Aetiopathogenesis of Scleroma*

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Scleroma has been known to affect human beings for nearly a century; von Hebra being the first to report this condition in 1870. He described it as a form of cutaneous cancer. However, the precise pathogenesis of the disease still remains controversial.

There are two views:

(1) Many authors including Hara *et al.* (1947); Kauffmann (1948); Levine (1951); support the bacterial theory propounded by Von Frisch (1882), who isolated a Gram negative bacillus from nasal lesions of scleroma patients.

(2) Second school of thought believes that the disease is caused by a filterable virus (Cunning and Guerry, 1942; Reyes, 1946; and Zwiefach, 1955). They believe that Klebsiella rhinoscleromatis is a normal commensal in the upper respiratory tract or a secondary invader.

Chamberlain (1936) and Putschowsky (1945) observed the course of the disease. The latter divided it into four different clinicopathological stages: (i) early catarrhal stage; (ii) atrophic stage; (iii) granulomatous stage and (iv) fibrotic stage.

It is evident that the precise aetiopathogenesis of the condition is far from clear. No mention of control series of bacteriological investigations of the upper respiratory tract is available. The aim of this study is to present the pathological aspects of this condition.

Material and Methods

Twenty-five cases with clinical suspicion of scleroma involving the upper respiratory tract, formed the basis of this study.

Two pieces of tissues were obtained from the suspected lesion under aseptic conditions.

(*a*) One piece was preserved in 10 per cent. formol saline solution. Paraffin embedded sections were stained with routine haematoxylin and eosin technique and with P.A.S. and Giemsa's techniques wherever indicated for intracellular organisms. This helped in confirming the diagnosis.

The secretions from the suspected lesions as well as the tissues suspended in isotonic saline were inoculated. The culture media used for this purpose were blood agar and MacConkey's agar. The secretions

* Read at 19th Annual Conference of Otolaryngologists, India, in January 1967.

https://doi.org/10.1017/S0022215100070158 Published online by Cambridge University Press

were directly smeared over the culture media, however, the tissues were well macerated before inoculation. The growth was observed after 24 to 48 hours of incubation at 37°C. The suspected colonies of Klebsiella group were further identified with the help of Gram's staining, motility test and detailed biochemical reactions. The vitro-sensitivity of the organisms was done against Furadentin and antibiotics viz. penicillin, streptomycin, chloramphenicol, oxytetracycline, chlortetracycline, reverine and erythromycin. The results were recorded after 24 hours of incubation at 37°C. The clear zone around the antibiotic disc was the index of sensitivity. This served as a guide in the treatment of the cases.

An equal number of apparently healthy individuals were studied for the bacterial flora of the nose, pharynx and/or larynx. This served as a control group.

Observation and Results

The nose was involved in 100 per cent. of the patients and was the primary site in every case. However, pharynx and larynx were involved in 56 per cent. and 52 per cent. of the cases respectively.

(i) *Clinicopathological Staging*

Most of the patients presented in the granulomatous stage (Fig. 1). It was recorded in 21 cases (84 per cent.), having nasal lesions, 7 of pharyngeal (50 per cent.) and 7 of the laryngeal lesions (53·8 per cent.). The atrophic stage was the next mode of presentation, involving 28 per cent., 50 per cent. and 53·8 per cent. of the nasal, pharyngeal and laryngeal lesions respectively. The details appear in Table I.

TABLE I.
SHOWING CLINICOPATHOLOGICAL STAGING (25 CASES).

Clinicopathological Stage	Nose (25 Cases)		Throat (14 Cases)		Larynx (13 Cases)	
	No. of Cases	Percentage	No. of Cases	Percentage	No. of Cases	Percentage
Early catarrhal stage	1	4	0	—	4	30·8
Atrophic stage..	7	28	7	50	7	53·8
Granulomatous stage	21	84	7	50	7	53·8
Cicatricial stage	2	8	4	28·6	2	15·4

Note: Due to the presence of more than one stage in the same lesion, the number exceeds the total number of cases, i.e. 25, and hence the total percentage as well.

Bacteriological Examination

(i) *Secretions. Klebsiella rhinoscleromatis* was isolated from nasal secretions in 5 cases (20 per cent.); however, 4 cases (30·8 per cent.) with laryngeal involvement showed positive culture.

