Rhinoscleroma: a clinicopathological study from the Gulf region

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ABSTRACT

Introduction: Rhinoscleroma is a chronic progressive inflammatory disease of the upper respiratory tract. We report a clinicopathological series from the Gulf region.

Methods: The clinical and pathological features of patients diagnosed with rhinoscleroma at three main hospitals in Saudi Arabia and Bahrain over a 20-year period are presented. Archived glass slides and paraffin blocks from these patients were retrieved from the pathology files for review. Special stains were performed whenever indicated. Biopsy material and clinical data from 25 patients formed the basis of this study.

Results: Most of the patients were young females with a median age of 24 years. The nose was involved in all cases with frequent extension to other parts of the upper respiratory tract. The provisional clinical diagnoses included syphilis, midline granuloma and malignancy. The histological differential diagnoses included leprosy, malakoplakia and metastatic renal cell carcinoma.

Conclusion: Rhinoscleroma is rare in Saudi Arabia and Bahrain. Awareness of possible clinical presentations and early diagnosis will significantly reduce the morbidity caused by this disease.

Keywords: *Klebsiella rhinoscleromatis*, nasal inflammatory disease, nose, respiratory tract infection, rhinoscleroma, upper respiratory tract

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INTRODUCTION

Rhinoscleroma is a chronic progressive inflammatory disease of the upper respiratory tract, affecting mainly the nasal passages.[1–3] The name rhinoscleroma was first used in 1870 by Von Hebra and Kaposi when describing a lesion in the nose which they labelled as a form of sarcoma.[4] In 1877, Mikulicz described the histological features of this disease in detail and established its non-neoplastic inflammatory nature.[5] Von Frisch identified the causative agent of this lesion in 1882 as a Gram-negative coccobacillus, now known as *Klebsiella rhinoscleromatis*.[6,7] Rhinoscleroma affects most parts of the respiratory tract. It usually starts in the nose, which is affected in most cases, and then spreads to other parts such as the pharynx, which may be involved in about 50% of cases.[8] Other affected sites include the eustachian tube,[9] maxillary antrum,[10] oral cavity,[11] larynx,[12] orbit,[13] trachea and bronchi.[14,15] Extension to the adjacent skin has also been reported.[16]

Rhinoscleroma is usually divided clinically and pathologically into three stages, namely: the catarrhal (or atrophic) stage, the proliferative (or granulomatous) stage, and the fibrotic (or sclerotic) stage.[17] The histological findings are more characteristic and diagnostic in the proliferative stage. The catarrhal stage has no specific features that a pathologist can recognise. If clinically suspected, a nasal swab for culture to isolate the microorganisms would confirm the diagnosis.[18] Rhinoscleroma is widely but unevenly distributed throughout the world, often occurring in focal specific geographical areas. A large endemic area is present in Eastern Europe, extending into the Ukraine and around the Black and Caspian Seas.[19] The disease had been reported in many countries in the Middle East, tropical Africa, India, Southeast Asia, Central and South America.[20–25] There are only two previous case reports from Saudi Arabia.[26,27] There have been no previous cases reported in Bahrain. This prompted us to report our experience on the clinicopathological aspects of this disease in those two countries in the Gulf region.

METHODS

All cases diagnosed as rhinoscleroma or chronic nasal inflammation of uncertain aetiology over the period 1980–2005 at three main hospitals (King Fahad in the Eastern Province of Saudi Arabia, Salmaniya Medical

Table I. Clinical data of the 25 cases.

