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Inhibitory Effect of Tuberculo-protein Complex, Tubercin-3, on Three Cases of Lepromatous Leprosy

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ABSTRACT

Three cases of leprosy were successfully treated with a tuberculo-protein complex, Tubercin-3, which was prepared from Mycobacterium tuberculosis by Chung (J. Korean Med. Ass. 17:427-431, 1974) and no noticeable side effects were observed.

The three cases were brought to us without leprosy medication since their disease was recently diagnosed. Daily inoculations of Tubercin-3, 1.0 microgram on the forearm, subcutaneously for 8 months in Case 1, 7 months in Case 2, and 6 months in Case 3, cleared them of their lepromatous lesions.

INTRODUCTION

Recently many researchers have attempted to treat cancer of both humans and animals by stimulating the reticulo-endothelial system through inoculations of BCG and its extracts (Bast, Jr. et al., 1974), expecting an enhancement of T-cell related immunity.

In 1973, Gajl-Peczalska et al. and Dwyer et al. found significant increase in B-cells and a decrease in T-cells in the peripheral blood among a group of lepromatous leprosy patients. Since lepromatous leprosy was due to Mycobacterium leprae infection we decided to use a substance for immunogenecity enhancement. We tried Tubercin-3 a low molecular weight protein complex prepared from tuberculosis bacteria in these severe cases of lepromatous leprosy.

CASE REPORTS

Case 1 (Fig. 1—4)

A 20-year old woman was referred to Presbyterian Hospital on February 4, 1974, for evaluation of her chronic severe skin disease for which she once attempted suicide. A year prior to this admission, she had suffered from a round 1 cm diameter reddish macular skin lesion on her chest which had then widened. New macules appeared and develeped into geographic lesions. Six months from the appearance of her first chest lesion, reddish macules and several small nodular lesions were noticed on the face and were treated with various antibiotics without effect.

When this patient was 5 or 6 years old, her mother developed leprosy. As a result, the patient was cared for at home of a relative.

On admission she showed many various sizes of typical lepromatous nodules on her face

(Fig. 1) with some degree of edema and irregular sized reddish lepromatous macules on her back and thorax. The patient was a well oriented and a moderately well nourished young woman who measured 156 cm in height and weighed 54.5 kg. On physical examination. there were no serious complaints except for those mentioned above. Chest X-ray was unremarkable. Routine urine, stool and blood examinations turned out to be within normal limits. The PPD test showed a weak positive reaction (5 mm×7 mm), bacillary index of the leprosy was 3.66, granularity index 2.0 and DRL test negative.

The Tubercin-3 treatment was initiated on February 18, 1974 with a daily subcutaneous injection of 1.0 microgram Tubercin-3 per 1.0 ml of saline on the patient. The edematous appearance of the face lessened within a month but the nodules remained on the face. The lesions on the chest and back were unchanged.

By May, most of the nodules of the face had disappeared except for two comparatively big nodules. Geographical lesions on her chest and back had completely disappeared. Bacillary index at that time showed 3.50, granularity index 6, and PPD positive (10 mm×12 mm). After 8 months of therapy, the patient's face appeared normal and no lepromatous lesions were noted on her body surface. Tubercin-3 treatment was discontinued on October 20, 1974. At follow-up examination on February 20, 1975 (a year after the beginning and 4 months after the cessation of therapy), the patient's skin appeared to be completely normal.

Case 2 (Fig. 5—6)

A 9-year old girl was brought to the leprosy clinic of the Presbyterian Hospital on April 4, 1974, by her father who had a leprosy history. She had a reddish tumor growing progressively on the chin and multiple reddish macules on the face, chest and abdomen. Her father reported that the lesion on the left cheek was first noticed as a small reddish macule in January 1974. It then gradually widened with increasing red coloration. In February, a corn size nodule had appeared on the chin. By the time of her admission in April, it had grown to walnut size. At the same time, several 4—5 cm in diameter reddish macular skin lesions also developed on her chest and abdominal area.

The patient was a moderately well nourished and well oriented girl who measured 116 cm in height and weighed 20.5 kg. On dermatological examination, there were elastic reddish walnut size lepromatous plaques on her chin; the reddish lepromatous macules covered all of the left cheek area; and several hypopigmented, hyperthetic typical leprosy lesions of 8—10 cm in diameter on her chest and abdomen.

Routine physical examination was within normal limits. Laboratory studies were within normal limits for complete blood cell counts, urinalysis, fasting blood sugar, and non protein nitrogen. DRL test for syphilis was nonreactive. The bacillary index for leprosy showed 3.5, granularity index 2.0, and the PPD test was negative in 48 hours. Chest X-ray appeared to be within normal limits. The patient was started on systemic Tubercin-3 treatment on April 10, 1974 with a daily subcutaneous injection in the forearm of 1.0 microgram of Tubercin-3 dissolved 1 ml of normal saline.

