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Upper respiratory tract involvement in sarcoidosis and its management

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Upper respiratory tract involvement in sarcoidosis and its management. R. Wilson, V. Lund, M. Sweatman, I.S. Mackay, D.N. Mitchell.
ABSTRACT: Of some 750 sarcoidosis patients, 27 were found to have involvement of their nasal mucosa. Most had multisystem disease, which was usually chronic. Nasal stuffiness or blockage and crusting were the major symptoms, and were usually present at the first presentation with sarcoidosis. The larynx was involved in five cases. The Kveim test was positive in twelve of the fourteen patients in whom it was performed, serum angiotensin converting enzyme was frequently elevated and sinus radiographs were often abnormal. Topical medication improved symptoms in some patients, but the majority required systemic corticosteroids. It was possible to withdraw medication completely after seven years in only one patient. Relapse was encountered during reduction of dosage in other patients. Random biopsy of macroscopically normal nasal mucosa did not yield histological support for a diagnosis of sarcoidosis in twelve out of thirteen patients, but upper respiratory tract lymphoid tissue may contain granulomas in patients with sarcoidosis.
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The intrathoracic portion of the respiratory tract is frequently involved in sarcoidosis, and it is therefore surprising that involvement of the upper respiratory tract (URT) is only rarely seen [1–7]. However, rhinological examination is often omitted in patients with sarcoidosis [1], perhaps leading to an underestimation of the incidence.

In 1905 BOECK [8] first described granulomatous infiltration of the nasal mucosa in a case with multisystem sarcoidosis. Since that time, a number of case reports and case series have appeared in the literature, but many of these are selected patients from specialist centres, and relatively few papers have reviewed all patients presented to a general sarcoidosis clinic [2, 3]. During two years (1984–6) we questioned 2,233 patients who attended our sarcoidosis clinic about URT symptoms, and present our findings, with respect to involvement in sarcoidosis.

Methods

Clinical study

Patients with URT symptoms were selected from new referrals and those patients already attending the sarcoidosis clinic. They usually had a clinical examination, chest radiograph, Kveim test and the following blood tests: full blood count, sedimentation rate, serum calcium and serum angiotensin converting enzyme (ACE). They were then seen in the ear, nose and throat (ENT) clinic and received a full ENT examination including indirect laryngoscopy, sinus radiographs, and if abnormalities were observed, a nasal mucosal biopsy or upper respiratory tract lymphoid tissue biopsy. Patients were jointly managed between the two clinics, with regular assessment at time intervals, depending upon their clinical status.

In order to assess the incidence of histological involvement with sarcoidosis of the macroscopically normal nasal mucosa, thirteen patients had a nasal mucosal biopsy during investigation of suspected sarcoidosis (which was subsequently confirmed).

Results

Clinical study

During the study, 2,233 patients were seen in the clinic, some 750 of whom were subsequently confirmed to have sarcoidosis. Twenty-seven patients (13 men, 14 women, mean age 41 yr, range 22–63 yr) were found to have changes of the nasal mucosa suggestive of involvement with sarcoidosis. All had clinical and histological evidence of non-caseating epithelioid cell granulomatosis in other organs (table 1) to support the diagnosis. Sarcoidosis had been present for less than one year and up to 20 yr, mean age 4.4 yr. Eleven patients were British, fifteen West Indian and one Spanish.

Patients' symptoms are shown in table 2. Nasal stuffiness or blockage, and crusting were very common. When a discharge was present, it was often purulent and/or bloodstained. Nasal symptoms were present at the onset of sarcoidosis in eighteen patients, but developed later in the course of the disease in nine patients (1–9 yr after the onset of sarcoidosis, mean age 3 yr).