Case no.	Age/gender	Clinical findings
1	60 M	Depressed nose, nodule left zygoma, crusting nasopharynx.*
2	23 F	Hoarseness of voice, bilateral nasal masses, subglottic mass.
3	21 F	Nasal obstruction, bilateral polypoid nasal masses, subglottic mass.
4	17 M	Epistaxis, bilateral nasal nodules, atrophic nasal mucosa, crusting nasopharynx.
5	50 F	Hoarseness of voice, nodule right nasal septum, subglottic mass.
6	52 F	Difficulty in breathing, bilateral nasal crusts, subglottic mass and stenosis.
7	18 F	Ulcerating mass in palate, extension to nasopharynx, bilateral nasal masses and otitis media.**
8	23 M	Mass right nostril, tracheal polyp, opacities in ethmodial air cells, subglottic ulcerative lesion.***
9	55 F	Fleshy mass right nasal cavity, extension to nasopharynx. X-ray opaque maxillary sinuses.**
10	15 M	Epistaxis, bilateral nasal obstruction due to fleshy masses, subglottic mass.
11	25 F	Complete nasal block due to a mass infiltrating both nasal cavities.
12	40 F	Both nostrils completely blocked with whitish soft tissue masses.
13	12 F	Infiltration and crusts in both nostrils, extension to nasopharynx.
14	36 F	Fleshy mass left nostril, subglottic mass.
15	19 M	Swelling lateral sides of both nasal vestibules.
16	20 M	Crusting of nasal activities and subglottic mass.
17	52 F	Friable mass septum and lateral walls of both nostrils.
18	66 M	Nasal obstruction, markedly hypertrophied and polypoid inferior turbinate.****
19	19 F	Fleshy masses blocking nasal cavities, mass in palate.
20	22 F	Hoarseness of voice, granulation and crusts in both nostrils, subglottic mass.
21	18 F	Epistaxis, ulcerating masses in both nostrils and palate.***
22	50 F	Epistaxis, ulcerating masses in both nostrils and palate.***
23	28 F	Nasal obstruction, whitish fleshy mass left nostril, otitis media nasopharyngeal thickening.
24	24 F	Extensive lesion in left nostril, opaque left maxillary sinus by X-ray, subglottic fleshy nodule.
25	25 F	Ulcerating mass both nostrils, destruction of septum. Similar mass in palate, subglottic nodules.

Provisional clinical diagnosis: *syphilis; **midline granuloma; ***malignancy; ****vasomotor rhinitis

Complex in Bahrain, and Bahrain Defence Force) were investigated. Histological slides were re-examined and in those considered to have rhinoscleroma, further sections were cut and stained by periodic acid schiff, Giemsa and Warthin-Starry techniques. Histologically, all cases were classified into one of the three morphological stages of rhinoscleroma, namely: catarrhal, proliferative (granulomatous) and fibrotic (sclerotic).

RESULTS

A total of 29 cases met the criteria of rhinoscleroma. Four cases were excluded from the study due to lack of clinical information. 20 of the patients were Saudis and five were Bahrainis. There were 18 females and seven males. Patients' ages ranged from 12 to 66 years, with a median of 24 years. The provisional clinical diagnoses and findings are listed in Table I. Histologically, 19 of the cases were at the proliferative (granulomatous) stage and six were at the fibrotic (sclerotic) stage. None of the cases were at the catarrhal (atrophic) stage.

The histological features were most characteristic in the proliferative stage. The epithelium showed various degrees of hyperplasia and the underlying stroma contained a mixed inflammatory infiltrate consisting of foamy histiocytes (Mikulicz cells), plasma cells, lymphocytes, and polymorphs. Fibrosis was either minimal or absent (Fig. 1). Mikulicz cells had small pyknotic centrally- or peripherally-located nuclei. Some contained single or multiple cytoplasmic vacuoles. The cells were usually arranged in sheets. Multinucleated cells with the same nucleo-cytoplasmic characteristics of Mikulicz cells were sometimes seen (Fig. 2). Few cases showed groups of histiocytes with abundant eosinophilic cytoplasm. The plasma cells were more prominent than lymphocytes. They were distributed evenly with a tendency to aggregate around blood vessels. Russell bodies were easily seen mostly intracellularly. Cells with eccentric nuclei and voluminous, eosinophilic cytoplasm, the so-called Unna cells, were seen in abundance in three cases (Fig. 3). Neutrophil polymorphs were present in all cases, mostly forming microabscesses. The stroma was vascular, the vessels were mostly small capillaries with

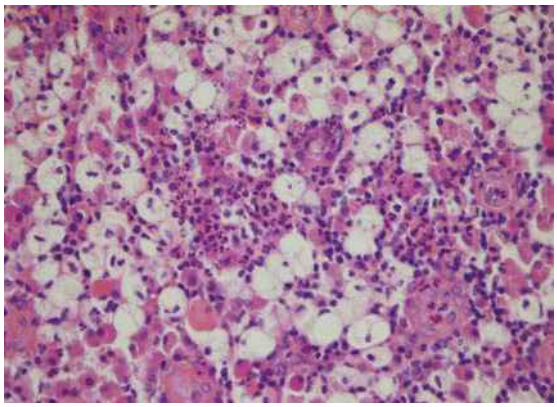

Fig. 1 Photomicrograph shows the typical mixed inflammatory cell infiltrate of rhinoscleroma consisting of neutrophils, lymphocytes, plasma cells and Mikulicz cells (Haemotoxylin & eosin, × 400).

