ABSTRACT

Aim: Rhinoscleroma is a rare disease hence the diagnosis can be difficult and delayed because of its clinical polymorphism. This article aims to review the entity and depict one of the treatment modalities for the same.

BACKGROUND: Rhinoscleroma is a chronic granulomatous, slowly progressive disease affecting the nose and other respiratory tract structures, endemic in some areas of southern and central Europe, Africa and the USA. The first evidence of patients with scleroma was in a Mayan Indian terracotta head dated between 300 and 600 AD depicting the typical nasal proliferative lesions of this disease. Hebra and Kohn in 1870 first described the condition as “rhinoscleroma” and considered it a neoplastic growth. Its inflammatory nature was first suggested by Gerber. Mikulicz, in 1877, described the typical foamy cells identified in biopsy specimens. Later in 1882 Von Frisch isolated K. Rhinoscleromatis. At the International Congress of Otolaryngology in 1932, Belinoff proposed the term scleroma respiratorium for this condition because not only the nose and upper respiratory airways are involved, but the lower respiratory tract also gets affected.

CASE DESCRIPTION: The clinical and pathological features of patients diagnosed with rhinoscleroma are presented. A 45 years old female patient with a chief complaint of dull localized pain which aggravated during meals and subsided after medication. The swelling had gradually increased in size on right side of the face. She also had a complaint of watery nasal discharge associated with common cold along with nasal obstruction and difficulty in breathing during lying down position. Post histopathological confirmation of our diagnosis, we performed debulking of the lesion intraorally and Ciprofloxacin 750 mg twice daily for 6 weeks along with the Augmentin 625mg thrice daily for 4 weeks and Metrogyl 400 mg thrice daily were given for 1 week, all from the day of debulking.

Conclusion: A combination of debulking and antibiotic therapy apparently produced satisfactory results for our patient. A study comparing this method of treatment with other treatment methods, such as the use of pharmacotherapy alone in such patients, with a longer follow up would be of considerable interest.

Clinical Significance: A combination of debulking and antibiotic therapy can be taken into consideration as surgery results in immediate symptomatic relief and decrease the microbial load thereby increasing the sensitivity of the pharmacological therapy.

Keywords: Rhinoscleroma, Klebsiella Rhinoscleromatis, Nasal Inflammatory Disease, Chronic Granulomatous Infection, Medical and Surgical treatment.


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mobility in all the teeth of the side involved was observed. (Fig.1b) Investigations ordered included routine blood investigations, histopathology and radiological imaging in the form of an orthopantomograph. (Fig.2)

After taking a specimen for histopathology, the patient was started with Augmentin 625mg one tab thrice daily and Ibuprofen 400 mg one tab thrice daily for 5 days. The histopathological findings were section showing few bone trabeculae and fibrous connective tissue. Fibrous connective tissue had infiltration by large number of lymphocytes, plasma cells and mononuclear’s. Several multinucleated giant cells were seen. In between the inflammatory exudates, there were masses of histiocytes and macrophages with abundant clear or vacuolated cytoplasm. These cells had ovoid vesicular nuclei. Small foci of necrosis were also seen confirming the diagnosis of Rhinoscleroma. (Fig.3)

Post histopathological confirmation of our diagnosis, we performed debulking of the lesion intraorally under conscious sedation and local anesthesia. (Fig.4 & 5) Primary closure was done using 3-0 Vicryl sutures. (Fig.6) Ciprofloxacin 750 mg twice daily for 6 weeks along with the Augmentin 625mg thrice daily for 4 weeks and Metrogyl 400 mg thrice daily were given for 1
week, all from the day of debulking.

Post treatment, the patient was followed up for a period of 2 months during which, the swelling continued receding (Fig. 7.1a and 7.1b) and after this the patient was lost to follow up.

DISCUSSION

Rhinoscleroma is a chronic granulomatous, slowly progressive infection that affects the nose and other respiratory tract structures which is endemic in some areas of southern and central Europe, Africa and the USA[7]. Migration of population currently responsible for more and more sporadic spread of cases in regions spared before then by this disease[8]. It was first described in 1870 by dermatologist Ferdinando Von Hebra and laterally named respiratory scleroma, which emphasizes involvement of upper airways[9]. Unusual sites are the middle ear[10] and the lower respiratory tract[11]. Other affected organs include the paranasal sinuses[12], eustachian tubes[13], orbital tissues[14], skin close to the affected mucosas[15], and the brain[16]. It occurs frequently in the nasal fossa, eventually extending itself to the larynx, the rhinopharynx, the mouth and the paranasal sinuses; the lips, trachea, and bronchi may also be affected to a lesser degree. Our patient had an involvement of right Maxillary Sinus, swelling on the right middle and lower third of face (extending from the infraorbital margin to the lower border of the mandible and ala of the nose to the zygoma.), nasal obstruction and obliteration of the right maxillary vestibule in relation to the 1st & 2nd premolars.

