A CASE OF LEPRA REACTION TREATED WITH CORTROPINE (ACTH)

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Lepra reaction is seldom seen in Norway, only one such case having been observed since 1931. The number of cases of active leprosy in Norway during this period was, however, very small.

It is possible that lepra reaction is an expression of an increased salutary process, and it has been maintained that the reaction depends to a certain extent on an allergic factor. It has also been pointed out that reactional conditions are comparatively common as a sequel to active treatment of the disease itself. To judge by the literature on the subject this reaction is not a desirable complication, as the patient's condition may be worse after it than it was before. Hitherto it has seemed that there was no treatment capable of arresting lepra reaction. Now, however, it would seem that we have such a remedy in corticotropin (ACTH)

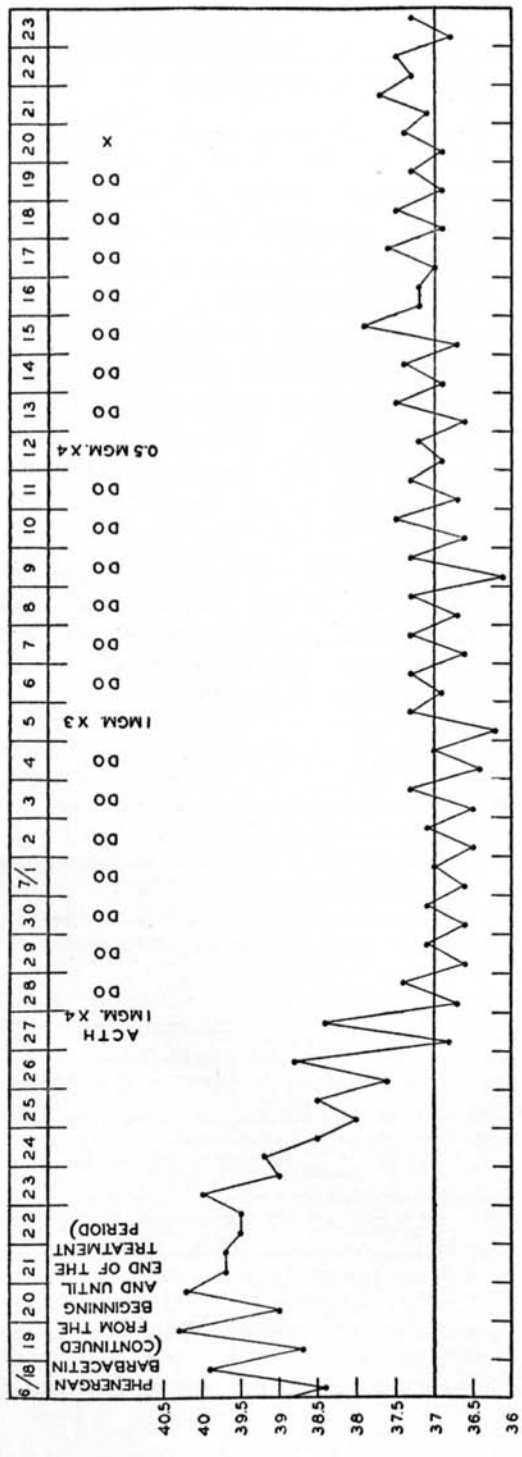
REPORT OF CASE

A man (S.M.), born in 1925, was admitted on January 10, 1951, to the Leper Hospital in Bergen. There was a history of much leprosy in his family and his mother and two maternal uncles had suffered from it. His mother was admitted to the hospital in 1931 with severe leprosy of the nodular form, and she died in 1933. Since 1931, neither the patient nor any of his brothers or sisters have been in contact with a case of leprosy. The father is healthy. Of a total of ten children, three died quite young. Four of the seven survivors are healthy, whereas three (one woman and two men) were found in 1950 and 1951 to be suffering from leprosy.

The patient had been perfectly well until 1940, when he noticed that his hands had begun to be frail and weak. Accordingly, he consulted a neurologist, who diagnosed a disease of unknown origin of the peripheral nervous system and prescribed electrical treatment.

The patient's condition remained unchanged until the summer of 1950, when he noticed that a rash had begun to appear on the trunk and limbs, and nodules on the thighs and legs. He did not consult a doctor about this rash, as it did not trouble him. It was not until his sister was found to be suffering from leprosy that he presented himself for examination.