After one month of therapy, the patient's lepromatous macules on her left cheek were decreased considerably in size and in the reddish coloration. The lepromatous nodular plaque on the chin showed a decrease in size and the hypopigmented macules on the chest and abdomen also decreased in size. By July 1974,

the lepromatous macules on the left cheek had almost disappeared leaving slight pigmentation. The nodular plaque on the cheek also showed significant shrinkage and most of the macules on the chest and abdomen had disappeared.

After 6 months treatment, lepromatous macules on the left cheek had completely subsided leaving a faint brownish coloration. The nodule on her chin had flattened almost to the normal skin level and the leprosy macules on her chest and abdomen disappeared completely. Scratch biopsy from the lesion on her chest and abdomen disappeared completely. Scratch biopsy from the lesion on her chin showed a bacillary index of 3.6 and a granularity index of 5.0. PPD test was positive (5 mm×7 mm) which had been negative on admission. Tubercin-3 treatment was discontinued on November 14, 1974.

At the follow-up examination in March 1975 (a year after the beginning and 4 months after the cessation of therapy), the patient's face appeared normal and no skin lesions were detected on the chest or abdomen.

Case 3 (Fig. 7—8)

A 33-year old woman was admitted to the Presbyterian Hospital on April 11, 1975, for her skin disease. Physical examination on admission showed typical lepromatous leprosy on her face and body. Chest X-ray, routine urine, stool and blood examinations were within normal limits. The PPD test was negative, bacillary index of leprosy 5.16, granularity index 2.0, DRL test negative.

The Tubercin-3 treatment was initiated on April 20, 1975 with daily subcutaneous injections of 1.0 microgram Tubercin-3 per 1.0 ml of saline into the forearm of the patient. The progress of the disease showed similar patterns to the two cases above. Bacillary and granularity indices during the treatment were as follows:

Date of Examination	Bacillary Index	Granularity Index
Apr. 11	5.16	2
Jun. 20	4.83	4
Aug. 20	4.50	4
Oct. 20	4.50	5

PPD also turned positive on August 10. Until and up to October 1975, the edematous appearance of the face lessened 50% of the lepromatous nodules subsided and lepromatous lesions of the body surface were almost gone. Treatment is still continuing with significant imporvement.

DISCUSSION

In 1939, Fernandez, inoculated BCG into leprous children, whose tuberculin and lepromin test were negative. This induced both tests to become positive. He also suggested that BCG inoculation would help the prevention and treatment of leprosy.

Kim *et al.* (1970) reviewed the studies of BCG on leprosy since Fernandez (1939). They concluded in 1970, that it was difficult to eliminate circumstantial verification of patient groups (such as location, social class, wealth, etc.) and expect reliable data on such tests due to the long duration of incubation periods in this disease. Even the murine leprosy experiments with BCG did not conclusively prove the effectiveness or prevention of the disease. Kim *et al.* (1970) re-examined the effectiveness of BCG on murine leprosy and reported that it helped the prevention of the disease to some degree. In 1959, Old *et al.* reported the inhibitory effect of BCG inoculation on transplanted tumors in the mouse. They explained this phenomena with the suggestion that BCG inoculation stimulated the reticulo-endothelial sys-

tems. Gajl-Peczalka *et al.* (1973) and Dwyer *et al.* (1973) studied the number of T-cells and B-cells in peripheral blood of 26 cases of leprosy patients, calculated the ratio of T and B lymphocytes and observed the reduction of T-cells among them as compared to normal controls. During his study on isolation of the effective substance for the enhancement of reticulo-endothelial system, Chung (1974) was able to extract low molecular protein complex, Tubercin-3 from tuberculosis bacteria. He used it to obtain clinical improvement in 10 cases of patients with stomach cancer. Kim *et al.* (1976) observed that the exocrine function of stomach, pancreas and liver are little, or not at all, affected by the intraperitoneal Tubercin-3, BCG, OK-432 (Picibanil) or H-11 extract (Urine peptide) even after massive or repeated doses in rats.

Although Koch's postulates have never been fulfilled, leprosy is still considered to be a mycobacterial infection and it is on the basis that we used Tubercin-3 on leprosy cases and were able to improve the condition of the cases significantly. There has not been any side effect for these patients during the period of the treatment.

It is interesting to note that in Case 2 and in Case 3, PPD negativity turned to positive during the treatment. Tubercin-3 proved to be effective in the treatment of lepromatous leprosy as discussed in this paper. It may also be useful in the treatment of the disease due to the deficiency of delayed hypersensitivity.