Several predisposing factors such as living under conditions of poor hygiene and nutritional deficiencies have been described and are apparently necessary for transmission of the disease[17]. Our patient belongs to the lower socio-economic strata whose oral (and general) hygiene was just satisfactory and nutritional status moderate.

The infection is due to Klebsiella Rhinoscleromatis, first described by Von Frisch in 1882[18]. A capsule Gram-negative rod-shaped bacteria, 2.5 micrometer in length which, along with K. Pneumoniae, K. Ozanae, K. Oxytoca and others, belong to the family Enterobacteriaceae. K. Rhinoscleromatis has a complex capsule cover and many fimbriae, which are responsible for the microorganism’s ability to adhere to host cells[19].

Humans are the only identified host of K. Rhinoscleromatis[20]. Rhinoscleroma is minimally contagious and requires extended and close contact for spread. Transmission results most probably through large amount of contaminated airborne particles, which are expelled by coughing and sneezing, or by contact with contaminated fomites[21]. The infection starts in the nose where the squamous epithelium of the vestibule abuts on the columnar ciliated epithelium of the nasal cavity. Similarly, infection in the glottis begins where the squamous epithelium of the vocal cord merges with the respiratory type of the subglottic region of the larynx. The disease often spreads to the maxillary antrum; it may also involve the ethmoidal sinuses, a site often overlooked[22]. Most of these changes contributing to the chronicity of Rhinoscleroma occurs in the subepithelial tissue during proliferative phase of the disease. These critical changes include factors leading to histiocytes transformation into Mikulicz cells, the inability of these cells to uniformly destroy Klebsiella, their rupture liberating viable Klebsiella and the intrinsic resistance of the pathogen microbe[23]. The presence of K. Rhinoscleromatis is not enough for the development of the disease; since contact for many years of a patient with healthy individuals may not necessarily bring about the infection in the latter. This has led to the suggestion that susceptibility of the host is important to develop the disease[24]. Cellular immunity is probably impaired in infected people. Peripherally, a reduction in CD4+ lymphocytes and a significant elevation in the numbers of CD8+ lymphocytes, so the CD4/CD8 ratio into the lesion is decreased, possibly inducing a diminished or altered T-cell response[25]. Humoral immunity response does not control the infection, probably due to the intracellular nature and copious mucin coat of the bacteria, or due to the non specific nature antibody of the response of the host. Whether these defects are acquired after infection or already present in predisposed individuals remains uncertain[26].

After mucosal invasion by the bacteria, the acute inflammatory response is inefficient, the neutrophils phagocitize Klebsiella, but appear to die too soon, before digestion finishes, releasing viable bacteria. Histiocytes continue with phagocytosis, and their phagosomes undergo massive dilatation. They thus
Rhinoscleromatis, and eventually rupture, releasing the bacteria into the interstitium[23]. The altered proportion of CD4+ and CD8+ lymphocytes in the lesion may produce disabled macrophages, allowing bacterial multiplication inside them and an ineffectual delayed type

**Hypersensitivity Response[27]:** The disease presents with mean age of occurrence as 15 and 35 years of age[28] and is more frequent in women than in men with female: male ratio of 13:1[29]. As can be expected from this sex predilection, our patient was female albeit 45 years of age. Terry S. Becker, in a study, reported that usually the patient complains of symptoms similar to the common cold with rhinorrhea, headache, variable dyspnea, and fetid odor[30]. Our patient displayed a similar clinical picture besides a complaint of dull localized pain.

**Clinically, four stages may be recognized[31]:**

1. **The catarrhal stage** characterized by mucopurulent nasal discharge.
2. **The granulomatous stage,** when several small nodules are present in the nose, larynx, pharynx or bronchi.
3. **The atrophic stage.**
4. **The sclerotic stage** which lead to crusting and partial to total obstruction of the nasal and airway passages.