Changes in the nasal mucosa were most frequently

Table 1. - Other organs affected by sarcoidosis in twenty-seven patients with nasal involvement

Organ	Number of patients
Lung	18
Skin	15
Lupus pernio	7
Peripheral lymph nodes	8
Lacrimal glands	4
Bone	5
Eyes	6
Conjunctiva	3
Uveitis	3
Brain	3
Joints	3
Spleen	1

Table 2. - Clinical symptoms in twenty seven patients with nasal sarcoidosis

Symptom	Number of patients
Stuffiness or blockage	24
Crusting	17
Bloodstained discharge	10
Purulent discharge	8
Facial pain	6
Mucoid discharge	4
Stridor	3
Anosmia	1

seen over the septum and/or inferior turbinates. Pale yellowish, slightly raised excrescences were seen to project from the mucosa, were firm to touch and occasionally formed plaques. The mucosa was often hypertrophied causing airway obstruction. Surface erosion and crust formation were commonly seen. Slight bleeding occurred but prolonged epistaxis did not. Septal perforation was observed in four patients, three of whom had had submucous resection, although one patient had had no previous nasal surgery. Three other patients had had submucous resection (two patients two years previously and one patient six years previously) without subsequent perforation. In two patients there was a collapse of the bridge of the nose due to destruction of septal cartilage and in one of these nasal bone involvement was demonstrated radiographically. Hypertrophy of lymphoid tissue causing granularity of the posterior pharyngeal wall was seen in two cases. On indirect laryngoscopy, abnormalities of the larynx were seen in five patients; granularity of the inferior surface of the epiglottis in one patient; asymptomatic, inflammed and oedematous vocal cords in one patient; grossly inflammed and granular arytenoid folds causing stridor in two patients; and in one patient with chronic involvement, the whole of the larynx was inflammed and scarred with distortion of normal architecture.

Histological confirmation of nasal involvement was obtained in 21 patients; in two patients the biopsy performed was superficial and showed an inflammatory infiltrate only; in three patients a biopsy was considered inadvisable and one patient refused biopsy. In nine patients the chest radiograph was completely normal. The result of the investigations are summarized in table 3. The Kveim test was positive in all but two of the patients on which it was performed, and in both of these patients systemic prednisolone was commenced because of stridor before biopsy was taken. In six patients sinus radiographs were normal, in ten there was bilateral mucosal thickening, and in four a maxillary sinus was opaque. These changes may be due to sarcoidosis or secondary to infection, but it is noteworthy that histological confirmation of sinus mucosal involvement was sought and obtained in two patients.

The need for systemic treatment was determined by the overall activity of the sarcoidosis rather than URT symptoms alone. Two patients received no treatment. Topical medication was used as the initial treatment in nine patients. An alkaline nasal douche was used to remove crusting and secretions before betamethasone nose drops (Betnesol, Glaxo) were administered, two drops to each nostril, in the head down and forwards position [9], twice daily. Two patients achieved satisfactory control of symptoms with this regimen, four patients found it no help and three felt topical treatment was some help but required systemic medication to satisfactorily control symptoms.

Twenty-two patients received systemic prednisolone, beginning at a high dosage (30–60 mg daily), which was gradually reduced over some months to a lower dosage, usually taken on alternate days. Satisfactory control of symptoms was achieved in all patients. However, in three of these relapses of URT

Table 3. - Results of investigations performed on patients with nasal sarcoidosis at the time of presentation

Investigation	Number of patients in which test was performed	Number of patients in which test was abnormal
Kveim test	15	13
Serum angiotensin converting enzyme*	22	17
Sinus radiographs	19	13
Sedimentation rate+	18	4
Serum calcium++	19	1
Full blood count**	19	1

*53-142 (mean 74), normal range 16-52 $nmol \cdot ml^{-1} \cdot min^{-1}$; +28-91 mm in the first hour (mean 56); ++2.98, normal range 2.20-2.62 $mmol \cdot l^{-1}$, **a normochromic normocytic anaemia

symptoms occurred whilst still taking a relatively high dosage. In each case, a reduction below 20 mg of prednisolone daily led to a relapse, although in one case the use of topical medication allowed a reduction to 10 mg of prednisolone daily. Hydroxychloroquine was used successfully in one patient, in whom corticosteroids were contraindicated because of obesity.

