Stomatitis and Dermatophytosis Coincident to Streptomycin Therapy

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Four cases of streptomycin stomatitis are presented together with three cases of eczematous dermatitis of the hands and feet coincident with streptomycin therapy, and attention is called to association of stomatitis with a vulvar mycotic lesion in one instance and concomitant stomatitis with severe trichophytoid lesions of hands and feet in another.

While the over-all series of treatment with streptomycin at this institution embraces a period of 28 months and 130 cases, it is notable that the pharyngeal ulcers to be described occurred relatively rarely in this series. Recrudescence of pre-existing trichophytosis was observed while the patient was undergoing streptomycin therapy. In each of the severe cases of eczematoid dermatitis to be described, a pre-existing trichophytosis of the feet was noted. In the light of the history of previous fungus infection, it is perhaps not illogical to infer that streptomycin therapy tends, in some cases at least, to give impetus to the trichophytosis already present.

Case 1: Pharyngeal and vulvar ulceration: W.C., a 22 year old white woman was admitted to Mississippi State Sanatorium on June 30, 1941. Admission diagnosis was bilateral, far advanced pulmonary tuberculosis. Auscultation revealed coarse, post-tussic rales throughout the right lung and expiratory wheeze over the subclavicular area. Coarse rales throughout left chest during both phases of respiratory cycle. Dullness to percussion was elicited at the level of the fourth rib anteriorly on right and an impaired note from the sixth to the ninth rib posteriorly on left side. Roentgenograms disclosed bilateral perihilar and mid-lung field infiltration, with fine featherly mottling of lung fields bilaterally almost through their entirety.

Streptomycin therapy was instituted on July 1, 1947, consisting of 2.0 grams daily parenterally and 0.5 gram by inhalation. A total of 85.0 grams was given. Blood counts, urinalyses and N.P.N. determinations were done periodically throughout the course and were within normal limits.

Pharyngeal ulcers were noted on August 25, 1947 (after 78.0 grams had been given). The ulcers were initially observed on the anterior pillars, the buccal mucous membrane, sublingually and on the vermilion border of the lips. Initially, they appeared as white two to four millimeter vesiculations which within 36 hours broke down to form five to eight millimeter craters eventually covered with shaggy, dirty white membrane.
Small vesicles appeared at the corners of the mouth and broke down to form fissures.

Smears taken repeatedly disclosed no specific organism. To prevent spirochetal infection, the membrane was removed from the ulcers and 10 per cent neo-arsphenamine in glycerin was applied topically followed by perborate mouth washes. Within 72 hours of the initial pharyngeal ulceration, vulvar ulcers following vesiculation were noted. Laboratory examination disclosed monilia and 2 per cent gentian violet was applied topically. Streptomycin was discontinued on September 5, 1947. Treatment of the lesions continued as above for 12 days. The ulcers, pharyngeal and vulvar healed. Re-institution of streptomycin (1.5 grams) resulted in recurrence of ulcers which again disappeared upon stopping streptomycin.

Case 2: Pharyngeal ulceration: R.F., a 21 year old white woman was admitted to this Sanatorium on June 4, 1948. Prior to admission she had right artificial pneumothorax for 14 months, inadvertently re-expanded. Immediate pre-admission history was that of easy fatigability, persistent cough with moderate expectoration. Intermittent hoarseness for preceding 90 days. Small hemoptysis one month prior to entrance. Rhonchi were heard in sub-clicular and inter-scapular areas on the right side. The findings were normal on the left side. A roentgenogram disclosed evidence of fibro-exudative lesion extending from apex to second inter-costal space anteriorly on right side. No unusual density was seen on the left side.

Bronchoscopy on June 17, 1948 revealed "considerable amount of granulation tissue near the carina... lumen of trachea reduced to about one-half its normal size." (Subsequent bronchoscopy revealed the right primary bronchus to be partially stenosed by granulation tissue). The patient was started on streptomycin on July 3, 1948. Thirty-one grams had been given by August 7 when vesiculations like those described in the previous case were noted. (She had been requested to report all paresthesias in the mouth). Although streptomycin was discontinued immediately, the lesions went on to crater formation within 48 hours. Neo-arsphenamine topically was used as in Case 1. The lesions cleared in five days. On August 12 streptomycin was re-started in 100.0 milligram doses. On August 14 (within 48 hours) vesicles and ulceration again appeared. (Total of 0.75 gram given). Faucial, buccal, sublingual and vermilion border of lips were the sites involved. This time the ulcerations persisted 10 days.