During the catarrhal stage there are foul smelling purulent nasal discharges and nasal obstruction; physical examination may demonstrate atrophy and crusting of the nasal mucosa or hyperemia and exudates in the respiratory tract mucosa. Our patient appeared to be in the first stage mentioned above because although there was a complaint of nasal obstruction and discharge, no nodules were detected on examination. The granulomatous stage is characterized by epistaxis, nasal deformity, hoarseness, anosmia and anesthesia of the soft palate; physical examination may find a bluish red and rubbery granulomatous lesion which evolves into a pale hard granulomatous mass. Sclerotic stage symptoms are similar to the previous stage; on physical examination the granulomatous lesions are surrounded by dense fibrotic tissue. Most patients are diagnosed in the granulomatous stage, because they are more symptomatic and other organs besides the nose may be involved[32]. Our patient complained of dyspnea only while lying down thus indicating partial obstruction.

Miller et al. reviewed the literature and reported that the initial symptom is nasal obstruction in 94% of cases followed by nasal deformity in 32%[33]. Interestingly, 10% of the lesions started as a swelling of the upper lip. Although our patient did not complain of nasal deformity or upper lip swelling, her right maxillary vestibule was obliterated in the region of the premolars. The same study showed that the palate is affected in 31% of cases, and the soft palate more frequently than the hard palate.

The upper lip ranks fifth (12% of cases). When the hard palate is affected, there is bone destruction produced by a progressive nodular infiltrate[34]. The nodular infiltration in the soft palate extends to the tonsillar fossa and oropharynx. Eventually, scarring can lead to forward tilting of the uvula and fibrous stenosis[35]. A report from the United States showed that 13 of 22 patients with Rhinoscleroma had laryngotracheal scleroma (LTS); nine had subglottic stenosis and/or glottic stenosis, and only 2 out of 22 cases had tracheal involvement limited to the first two tracheal rings[36]. Gaafar[37] described the endoscopic pattern of LTS in 11 patients; laryngeal involvement was diffuse and localized, tracheal lesions appeared granular or atrophic, and bronchial involvement caused bronchial narrowing. We found none of these features in our patient although a swelling extending from the right infra orbital margin to the right lower border of the mandible and the right ala of nose to the root of the ipsilateral root of zygoma, was evident. The infective nature of the disease was first suspected upon lymph node palpation during which the right submandibular lymph nodes were found to be tender, mobile and oval.

Our radiological findings were an abnormal bone pattern in the region of the right maxillary sinus with increased radioopacitiy and a radiolucent area in the apical third region of the right maxillary premolars besides dental findings, suggesting either maxillary sinusitis or a residual cyst. No radiographic appearance is pathognomonic for Rhinoscleroma. Sinus opacification may mimic sinuses of other etiologies. Turbinate atrophy is highly suggestive of Rhinoscleroma but must be differentiated by tissue culture from infection caused by Klebsiella ozaenae. The Rhinoscleromatous nasal mass ("Von Hebra Nose") is uncommon but may suggest carcinoma, especially in the presence of bone destruction[30]. Because the radiographic findings in Rhinoscleroma are nonspecific, diagnosis cannot be made based on radiographic criteria alone. The diagnosis can only be established by finding the characteristic organism, Klebsiella rhinoscleromatis, in appropriate tissue specimen or culture[30]. Specific diagnosis is made by the bacterial isolation by culture on blood or macconkey agar (positive in 50% to 60%) and by identification of histopathologic features and bacilli in biopsied lesions biopsies, using periodic acid-Schiff (PAS), Giemsa and Warthin - Starry stain[32]. These stains combined with immunoperoxidase staining using Klebsiella capsular type 3 antiserum increase accuracy and specificity of both histological and bacteriological diagnoses[38].

Differential clinical diagnosis at early stage is common rhinitis. At tumoral stage diagnoses of leprosy, tertiary syphilis, cutaneous tuberculosis, sarcoidosis and Wegener granulomatosis must be ruled out; when scar formation process occurs, destructive mycosis, mucocutaneous leishmaniasis on scar tissues and ozena must be evoked[39].

In addition, the disease may be mistakenly diagnosed as neoplastic disease, mucocutaneous leishmaniasis, leprosy, paracoccidi-
Rhinoscleroma: A Case Report with Review of Literature

The gross and histological appearance of Rhinoscleroma evolves through three stages. Initially, watery mucoid material with flecks of blood is noted on gross examination. Histological study reveals squamous metaplasia, acute inflammation, and granulation tissue. Later, Rhinoscleroma is expansive, tumorous, and multilobulated. On histological examination, plasma cells, with or without Russell bodies (reddish-violet elliptical structures, slightly bigger than plasma cells and felt to represent degenerated plasma cells), and Mikulicz cells (foamy histiocytes containing Klebsiella rhinoscleromatis) are seen. The overlying mucosa is hyperplastic. The late stage of Rhinoscleroma has the gross and histological appearance of scar tissue. Isolated foci of plasma cells and Mikulicz cells may be present[30].