An improved appearance of the nasal mucosa paralleled improvement in nasal symptoms, although the mucosa did not return to normal. In two patients taking oral corticosteroids, atrophic mucosal changes developed. It was only possible to withdraw systemic corticosteroids in one patient without a relapse of symptoms, either in the nose or some other manifestation of the disease. This Caucasian patient had bilateral hilar and right paratracheal lymphadenopathy, pulmonary mottling and nasal involvement. Corticosteroids were finally withdrawn after seven years, and the patient remains well one year later.

Biopsy of normal nasal mucosa

In thirteen patients with sarcoidosis but no nasal symptoms, a biopsy was taken from mucosa which appeared normal or only a little reddened. Eleven of the patients had intrathoracic involvement (four bilateral hilar lymphadenopathy alone and seven associated pulmonary involvement), one patient had neurosarcoidosis, and one patient had persistent hypercalcaemia, impaired gas transfer and a positive Kveim test. Epithelioid cell granulomas were seen in the biopsy of only one patient, and the other biopsies were either completely normal or had a scanty inflammatory cell infiltrate. The single positive histology was obtained from a patient with sarcoidosis involving the lungs, eyes, parotid glands, lacrimal glands and skin.

Involvement of adenoidal and tonsillar tissue

Two cases were seen, in whom histology of enlarged URT lymphoid tissue showed non-caseating granulomas. In the first case the adenoids were removed because of sleep apnoea, and in the second the tonsils because of recurrent sore throats. In both patients subsequent investigation revealed pulmonary sarcoidosis.

Discussion

We estimate that less than five percent of the patients attending our sarcoidosis clinic had symptomatic involvement of their URT. Other authors have suggested a similar incidence [1–7]. The nose was one of a number of organs involved in each patient, and the group in general exhibited long-standing, florid sarcoidosis. Therefore, it was not surprising to find a high proportion of West Indian patients (56%) in the nasal group, compared to our clinic population as a whole. We did not find the female predominance which is usually reported in nasal sarcoidosis [1–7].

The nasal symptoms, especially blockage and crusting, were often present at the onset of the disease, and because of their severity led to the patient seeking medical advice. A purulent nasal discharge was a major symptom in 30% of patients, and is a complaint that has not been emphasized in previous reports [1–7]. A hypertrophied nasal mucosa may have caused poor drainage and resulted in secondary bacterial infection. The findings, on examination, were as described by other authors [1–7], although the presence of polypoidal granulomatous masses [7] was not seen. Three out of six patients in our group who had had surgery, but only one out of 21 who had not, developed septal perforation. Nasal septal perforation has been reported, both after surgical procedures, notably submucous resection of the septum [2, 6, 10, 11], and after medical treatment alone [2, 6, 12]. Submucous resection should be avoided in sarcoidosis with nasal involvement.

The larynx was affected in five of our patients (19%), and the nose was also involved in each case. Involvement of the larynx alone is rare [1], and a previous study found a similar percentage of nasal sarcoid with laryngeal involvement [2]. The epiglottis is most frequently affected [12, 13], and the aryepiglottic folds, false vocal cords and ventricles are affected more frequently than the true vocal cords [6]. Generalized thickening of the mucosa can lead to airway obstruction, as in two of our patients, requiring urgent intervention with corticosteroids or even surgery. In later stages of the disease fibrosis can narrow and distort the airway.

In most of our cases (78%), nasal involvement was part of overt multisystem disease. Nasopharyngeal granulomas may be attributable to many causes, such as tuberculosis, leprosy, Wegener's granulomatosis, and cholesterol granulomas [14]. Other causes include congenital and acquired syphilis, scleroma and fungal infection [15]. Should the nose be the only evident site of granulomatous change the diagnosis may remain doubtful. In one third of our patients, the chest radiograph was normal, a much higher percentage than is usually encountered in sarcoidosis [16]. Four of the fourteen patients described by McKelvie *et al.* [1] had normal chest radiographs, but only 10% of the 53 patients described by James *et al.* [2], and none of the eleven patients described by Selroos and Niemistö [7]. Certainly the absence of an abnormal chest radiograph should not deter the diagnosis of URT sarcoidosis.

