Role of Antibiotics in Treatment of Rhinoscleroma Systematic Review of the Evidence

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By

Ibrahim Saad Abd El Salam Attia

(M.B.B.CH)

Alex. University-2004

Under Supervision of

Professor Dr. Mahmoud Ezz El-Dein El-Sammaa

Professor of ORL

Faculty of Medicine-Ain Shams University.

Dr. Aly Mohamed Nagy El-Makhzangy

Lecturer of ORL

Faculty of Medicine- Ain Shams University

Faculty of Medicine

Ain Shams University

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الدكتور / على محمد ناجى المخزنجى

مدرس جراحة الأنف و الأذن و الحنجرة

كلية الطب - جامعة عين شمس

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Aim of the Study

The aim of this study is to carry out a focused systematic review of the efficacy and outcome of different antibiotic treatments (whether desirable or adverse) on Rhinoscleroma.

Introduction

Definition:

Rhinoscleroma (RS) is a chronic, progressive, granulomatous infectious disease of the upper respiratory tract. The term "rhinoscleroma" was first coined in 1870 by Von Hebra. ***(De Pontual et al., 2008).***

Epidemiology:

Rhinoscleroma is frequently described as a rare disease in the West. Therefore, National and International Epidemiological data are scarce. ***(De Pontual et al., 2008).***

Though it remains a rare disease. It is endemic in parts of Asia, Africa, and South and Central America. It is particularly common in Egypt and Indonesia. Rhinoscleroma is now being seen with increasing frequency in south-east Europe, Poland, Hungary, south-west Russia, and in the south-western United States among Mexican populations. Endemic areas are thought to have common environmental factors favorable to the spread of the causative agent: poor nutrition, poor hygiene, and overcrowding in the homes. Close personal contact is thought to be necessary for spread of the disease. The vector may be an insect, but this has never been shown. ***(Lubin et al., 1981)***.

(Badrawy and El-Shennawy., 1974) cited that Handousa and Elwi in 1958 reported an average of forty cases per annum at Cairo University Hospitals and that El-Mofty in 1962 suggested that the incidence of scleroma in Egypt was decreasing as compared with preceding years and this was explained by the improvement in the standard of living**.**

Causative agent:

The causative organism is Klebsiella rhinoscleromatis, a gram-negative aerobic coccobacillus, as determined by histology, culture, and rising antibody titers in convalescent sera ***(Fajardo-Dolci et al., 1999).***

It is important to note that maximum positive isolations were recorded in the granulomatous stage. The granulomatous lesions could be rich in the causative organism, intracellularly or in interstitial spaces. Where the tissue was macerated well, the chances of positive culture improved. The disease process is more active in the granulomatous stage, thereby the chances of isolation of the organism are more. The lack of isolation in the cicatricial stage could be due to the decline of the disease during this stage and the tendency towards healing. ***(Sinha, et al., 1969)***.

Pathology:

Generally, the microscopic appearance is that of a granulomatous chronic inflammatory lesion with an infiltrate composed chiefly of plasma cells, mainly perivascular in distribution, and lymphocytes. Although the early and scarred end stages are non specific, the hallmarks of florid scleroma include Mikulicz's cells, plasma cells, Russell bodies, gram negative rods and hypertrophied epithelium. Mikulicz's cells are large and vacuolated (100-200 micron in diameter) with foamy cytoplasm in which gram negative, bipolar K. rhinoscleromatis may be seen with routine stains. The Russell bodies are much smaller than Mikulicz's cells, are refractive to light, and are believed to be degenerated plasmocytes. Russell bodies and Mikulicz's cells are not peculiar to scleroma, however, and other causes of chronic granulomas and neoplasia must be eliminated. The pseudo epitheliomatous hyperplasia of the mucosal epithelium seen may be confused with carcinoma. The amount of cellular infiltration varies with the stage of the disease. After many years cellularity is replaced by fibrosis, which gives the disease its clinical wooden hardness and the name scleroma. In general, a granulomatous respiratory tract lesion showing plasma cells, Russell bodies, Mikulicz's cells in which gram negative bacilli can be demonstrated and in which

no acid fast organisms can be found, is almost certainly scleroma. ***(Feldman et al., 1967).***