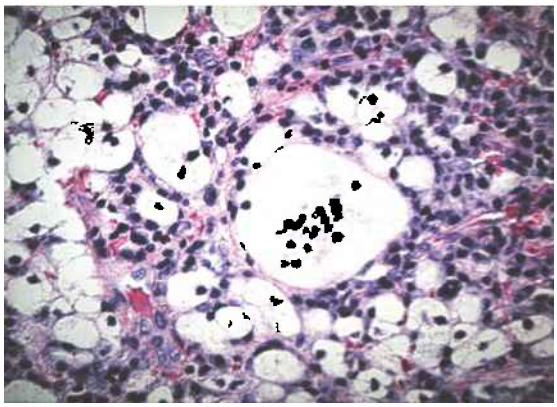

Fig. 2 Photomicrograph shows occasional multinucleated giant cells with foamy cytoplasm and small nuclei in a background of plasma cells, neutrophils and Mikulicz cells (Haemotoxylin & eosin, × 400).

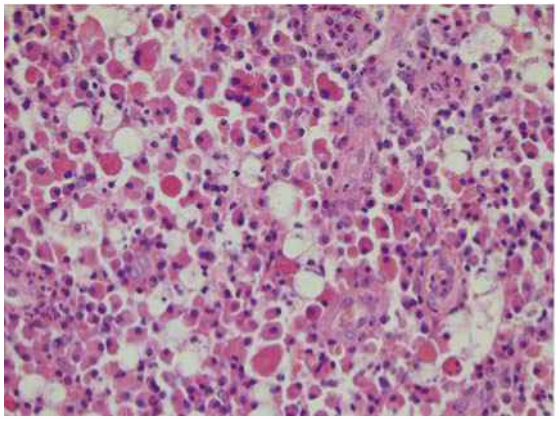

Fig. 3 Photomicrograph shows plasma cells with voluminous cytoplasm and eccentric nuclei, the so-called Unna cells (Haemotoxylin & eosin, × 400).

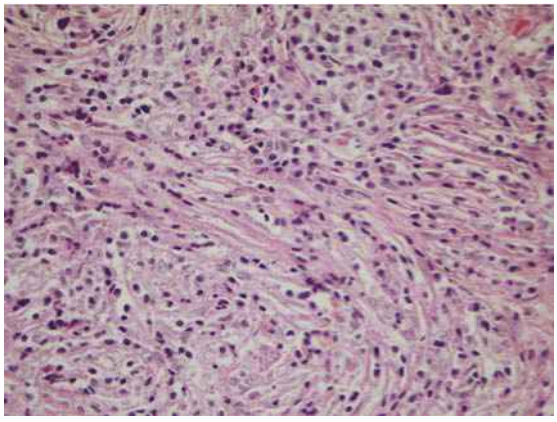

Fig. 4 Photomicrograph shows fibrotic stage with bands of fibrosis and scanty Mikulicz cells (Haemotoxylin & eosin, × 400).

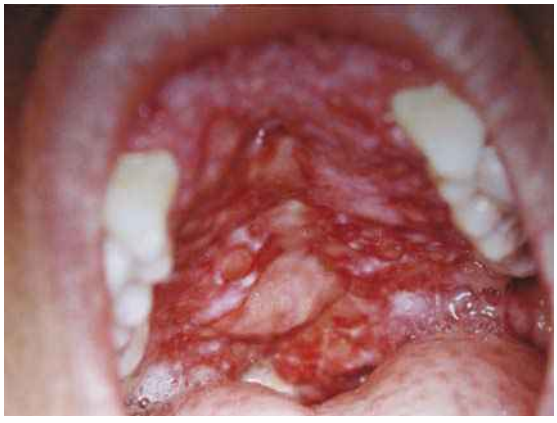

Fig. 5 Clinical photograph shows rhinoscleroma in the oral cavity involving the soft and hard palates.

prominent endothelial lining.

In the fibrotic (sclerotic) stage, there was prominent fibrosis with hyalinised collagen separating the inflammatory cells. Both Mikulicz cells and neutrophils were scanty. A moderate lymphoplasmacytic component was present. Vascularity was markedly diminished in this stage (Fig. 4). Intracellular short bacilli were identified in 19 of the 25 cases by the use of special stains. Although the microorganisms were sometimes easily seen in the haematoxylin and eosin-stained slides, they were best demonstrated using the Warthin-Starry stain.