Tubercin-3 did not induce antibody in several kinds of animals and did not react to PPD antibody *in vitro*.

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Case No. 1

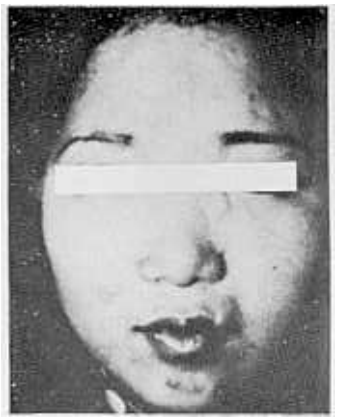

Fig. 1. Before treatment
Feb. 17, 1974

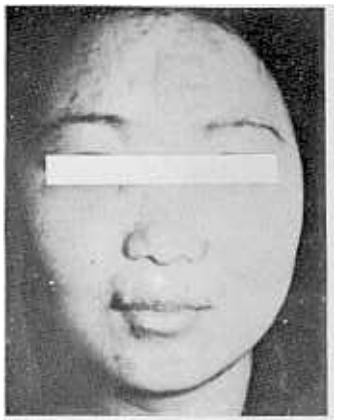

Fig. 2. T-3* treatment for a month Mar. 20, 1974

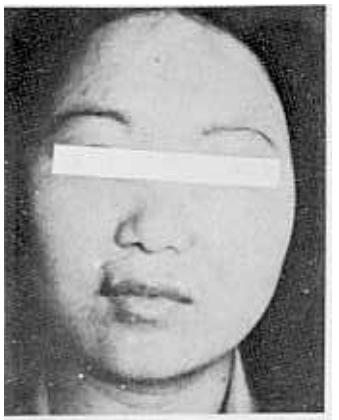

Fig. 3. T-3 treatment for two months
Apr. 20, 1974

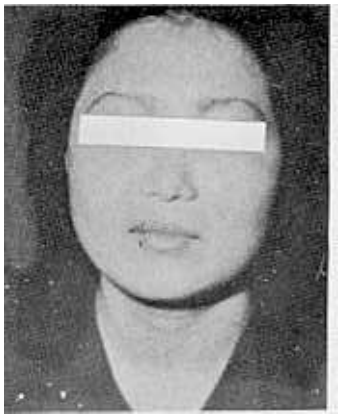

Fig. 4. T-3 treatment for eight months
Oct. 20, 1974
T-3* : Tubercin-3

Case No. 2

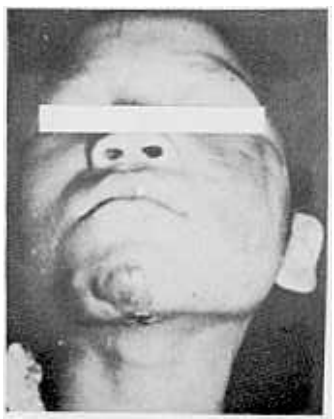

Fig. 5. Before treatment
Apr. 4, 1974

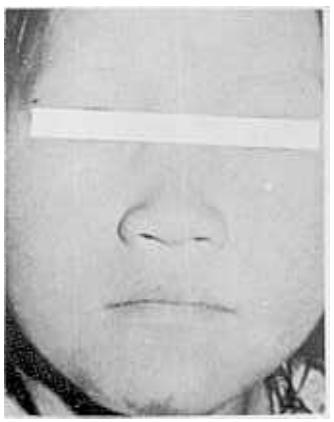

Fig. 6. T-3 treatment for 6 months
Oct. 4, 1974

Case No. 3

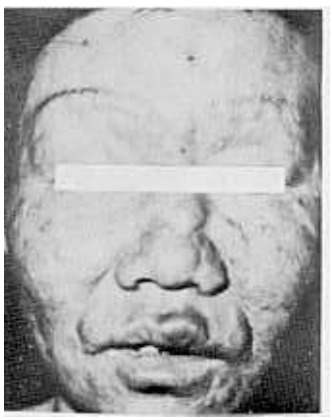

Fig. 7. Before treatment
Apr. 11, 1975

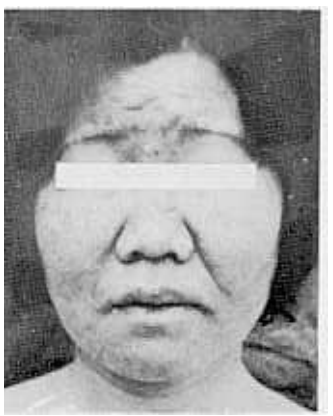

Fig. 8. T-3 treatment for 6 months
Oct. 20, 1975