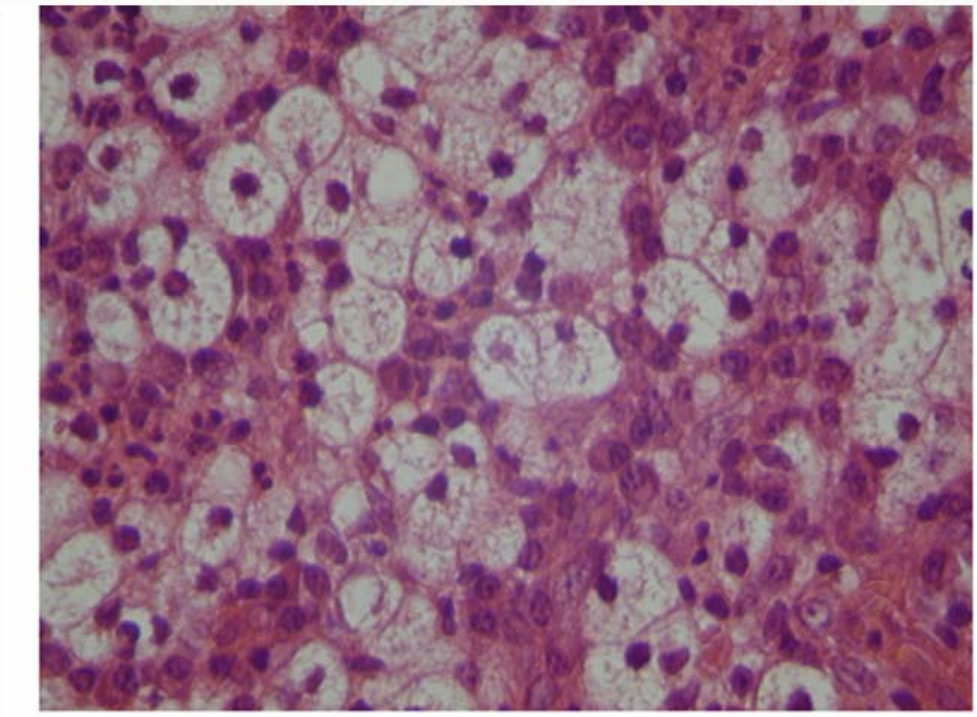

Fig. (1): Histological examination of a nasal biopsy; typical histocytic granulomatous histology of the rhinoscleroma at an advanced stage. The inflammatory infiltrates are mainly composed of characterstic foamy macrophages and plasmocytes ***(Coated from Botelho-Nevers et al., 2007).***

Diagnosis:

Various methods to confirm the diagnosis of rhinoscleroma include clinical presentation, culture from the affected area, biopsy of the lesion, serology and immunochemistry. A positive culture of *K. rhinoscleromatis* is diagnostic of rhinoscleroma because it is not found in normal

nasal secretions. A biopsy is taken from areas of active disease, with the nasal septum and anterior aspect of the inferior turbinate being easily accessible sites for this. Serological tests are diagnostic but are only of value when positive including complement fixation test and agglutination test. Also immunochemistry can be used as a diagnostic method for rhinoscleroma and this is especially important in cases where the histopathology is equivocal, the identification is based on that *K. rhinoscleromatis* is antigenically homogenous, in addition it has a unique antigenic formula O2K3, where O stands for the smooth somatic antigen and K for the capsular antigen, so we can apply immunoperoxidase technique for specific identification of the capsular antigen of *K. rhinoscleromatis*. ***(Shum et al., 1982)***.