DISCUSSION

Rhinoscleroma is a disease of the young, and females are more frequently affected than males. 13 of our cases were below the age of 25 years, with a median of 24 years. 18 were females and seven were males, with a female to male ratio of 2.5:1. The nose was involved in all cases. Although in our series, 11 cases showed laryngeal involvement, the nasopharynx was involved in six cases only. The low incidence of nasopharyngeal involvement in this series is probably due to difficulty of direct visualisation as the nasal cavities were usually blocked by crust and inflammatory masses.

Clinically, the differential diagnoses include all ulcerative and destructive lesions of the upper respiratory

tract and oral cavity.[28] Cases 7 and 9 were diagnosed clinically as midline granuloma. Case 7 showed, in addition to the upper respiratory tract lesions, an ulcerative mass in the oral cavity (Fig. 5). Case 1 was diagnosed as syphilis on account of a depressed nose, destruction of soft palate and a positive serology for syphilis. A false-positive serology for syphilis was reported previously.[29] Despite the prevalence of cutaneous leishmaniasis in this geographical zone, it was not confused with rhinoscleroma due to awareness of the former lesion. Histologically, 19 out of 25 cases (76%) in our series were classified as proliferative (or granulomatous) stage rhinoscleroma. The diagnosis can easily be made at this stage, as Mikulicz cells are easily seen, usually in aggregates or sheets in addition to the other cellular components.

The histological differential diagnoses of proliferative stage rhinoscleroma include lepromatous leprosy, malakoplakia, granular cell tumour and metastatic renal cell carcinoma. The polymorphonuclear microabscesses and vascular proliferation are not features of leprosy. Furthermore, *Mycobacterium leprae* can easily be demonstrated by the Ziel-Neelsen stain. The Mikulicz cell is a histiocyte, as demonstrated by light microscopy, electron microscopy and enzyme histochemistry.[30,31] It probably starts as a histiocyte with eosinphilic cytoplasm and later becomes vacuolated. If the cells with eosinophilic cytoplasm predominate, malakoplakia and granular cell tumour enter into the differential diagnoses. The rarity of malakoplakia at this site and the absence of Michaelis-Gutmann bodies will argue against the diagnosis. Granular cell tumour can be easily ruled out by the use of S100 protein immunostain. When Mikulicz cells are arranged in small groups, they might superficially resemble renal cell carcinoma.

Klebsiella rhinoscleromatis can be demonstrated in haematoxylin and eosin-stained sections and by other appropriate stains. We found Warthin-Starry the most helpful type of stain as it stained the organisms black, leading to easier detection. An explanation for the chronicity of rhinoscleroma probably lies in the type of tissue reaction induced, specifically in relation to the distribution of T-lymphocytes. For effective epithelioid cell transformation (and granuloma formation), T-cell segregation is a prerequisite, i.e. T4 and T8 cells should be separated and not admixed. In conditions such as rhinoscleroma and lepromatous leprosy, T-cell subtypes are diffusely distributed and freely admixed. As a consequence, there is ineffective epithelioid cell transformation and impaired granuloma formation, leading to inadequate elimination of the causative organism.[32]