Because a successive bronchoscopy disclosed the lesion (tracheal) to be progressing after an original regression due to the streptomycin, the bronchoscopist felt that streptomycin was the only recourse. Streptomycin was again administered on September 23, 1948. After 333.3 milligrams there was a return of vesicles, generalized capillary dilatation over the body-surface, peri-orbital oedema plus angio-neurotic oedema of the lips. The temperature was recorded at 102.4 degrees F. The patient complained of intense burning sensations over the entire body and paresthesia and burning in the pharynx. Pyribenzamine (50.0 milligrams) resulted in subjective relief from burning sensations. Erythema of body was reduced and oedema of the lips disappeared gradually. Only two 5.0 millimeter ulcerations in the pharynx were seen and these disappeared in 72 hours.
Case 4: Pharyngeal ulceration: S.D.L., a 16 year old white female was admitted April 21, 1948 with moderately advanced disease with a pronounced exudative component. Roentgenographically, soft mottling from the apex to the horizontal fissure was seen on the right side and a cavum one centimeter in diameter at the level of the first rib anteriorly. Two one by one centimeter exudative lesions in the first and second intercostal spaces respectively appeared on the left side. Right artificial pneumothorax was unsuccessful. Streptomycin was begun on April 26 at daily dosage of one gram and continued until August 24. The streptomycin was discontinued at this time because of the appearance of pharyngeal ulceration as described in preceding cases. At this time a total of 90.0 grams had been given. An attempt to re-start streptomycin resulted in re-appearance of the ulceration. Subsequent discontinuance of streptomycin resulted in healing of the pharyngeal lesions. It has not been the writer’s experience that pyribenzamine prevents a second appearance of pharyngeal ulcers; i.e., once streptomycin has been discontinued because of onset of ulcers, and is subsequently re-started. In this case the sputum was converted and remains negative as of September 25, 1948; the roentgenograms had shown excellent clearing of the exudative lesion.

Case 4: Pharyngeal ulceration: A.K.M., a 34 year old white male was admitted on May 29, 1948 with history of persistent cough (three months) and minimal expectoration. Chest examination disclosed no abnormal findings. A roentgenogram revealed peribronchial infiltration in lower one-half of left lung field. Sputum was Gaffky iv. Bronchoscopy on June 17 disclosed tuberculous bronchitis of left lower lobe bronchus without visible ulceration.

Streptomycin was begun April 21 with one gram daily. After 87.0 grams on October 7, a shaggy white membrane was seen over the aperture of Stenson’s duct which was treated locally with neo-arosphenamine. Streptomycin was discontinued. Smears cultured on Sabouraud’s medium were uninformative. The crater surrounding the opening of Stenson’s duct healed in five days after discontinuance of streptomycin. Concurrent sublingual and vermilion lip border lesions also healed. The lesions re-occurred on re-starting streptomycin. Successive bronchoscopies have revealed that the bronchial lesion in the left lower lobe has improved markedly.

Case 5: Recrudescence of dermatophytosis: W. de L., a 40 year old white man was admitted on May 14, 1948 with positive sputum and an infiltrative lesion confined to left apex roentgenographically. Left pneumothorax was instituted. Ineffective closed pneumonolysis was done on February 3, 1947. Inasmuch as the cavity would not close, pneumothorax was abandoned and he came to three stage thoracoplasty begun October 27, 1947 and completed December 16.

Between the first and second stages, the patient was highly febrile for several days. A check film disclosed widespread apparently tuberculous disease on operative side. Bronchoscopy at this time revealed no blockage of major bronchi. Streptomycin was begun November 5, 1947 at 2.0 grams daily in hope of controlling disease in ipsilateral side and prevention of spread to contra-lateral lung. The patient’s temperature approached normal and a check-film showed marked clearing. The second stage was done on November 25 and the third was finished as mentioned.
The course of streptomycin was continued until 145.0 grams had been given. At this time eczematous weeping lesions of hands were noted. Initially the lesions were vesicles which ruptured to liberate clear fluid. In later stages the overlying skin became undermined, sloughed and the corium was exposed. The skin sloughed from the terminal phalanges of the index, middle and ring finger of the right hand. The thumb had weeping lesions of lesser intensity. Boracic acid soaks, Lassar's Paste to the denuded areas plus touching up of ruptured vesicles with 2 per cent silver nitrate was accomplished. Streptomycin was continued at 145.0 grams. The aforementioned lesions did not abate in intensity for four weeks. Questioning and examination of the patient revealed tinea versicolor of feet admitted eight years. (Organism identified by laboratory examination). When the lesions were subacute, quinine bisulphate was used as powder. The lesions of the hands and feet were healed completely in eight weeks. This and the two succeeding cases had similar histories of co-existent dermatophytosis of the feet with comparable reactions under streptomycin therapy and are therefore listed.