Other reports have commented upon the association between nasal mucosal involvement and skin sarcoid, especially of lupus pernio [2, 6, 17]. We found skin sarcoid in 15 of 27 patients and lupus pernio in seven. There is an association between persistent skin infiltration and changes in the bones of the hands and feet [6, 18], and we found dactylitis in four patients with skin infiltration.

As the nasal mucosa is easily accessible, it would be an attractive site to biopsy in order to substantiate a diagnosis of sarcoidosis. However, biopsy of normal

mucosa yielded a positive result in only one case with multisystem sarcoidosis, a patient with a number of other easily accessible sites to biopsy. Two previous studies have reported a similarly poor yield, one of the six cases reported by WEISS [19], and none of the seven by SILTZBACH and BLAUGRUND [17]. In two cases reported here, lymphoid tissue removed for other reasons was found to contain granulomas, and caused investigation which led to a diagnosis of sarcoidosis. This confirms earlier observations that URT lymphoid tissue is a rich source of granulomas in patients with sarcoidosis [15, 20, 21].

Two patients have as yet not required treatment, however both have only recently been presented to the clinic. The majority of patients required systemic treatment of their sarcoidosis over a prolonged period, and this has been successfully withdrawn in only one patient. URT symptoms were controlled in every case. Others have reported a less favourable outcome [1, 22], but it is likely that in these cases either dosage or duration of treatment was not optimal. If nasal symptoms relapse whilst the patient is still taking a relatively high dosage of corticosteroid, local treatment may be used to allow a further reduction of oral medication. For example, local injections of a depot preparation of corticosteroid into thickened tissue have been found effective both in the nose and larynx [1]. Topical medication has been found useful by some authors [2, 11, 23], but ineffective by others. Benefit was found in five of our nine patients, and in one other patient it allowed oral medication to be reduced.

In summary, nasal involvement is quite rare, it generally occurs in patients with chronic multisystem sarcoidosis, does not usually occur without macroscopic changes in the mucosa, and causes severe symptoms. Biopsy of macroscopically normal nasal mucosa would not appear to be a useful investigation to support the diagnosis of sarcoidosis. Patients may be helped by topical therapy, but the majority will require oral corticosteroids to control either nasal symptoms or some other aspect of their disease.