REFRENCES

1. Hart CA, Rao SK. Rhinoscleroma. J Med Microbiol 2000; 49:395-6.
2. Lenis A, Ruff T, Diaz JA, Ghandour EG. Rhinoscleroma. South Med J 2001; 81:1580-2.
3. Omeroglu A, Weisenberg E, Baim HM, Rhone DP. Supraglottic granulomas in a young central American man. Arch Pathol Lab Med 2001; 125:157-8.
4. Von Hebra F. Rhinoscleroma: a new and unusual lesion at the nose in addition to histological findings by Dr M Khon. Wien Med Wochenschr 1870; 20:1-5.
5. Van Renterghem L, Joly B, Cabaret V, et al. Scleroma and rhinoscleroma, a diagnostic difficulty: review of literature with proposal of new observation. Cahier d'Otol Rhinol Laryngol 1993; 10:419-24.
6. Von Frisch A. Aetiology of rhinosclerosis. Wien Med Wochenschr 1882; 32:969-72.
7. Schwartz DA, Geyer SJ. Klebsiella and rhinoscleroma. In: Cornor DH, Chandler FW, Schwartz DA, et al, eds. Pathology of Infectious Diseases. New York: McGraw-Hill Professional, 1998:589-95.
8. Gamea AM. Role of endoscopy in diagnosing scleroma in its uncommon sites. J Laryngol Otol 1990; 104:619-21.
9. Soni NK, Hemani DD. Scleroma of the eustachian tube: salpingoscleroma. J Laryngol Otol 1994; 108:944-6.
10. Soni NK. Antroscopy in rhinoscleroma. J Laryngol Otol 1992; 106:697-8.
11. Carter TD. A brief discussion on scleroma (rhinoscleroma) with a report on some cases in Rhodesia. Cent Afr Med 1996; 12:159-61.
12. Iyengar P, Laughlin S, Keshavjee S, Chamberlain DW. Rhinoscleroma of the larynx. Histopathology 2005; 47:224-5.
13. Lubin JR, Jallow SE, Wilson WR, Grove AS, Albert DM. Rhinoscleroma with exophthalmos: a case report. Br J Ophthalmol 1981; 65:14-7.
14. Alfaro-Monge JM, Fernandez-Espinosa J, Soda-Merhy A. Scleroma of the lower respiratory tract: case report and review of literature. J Laryngol Otol 1994; 108:161-3.
15. Soni NK. Scleroma of the lower respiratory tract: a bronchoscopic study. J Laryngol Otol 1994; 108:484-5.
16. Diallo BK, Diallo M, Kane A, et al. [A new case of rhinoscleroma with skin extension]. Rev Laryngol Otol (Bord) 2004; 125:253-5. French.
17. Andraca R, Edson RS, Kern EB. Rhinoscleroma: a growing concern in the United States? Mayo Clinic experience. Mayo Clin Proc 1993; 68:1151-7.
18. Meyer PR, Shum TK, Becker TS, Taylor CR. Scleroma (Rhinoscleroma). A histologic immunohistochemical study with bacteriologic correlates. Arch Pathol Lab Med 1983; 107:377-83.
19. Hyams VJ. Rhinoscleroma. In: Binford CH, Cornor DH, eds. Pathology of Tropical and Extraordinary Diseases. Washington DC: Armed Forces Institute of Pathology, 1973:187-9.
20. Alavi K, Kohout E, Dutz W. Two cases of scleroma in Iran. J Clin Pathol 1971; 24:360-2.
21. Muzyka MM, Gubina KM. Problems of the epidemiology of scleroma. I. Geographical distribution of scleroma. J Hyg Epidemiol Microbiol Immunol 1971;15:233-42.
22. Okoth-Olende CA, Bjerregaard B. Scleroma in Africa: a review of cases from Kenya. East Afr Med J 1990; 67:231-6.
23. Wabinga HR, Wamukota W, Mugerwa JW. Scleroma in Uganda: a review of 85 cases. East Afr Med J 1993; 70:186-8.
24. Kim NR, Han J, Kwon TY. Nasal rhinoscleroma in a nonendemic area: a case report. J Korean Med Sci 2003; 18:455-8.
25. Salima K, Samia S, Mounir T, et al. [Rhinoscleroma: a report of 2 cases] Tunis Med 2005; 83:586-71. French.
26. Akhtar M, McArthur PD, Ashraf Ali M. Rhinoscleroma: ultrastructural study of a case before and after treatment. King Faisal Specialist Hospital Med J 1982; 2:23-30.
27. Maglad S, Satir AA. Rhinoscleroma – case report. East Afr Med J 1985; 62:420-2.
28. Shaw HJ, Martin H. Rhinoscleroma – a clinical perspective. J Laryngol Otol 1961; 75:1011-39.
29. Ryeyes E. Rhinoscleroma: observations based on a study of two hundred cases. Arch Dermatol Syphilis 1946; 54:827-33.
30. Hoffman EO, Loose LD, Harkin JC. The Mikulicz cell in rhinoscleroma: light, fluorescent and electron microscopic study. Acta Laryngol 1981; 91:595-604.
31. Gumprecht TF, Nichols PW, Meyer PR. Identification of rhinoscleroma by immunoperoxidase technique. Laryngoscope 1983; 93:627-9.
32. Modlin RL, Hofman FM, Meyer PR, et al. In situ demonstration of T lymphocyte subsets in granulomatous inflammation: leprosy, rhinoscleroma and sarcoidosis. Clin Exp Immunol 1983; 51:430-8.