Case 6: Recrudescence of dermatophytosis: P.B., a 42 year old white man was admitted to Mississippi State Sanatorium on April 18, 1948 with a diagnosis of far advanced bilateral pulmonary tuberculosis. Roentgenograms disclosed evidence of fibro-caseous disease with localizations, embracing the upper two-thirds of the left lung field. On the right side a 3.0 by 3.5 centimeter cavity was seen in the apex and fibro-caseous disease extending from the apex to the second intercostal space anteriorly. A tracheo-bronchial lesion was discovered on early bronchoscopy. Pneumothorax on the left side was unsuccessful (endobronchial lesion noted on right). Streptomycin was begun May 26, 1948 with 1.0 gram daily. This was discontinued August 28 after 81.0 grams had been administered. On August 25 an eruption of vesicular nature was noted on the hands. The vesicles ruptured and proceeded to weeping eczematoid type lesions involving three digits on the left hand. Coincident dermatophytosis of feet was present prior to streptomycin therapy and exacerbated during the course of treatment. There was previous history of chemical (paint factory) dermatitis three years before. Remedial measures previously mentioned were used topically. Pyribenzamine was ineffective. In this case as in the foregoing, the extant dermatophytosis on the feet became worse during streptomycin therapy. At this point, it must be mentioned that contact of hands and feet is unavoidable and is a factor. The emphasis, however, is on the recrudescence of the lesions.

Case 7: Pharyngeal ulceration and recrudescence of dermatophytosis: J.H.R., a 58 year old white man was re-admitted May 10, 1948 with far advanced bilateral pulmonary tuberculosis. A complicating vocal cord ulcer and an epiglottic implant were the indications for streptomycin. The roentgenograms disclosed evidence of fibro-caseous infiltration of the upper one-half of both lungs and basal emphysema. Streptomycin was begun on May 17 at 1.0 gram daily; discontinued August 23 after a total of 92.0 grams had been given. After 88.0 grams of streptomycin, it was noted that a dermatophytosis of the feet (present for 12 years) was progressively worse. Vesiculations which ruptured to leave superficial slough, were followed by beefy red,
weeping lesions of both feet. The existent dermatophytosis of the toes spread to involvement of one-half of the dorsum of each foot. Treatment locally as outlined previously was ineffectual. Resort to 2 per cent alum-
inum acetate proved more efficacious. Pyribenzamine was given in doses of 200.0 milligrams daily for two weeks.

After 90.0 grams of streptomycin, pharyngeal ulceration as in previous cases was noted. Marked fissuring of the mouth borders was also noted as in the first case cited. Subjective improvement of hoarseness and objective improvement of epiglottis and vocal cord lesions were noted. Streptomycin was continued until a total of 92.0 grams was given.

The dermatophytosis grew progressively worse with denudation and extremely slow re-epithelialization. The pharyngeal ulceration in this case progressed until the craters measured 8.0 millimeters in diameter. The objective in this case was achieved in that the epiglottic and vocal cord lesions healed. The pharyngeal lesions healed 18 days after onset (14 days after stopping streptomycin). The dermatophytosis healed 90 per cent after 12 weeks. Associated vestibular disturbance (vertigo) persists at present writing, nine weeks after streptomycin was discontinued.

**Commentary**

Observation of these complications of streptomycin therapy leads to the consideration of the following points: (1) Streptomycin reduces bodily resistance to pre-existing fungus infections (vid. trichophytosis) giving added impetus to these entities. Close observation is indicated when giving streptomycin in these cases. (2) Caution is called for in administering streptomycin to women with vaginal tract fungaceous infestations of any degree (vid. case 1). (3) Until further work with pharmaceuticals calculated to minimize streptomycin reactions, particularly stomatitis, proves efficacious, streptomycin had best be discontinued when such complications occur. Repeated efforts were made to re-start streptomycin in fractional doses with and without pyribenzamine to no appreciable avail.

**SUMMARY**

1) Four cases of pharyngeal ulceration occurring during strep-
tomycin therapy are presented.

2) Three cases of recrudescence of pre-existing dermatophy-
tosis are recorded.

3) One case was a combination of pharyngeal ulceration and vulvar ulceration.

4) One case represented combined pharyngeal ulceration and dermatophytosis.

**RESUMEN**

1) Se presentan cuatro casos de ulceración faringea que ocu-
rrieron durante el tratamiento con estreptomicina.
2) Se señalan tres casos de recrudecimiento de dermatofitosis pre-existente.
3) En un caso hubo coexistencia de ulceración faringea y vulvar.
4) En un caso hubo ulceración faringea y dermatofitosis.

REFERENCES