References

1. McKelvie P, Gresson C, Pokhrel RP, Jackson P. – Sarcoidosis of the upper air passages. *Br J Dis Chest*, 1968, 62, 200–206.
2. James DG, Barker S, Jash D, MacKinnon DM, Carstairs LS. Sarcoidosis of the upper respiratory tract (SURT). *J Laryngol Otol*, 1982, 96, 711–718.
3. McCaffrey TV, McDonald TJ. - Sarcoidosis of the nose and paranasal sinuses. *Laryngoscope*, 1983, 93, 1281–1284.
4. Reisner D. Boeck's sarcoid and systemic sarcoidosis: a study of 35 cases. *Am Rev Tuberc*, 1944, 49, 289–307 and 437 462.
5. Kämpfer R. – Über extrapulmonale organmanifestationen des morbus Boeck unter besonderer Beruchsichtigung der Schleimhaut der oberen Luftwege. *Prax Pneumol*, 1964, 18, 204–217.
6. Neville E, Mills RGS, Josh DK, MacKinnon DM, Carstairs LS, Geraint James D. – Sarcoidosis of the upper respiratory tract and its association with lupus pernio. *Thorax*, 1976, 31, 660–664.
7. Selroos O, Niemistö M. – Sarcoidosis of the nose. Including a report on a patient with large sarcoid polypi of the nasal mucosa. *Scand J Respir Dis*, 1977, 58, 57–62.
8. Boeck C. – Forgestzte untersuchugen über des multiple benign Sarkoid. *Arch Dermatol Syph, Wien*, 1905, 73, 301–332.
9. Chalton R, MacKay I, Wilson R, Cole P. – Double-blind, placebo controlled trial of betamethasone nasal drops for nasal polyposis. *Br Med J*, 1985, 291, 788.
10. Allison JR, Mikell PV. – Sarcoid associated with tuberculosis of the larynx; report of case. *Arch Dermatol Syphilol, Chicago*, 1932, 25, 334–343.
11. Hammond BL, Kataria YP. - Nasal sarcoidosis with septal perforation. *J Otolaryngol*, 1980, 9, 31–34.
12. Barmwater K. – Über Boeck's Sarkoid auf den schleimnäuten. *Hals-Nas U Ohrenarz*, 1936, 27, 259–264.
13. Lindsay JR, Pearlman H. – Sarcoidosis of the upper respiratory tract. *Ann Otol*, 1951, 60, 549–566.
14. Coup AJ, Hopper IP. - Granulomatous lesions in nasal biopsies. *Histopathology*, 1980, 4, 293–308.
15. Wilson R, Sweatman M, MacKay IS, Mitchell DN. – Adenoidal tissue as an aid to the diagnosis of sarcoidosis in childhood. *Thorax*, 1986, 41, 66–67.
16. Dunbar RD. – Sarcoidosis and its radiological manifestations. *CRC Crit Rev Diag Imag*, 1978, 11, 185–221.
17. Siltzbach LE, Blaugrund SM. – Sarcoidosis of the mucosa of the respiratory tract. Trans 43rd Ann Meet Am Broncho-esophagol Assoc, 1963, 25.
18. James DG. – Dermatological aspects of sarcoidosis. *Q J Med*, 1959, 28, 109–124.
19. Weiss JA. – Sarcoidosis in otolaryngology: report of 11 cases. *Laryngoscope*, 1960, 70, 1351–1398.
20. Schaumann J. – Sur le lupus pernio. Mémoire presénté en Novembre 1914 à la Societé Fraocaise de Dermatologie et de Syphiligraphie pour le Prix Zambaco. Stockholm, 1934.
21. Gravesen PB. – Lymphogranulomatosis benigna. Odense: I Kommission hos Andelsbogtrykkeriet, 1942.
22. Dowie LN. – A short review of sarcoidosis with a report of three cases with involvement of the nasal mucosa. *J Laryngol Otol*, 1964, 78, 931–936.
23. Maillard AA, Goepfert H. - Nasal and paranasal sarcoidosis. *Arch Otolaryngol*, 1978, 104, 197–201.

RÉSUMÉ: Sur 750 patients atteints de sarcoïdose, 27 ont une atteinte de la muqueuse nasale. La plupart avait une maladie multisystémique habituellement chronique. Un enchifrènement, une obstruction nasale et des croûtes étaient les symptômes principaux et étaient habituellement présents lors du diagnostic de sarcoïdose. Il y a eu 5 cas d'atteinte laryngée. Le test de Kveim était positif chez 12 des 14 patients chez lesquels il a été exécuté. L'enzyme de conversion de l'angiotensine était fréquemment augmenté et les radiographies des sinus étaient souvent anormales. Une médication locale a amélioré les symptômes chez certains patients mais la majorité d'entre eux ont eu besoin de cortico-stéroïdes systémiques. Ce n'est que chez un seul patient que l'on a pu arrêter la médication complètement après 7 années. Chez les autres, on a observé une rechute au cours de la diminution du dosage. Une biopsie aveugle d'une muqueuse nasale macroscopiquement normale n'a fourni aucun argument histologique pour le diagnostic de sarcoïdose chez 12 des 13 patients mais les tissus lymphoïdes des voies respiratoires supérieures peuvent contenir des granulomes chez les patients atteints de sarcoïdose.