The disease progresses in three stages: (1) The catarrhal stage: The histopathology of this stage was squamous metaplasia, subepithelial infiltrate of neutrophils, and general granulation tissue. (2) The hypertrophic stage: Histopathological shows an infiltrate of chronic inflammatory cells, "Mikulicz cells" and "Russell bodies" were visualized as hallmark for diagnosis of Rhinoscleroma. (3) The sclerotic stage: Histopathological includes large amount of fibrous and cicatricial tissues and few or no Mikulicz cells or Russell bodies[23,41].

In the pre-antibiotic era, the mainstay of therapy for scleroma was surgery, particularly in the late fibrotic stage with airway problems due to obstruction or disfigurement. Now, Rhinoscleroma treatment involves prolonged antibiotic therapy, in an attempt to eradicate K. Rhinoscleromatis.

In vitro, these bacteria are inhibited by clinically achievable concentrations of amoxicillin - clavulanate, chloramphenicol, trimethoprim - sulfamethoxazole, cephalosporins, streptomycin, tetracyclines and ciprofloxacin[42]. However, in vivo, antibiotics with demonstrated efficacy are streptomycin, doxycycline, tetracycline, rifampicin, second- and third-generation cephalosporin, sulfonamides, clofazimine, ciprofloxacin[43] and ofloxacin[44].

Systemic streptomycin was the first drug to be used successfully and for years it was the drug of choice but it has severe side-effects, especially in the vestibular system, and the bacterium has now acquired resistance. When tetracycline was introduced it had the facility of oral administration, but it required prolonged therapy in terms of months or years with poor patient compliance. Tetracycline is to be avoided in the pediatric age group and during pregnancy because of teeth staining[45]. Rifampicin has also been shown to have good results, but patient's receiving rifampicin must be closely monitored for sign of toxicity. To avoid the systemic effects of rifampicin, topical rifampicin has been used with good results[46]. Trimethoprim-sulfamethoxazole has been found to be effective, and its low cost is especially important in third world nations[47].

Most recently, quinolones have been reported as adequate treatment[48]. Ciprofloxacin, a fluoroquinolone, is an antibiotic with excellent tissue penetration and a broad antibacterial spectrum of action. Adverse effects are comparatively few and include gastrointestinal symptoms in three to six per cent of patients. Its use is not recommended in patients under 12 years of age because of the risk of arthropathy. Ciprofloxacin has the advantage of twice-daily administration, that may improve compliance for long courses of therapy. Another theoretical advantage is that the quinolones are concentrated within macrophages[49]. Ciprofloxacin, 250-500 mg administered twice daily for four weeks, was shown to have excellent clinical efficacy in an area of Mexico where scleroma is endemic[50]. There have been other case reports of Rhinoscleroma cured with ciprofloxacin but the appropriate duration of antibiotic therapy has not been established yet.

We reasoned that, since debulking would immediately reduce microbial load and provide symptomatic relief, and also, since K. rhinoscleromatis is highly sensitive to fluoroquinolones and penicillin's, we used a combination of surgery and antibiotic pharmacotherapy for treating this patient. Metronidazole was used to inhibit anaerobic infection, if present during the procedure. Ciprofloxacin 750 mg and Augmentin 625 mg, which is a combination of Amoxicillin and Clavulanic acid, were used for a period of 4 weeks to treat this infection. Ciprofloxacin 750 was continued for another 2 weeks as a prophylactic measure. Ciprofloxacin is cheaper in the long run than drugs with a lower initial cost that required longer periods of administration.

Borgstein et al.[50], (1993), reported that 89% of biopsy culture of this lesion was negative two months of use of ciprofloxacin for four weeks, and after six months clinical improvement was significant and relapse rate low.

CONCLUSION

A combination of debulking and antibiotic therapy including Ciprofloxacin 750 mg, Amoxicillin 500 mg and Clavulanic Acid 125 mg for 4 weeks, followed by a 2 week period of Ciprofloxacin 750 mg prophylaxis apparently produced satisfactory results for our patient. Surgery resulted in immediate relief from the nasal obstruction. Post treatment, the patient was followed up for a period of 2 months during which, the swelling continued receding and after this the patient was lost to follow up. A study comparing this method of treatment with other treatment methods, such as the use of pharmacotherapy alone in such patients, with a longer follow up would be of considerable interest.

CLINICAL SIGNIFICANCE

A combination of debulking and antibiotic therapy can be taken into consideration as surgery results in immediate symptomatic relief and decrease the microbial load thereby increasing the sensitivity of the pharmacological therapy.
REFERENCES


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