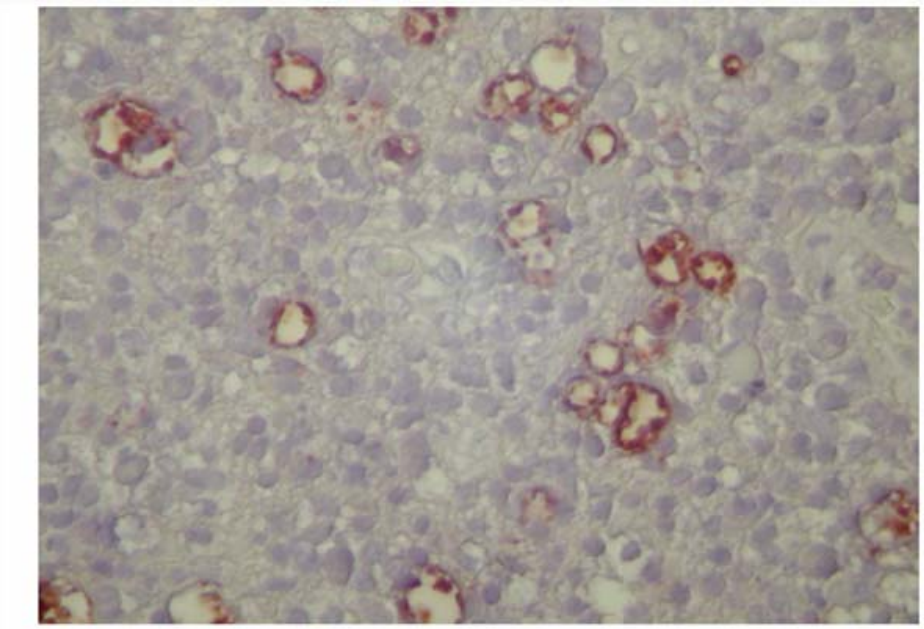

Fig. (2): Klebsiella rhinoscleromatis is detected by immuno-histochemical examination using the patient's own serum at a dilution of 1:500. Bacilli are packed as coarse immunopositive material in foamy macrophage cytoplasm (hematoxylin counter stain, original magnification ×400. ***(Coated from Botelho-Nevers et al., 2007).***

Clinically, scleroma is a progressive granulomatous disease with insidious onset and indolent course, commencing in the nose and eventually extending into the nasopharynx, oropharynx, larynx and sometimes the trachea and bronchi.

Three overlapping stages are described in rhinoscleroma: atrophic, granulomatous (proliferative or nodular) and sclerotic (cicatricial or fibrotic). 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. In the granulomatous stage there are 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, Figure (3) shows a patient with bilateral granulomatous lesions.

Fig. (3): ***(Coated from Shubich and Aguilar., 1979).***

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 ***(Maguina et al., 2006).***

Treatment:

Rhinoscleroma remains a difficult entity to cure, and relapses are common. Currently, the recommended treatment of rhinoscleroma consists of a combination of surgical debridement and long-term antibiotic therapy. Treatment is also stage-dependent. ***(Borgestein et al., 1993)***.

Prolonged antimicrobial treatment is required to cure rhinoscleroma. Streptomycin in combination with tetracycline has long been regarded as the standard treatment although rifampin has more recently been found to be effective either by topical application or oral ingestion.

Several antibiotic regimens are likely to be more effective and are certainly more easily administered than streptomycin and tetracycline. Clinical trials that examine the clinical effects of co-trimoxazole, ciprofloxacin, and newer cephalosporins appear to be warranted.

Two further features of rhinoscleroma might appear to support the use of ciprofloxacin or rifampin. First, since this disease is generally limited to the tissues of the upper respiratory tract, clinical efficacy may be dependent on the antibiotic levels that can be achieved in nasal secretions. Ciprofloxacin and rifampin both concentrate in these secretory