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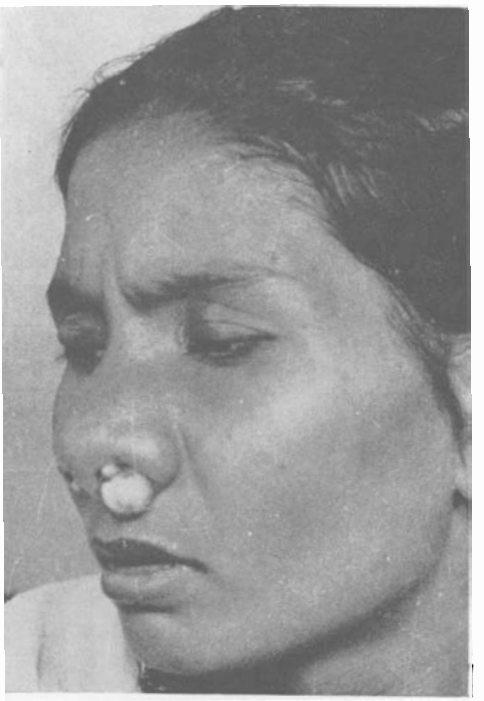


FIG. 1.
Showing a case in granulomatous stage involving nose.

TABLE II.
SHOWING THE RELATIONSHIP OF MATERIAL CULTURED AND POSITIVE RESULTS.

Site	No. of Cases Studied	Secretions		Tissue Biopsy	
		No. of Positive Cultures	Percentage	No. of Positive Cultures	Percentage
Nose	25	5	20	11	44
Throat	14	0	10	2	14·3
Larynx	13	4	30·8	3	23·8

Note: No. of positive cultures shown exceeds the total number of 15 as in some cases the organisms were isolated from more than one site.

(ii) *Tissue for Culture.* The pathological tissue was inoculated in all the nasal lesions (100 per cent.); 69·23 per cent. of the laryngeal and 35·64 per cent. of the pharyngeal lesions. It is evident from Table II that 44 per cent. of the nasal lesions, 23·8 per cent. of the laryngeal and 14·3 per cent. of the pharyngeal lesions yielded positive culture of *K. rhinoscleromatis* by this method.

In all, 15 out of 25 cases (60 per cent.) revealed positive isolation of *K.*

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rhinoscleromatis by tissue inoculation as compared to 7 cases (28 per cent.) by the secretions cultured.

The positive isolation rate of *K. rhinoscleromatis* was affected by the prior streptomycin therapy in a good number of patients (52 per cent.). It may be mentioned that *K. rhinoscleromatis* could be isolated in all the untreated cases (48 per cent.); see Table III.

TABLE III.

RELATIONSHIP OF POSITIVE CULTURE WITH PRIOR TREATMENT.

	No. of Cases	Percentage	Positive Culture	
			No. of Cases	Percentage
Treatment taken already	13	52	3	12
No treatment taken already ..	12	48	12	48
Total	25	100	15	60

Antibiotic Sensitivity Tests (Fig. 2)

Eleven out of fifteen strains (73·3 per cent.) were recorded to be most sensitive to streptomycin. However, in 2 cases (13·3 per cent.) it was most sensitive to chloramphenicol and to oxytetracycline (terramycin) in another 2 cases (13·3 per cent.).

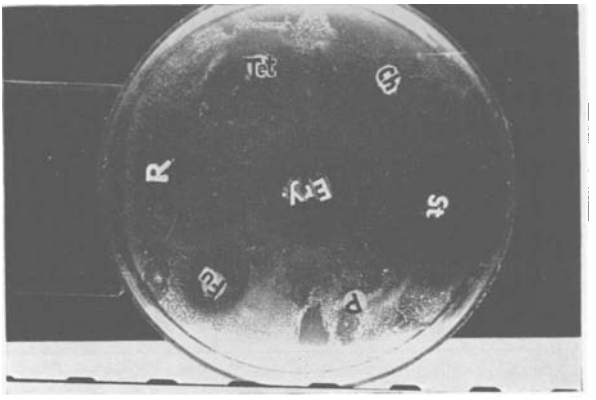


FIG. 2.

