal fibrotic masses narrowing the nasal airway, and a third with subglottic narrowing. In a postscript,[5] Roberts added a further two cases of nasal disease. All showed this characteristic angiocentric fibrotic pattern, with an abundance of eosinophils in the early lesions. All Roberts' cases were female, between 27 and 59 years fo age. One of these cases developed a patch of granuloma faciale six years later (see Table I).

Nasal disease affects the mucosa of the lateral nasal wall and septum. This helps to differentiate EAF clinically from mid-line granulomatous diseases, that tend not to affect the lateral wall. Furthermore, ulceration does not occur, and the mucosa remains smooth over the fibrotic swellings. This lack of ulceration also helps to differentiate EAF from eosinophilic ulcer of the tongue. Histologically, eosinophilic ulcer shows a different pattern of inflammation and fibrosis,[9] remains unifocal, resolves spontaneously, and does not recur.[10]

Three of the six nasal cases affected the septum alone at initial presentation.[2,5,6] These patients underwent a septoplasty, that improved symptoms initially. It would be easy to assume that a thickened, fibrotic septum had resulted from a previously undiagnosed organized septal haematoma, but a recurrence would be unlikely if an adequate resection had been performed. All cases with nasal disease eventually experienced multiple recurrences, and showed little or no response to oral or intra-lesional steroid injections,[4] except the most recent case[6] who still had a reasonable airway at 12 months following surgery.

Fageeh *et al.*[3] added the second case of EAF to affect the subglottis, in a 25-year-old female. Both cases of subglottic disease to date required tracheostomy for airway compromise initially. Later, a laryngotracheoplasty was performed and reported as being successful in both cases, but again, no follow-up information is available in either report to comment on long-term benefit.

If granuloma faciale is present, this gives a clue to the diagnosis. So far, this seems to be more likely in males. Two of the three affected males (the first case[1] and our case) had multiple facial plaques appearing within six months of the onset of nasal symptoms. The third male[6] was followed up for 18 months after onset of symptoms (one year after surgery), but had not developed granuloma faciale, nor a recurrence of his nasal obstruction, by that time. Only one female of six developed granuloma faciale as a single patch, six years after the development of nasal disease.[4] This sex difference may be related to the higher incidence of granuloma faciale in males.

All patients were otherwise healthy, and suffered no systemic symptoms. Investigations have been normal in all reported cases, including full blood count, white cell count, peripheral eosinophils, ANCA, and chest X-rays. The presence of eosinophils locally suggests a possible allergic cause, although if this were the case one might expect a better response to steroids. Only three patients were

TABLE I

SUMMARY OF ALL REPORTED CASES OF EAF

Case	Age	Sex	Region	Granuloma faciale	Paper ref:
1	49	M	Nasal (lateral)	Multiple, 6 months	Holmes and Panje,[4]
2	27	F	Nasal (lateral, septal)	No	Roberts and McCann,[2]
3	33	F	Subglottis	No	Roberts and McCann,[2]
4	59	F	Nasal (lateral, septal)	Single, 6 years	Roberts and McCann,[2]
5	25	F	Subglottis	No	Fageeh *et al.*[3]
6	54	F	Nasal (septal)	No	Roberts and McCann,[5]
7	50	F	Nasal (lateral)	No	Roberts and McCann,[5]
8	51	M	Nasal (septal)	No	Matai *et al.*[6]
9	38	M	Nasal (lateral, septal)	Multiple, 6 months	Burns present paper

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known to be 'allergic', one to penicillin, one had hay fever and another had urticaria. Our patient had psoriasis. Furthermore, there has been no evidence of generalized allergic vasculitis, and immunohistochemical stains have failed to show any evidence of immune-complex deposition around the involved small vessels.[2]

Conclusion

Both granuloma faciale and EAF appear to run a chronic, indolent, self-limitng course, usually remaining unchanged once fully developed. The histological similarity between these two conditions and their association in three of the nine cases of EAF currently described is strong evidence to support that they represent the same pathologic process.

This diagnosis should be considered when patients require multiple revisions for nasal obstruction, particularly when there is a thickened nasal septum or fibrosis of the lateral nasal wall. Cases of subglottic stenosis occurring in adults with no prior history of respiratory difficulties or intubation are difficult to account for, some of which may be caused by EAF.

Various treatments have been tried with only partial success, including surgical resection, which tends to lead to recurrence. This is also seen commonly in surgery for granuloma faciale plaques on facial skin. Laryngotracheoplasty seems to have been effective in both cases of EAF affecting the subglottis, but there is limited follow-up information available.

It should also be borne in mind that this entity is only recently described with handful of cases, and is not widely known. Many pathologists may not be able to offer a report more specific than 'fibrosis'. This has certainly been the problem up until now, but as more cases are identified and awareness is heightened, the presence of eosinophils and the characteristic pattern of fibrosis should become more widely recognized as diagnostically significant.

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References

1 Konohana A. Extrafacial granuloma faciale. *J Dermatol* 1994;**21**:680–2
2 Roberts PF, McCann BC. Eosinophilic angiocentric fibrosis of the upper respiratory tract: a mucosal variant of granuloma faciale? A report of three cases. *Histopathology* 1985;**9**:1217–25
3 Fageeh NA, Mai KT, Odell PF. Eosinophilic angiocentric fibrosis of the subglottic region of the larynx and upper trachea. *J Otolaryngol* 1996;**25**:276–8
4 Holmes DK, Panje WR. Intranasal granuloma faciale. *Am J Otolaryngol* 1983;**4**:184–6
5 Roberts PF, McCann BG. Eosinophilic angiocentric fibrosis of the upper respiratory tract: a postscript. *Histopathology* 1997;**31**:385
6 Matai V, Baer S, Barnes S, Boxer MA. Eosinophilic angiocentric fibrosis. *J Laryngol Otol* 2000;**114**:563–4
7 Anderson CR. Dapsone in granuloma faciale. *Lancet* 1975;**1**:642
8 Guill MA, Aton AK. Facial granuloma: Responsive to dapsone therapy. *Arch Dermatol* 1982;**118**:332–5
9 Tang TT, Glicklich M, Hodach AE, Oechler HW, McCreadie SR. Ulcerative eosinophilic granuloma of the tongue. A light and electron-microscopic study. *Am J Clin Path*1981;**75**:420–5
10 Movassaghi K, Goodman ML, Keith D. Ulcerative eosinophilic granuloma: a report of five new cases. (Review) *Brit J Oral Maxillofacial Surg* 1996;**34**:115–7

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