Antibiotic sensitivity test *in vitro*. The different antibiotic discs used:

Ch. — Chloramphenicol
P. — Penicillin
R. — Reverine
Ery. — Erythromycin
St. — Streptomycin
Fu. — Furadentin
Tet. — Tetracycline

Relationship of Positive Culture to Clinicopathological Staging

The maximum number of positive cultures were isolated from the granulomatous lesions from all the sites i.e. 11 out of 21 nasal lesions

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(52·3 per cent.); one out of 7 from pharynx (14·3 per cent.), and 2 out of 7 from larynx (28·6 per cent.) in the granulomatous stage yielded positive culture. The incidence of positive culture was next common in atrophic lesions from different sites.

TABLE IV.
SHOWING ANTIBIOTIC SENSITIVITY TESTS OF *K. RHINOSCLEROMATIS* (15 STRAINS)

Name of Antibiotic	No. of Strains	Percentage
Streptomycin ..	11	73·3
Oxytetracycline..	2	13·3
Chloramphenicol	2	13·3

It was noticeable that all the strains were resistant to penicillin.

TABLE V.
RELATIONSHIP OF POSITIVE CULTURE TO CLINICOPATHOLOGICAL STAGING.

Clinicopathological stage	Nose			Throat			Larynx		
	No. of Cases	No. of Positive Cultures	Percentage	No. of Cases	No. of Positive Cultures	Percentage	No. of Cases	No. of Positive Cultures	Percentage
(i) Catarrhal	1	1	100	—	—	—	4	—	—
(ii) Atrophic	7	2	28·6	7	1	14·3	7	2	28·6
(iii) Granulomatous	21	11	52·3	7	1	14·3	7	2	28·6
(iv) Cicatricial	2	—	—	4	—	—	2	—	—

Note: In some of the cases, overlapping of clinicopathological stage and culture was because of positive culture from more than one site in some cases.

Bacteriological Study in Control Cases

It is important to record that no positive culture of *Klebsiella rhinoscleromatis* was obtained from nasal, pharyngeal and/or laryngeal secretions in a control group of 25 cases.

Discussion

Is *K. rhinoscleromatis* a normal commensal of upper respiratory passages? Babes (quoted by Watkins, 1952) recovered Frisch bacillus in 50 per cent. of cases of chronic inflammations of nasal mucosa. Levine (1951) studied 532 patients with diseases of ear, nose or throat other than scleroma, and concluded that *K. rhinoscleromatis* did not occur in the nose and throat of patients who did not have scleroma. The failure to isolate *Klebsiella rhinoscleromatis* in the study of 25 apparently healthy individuals supports the contention that it is not a normal commensal.

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The present study supports the widely favoured bacterial theory. *K. rhinoscleromatis* could be isolated in all the cases of the untreated group, however, the poor isolation rate of the organism in others, could be due to previous streptomycin treatment taken by the patients. Steffen and Smith (1961) confirmed the postulation, by reproducing the lesions of scleroma. They inoculated *K. rhinoscleromatis* in albino mice by intranasal and intra-cerebral routes. This view was further favoured by immunofluoresence antibody technique undertaken by Hoffman (1963) and electronmicroscopic studies of the pathological lesions by Fisher and Dimling (1962).

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.

The *in vitro* sensitivity tests in the present study support the mostly held concept that streptomycin is the best antibiotic against this condition.

Conclusions

We can conclude that:

(i) Most of the patients attend the hospital when the lesion is well advanced, i.e. the granulomatous stage.

(ii) *K. rhinoscleromatis* could be isolated in 60 per cent. of the cases. The results were affected by the previous treatment.

(iii) The isolation of the causative organism is more frequent when the macerated tissue is inoculated (60 per cent.) as compared to secretions (23 per cent.). Further, the positive cultures were more frequently isolated in the granulomatous stage, the most active form of the disease.

(iv) The study of the smears of otherwise normal nose, pharynx and larynx revealed that *K. rhinoscleromatis* is not a normal commensal of these regions.

(v) The sensitivity tests *in vitro* reveal that the most effective antibiotic at our command is streptomycin. However, oxytetracycline and chloramphenicol are also useful against certain strains.

Acknowledgments

We are thankful to the Dean, All India Institute of Medical Sciences, New Delhi, for permitting us to publish a part of the thesis, submitted for the degree of M.S. (Otorhinolaryngology).

https://doi.org/10.1017/S0022215100070158 Published online by Cambridge University Press

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https://doi.org/10.1017/S0022215100070158 Published online by Cambridge University Press

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