On admission to the hospital (January 10, 1951) the peripheral nerves of his face and limbs were found to be involved. There was slight hypoesthesia of the left side of his face and slight paresis of his left orbicularis oculi. There was also hypoesthesia of all the sensory functions from the



TEXT-FIG. 1. A portion of the temperature chart of the case reported, beginning on the thirtieth day of the febrile period, showing the prompt apparent effect of the administration of corticotropin despite the small dosage employed.[1]

[1] For consideration of space this chart (redrawn from the original one supplied) does not include the earlier part of the febrile period.—EDITOR.

fingers, to a point in the middle of the upper arms. The fingers showed slight flexor contracture, and there was marked atrophy of the muscles of the hands. Both ulnar nerves were tender on pressure and slightly thickened. Hypoesthesia was also observed from the toes to a point in the middle of the thighs, but there was no definite paresis or atrophy of the muscles of the legs. The peroneal nerves on both sides were tender on pressure.

The patient presented an extensive maculopapular rash. On the limbs there were numerous patches, large and small, to some extent confluent. The thighs and legs presented numerous sharply defined nodules of a firm, elastic consistency. A biopsy showed a leproma with numerous typical leprosy bacilli.

The sedimentation rate was 25; hemoglobin (Sicca colorimeter) was 88 per cent; the erythrocytes numbered 4.3 millions, and the leucocytes 9,200.

Treatment with promin solution (5 ml.) was started at once, being given every day in series of two weeks with an interval of one week. This treatment was well tolerated. The patient remained quite well. His general condition improved, and there was definite retrogression of the clinical symptoms.

On May 19, 1951, however, a change set in and a rash appeared. It began as definitely raised, sharply defined, bright red infiltrations, of about the size of an almond, on both upper eyelids. His evening temperature was 39.5°C. and he felt unwell, suffering from fleeting pains in the limbs. During the next few days the infiltration of the thighs grew steadily larger, and those over the nose became confluent and spread upwards to the forehead. New infiltrations of the same appearance and character also developed on the arms and legs. There was, however, absolutely no flare-up of the old rash, neither of the patches which had now diminished greatly nor of the nodules of the thighs and legs.

There was violent pain in the peripheral nerves, a few of which were very tender on pressure. The auricularis magnus on the right side of the neck was in particular excessively tender, and as thick as a pencil. After only a few days the patient noticed increased loss of sensation in his hands and feet; the hands became weaker, and a definite bilateral peroneus paralysis set in.

After this condition had lasted about two weeks, the evening (peak) temperatures ranging between a maximum of 39.8°C. and a minimum of 38.6°C., there ensued a period during which the trend was somewhat downward, to only 38°C. on the 25th day, and the patient felt a little better. After that, however, the temperature increased steadily to a maximum of 40.3°C. on the 32nd day, and the patient seemed to be very exhausted; he felt tired and listless, and his appetite was very poor. The sedimentation rate was now 100. Definite anemia had developed, and the hemoglobin was 70 per cent, it having been 93 per cent 14 days before the reaction. The curve for the last three days of this period of rise, and until the end of the treatment period, is shown in Text-fig. 1.

As soon as the reaction began the patient received treatment with sedatives and an antihistamine preparation with protracted action (phenergan). The treatment had no effect apart from the relief and sleep it afforded.

I now decided to give ACTH (cortropin) a trial in the hope of stopping the reaction, and this was started on June 27, on the 40th day of the reaction. By mistake, very small doses were given—1 mgm. four times a day for eight days, 1 mgm. three times a day for seven days, and then 0.5 mgm. four times a day for eight days. The treatment previously given (barbacetin and phenergan) was continued. During this treatmet period the eosinophil cells were counted and the blood pressure measured each day. These examinations revealed no great changes; the eosinophil count ranged between 500 and 200 and the blood pressure between 120/90 and 140/120. The blood sugar was normal all the time.

The results were striking. The patient became afebrile, as shown in the chart, as early as the second day after the institution of the treatment. His general condition improved so much that he was able to get up on the twelfth day of the treatment. His appetite improved greatly, and the pain diminished. The rash disappeared gradually, and the pareses diminished considerably. The improvement continued after the treatment with cortropin was discontinued, although he still developed a few new bright red infiltrations on arms and legs. These infiltrations were not, however, accompanied by general symptoms or signs of new involvement of the peripheral nerves.

A biopsy of one of these lesions led to the following report:

Under the microscope the specimen of tissue is seen to be covered by flat epithelium in several layers, with cornification. In the corium, and further down in the subcutis, a nodular infiltration consisting of macrophages, lymphocytes and a few scattered granulocytes can be seen. The cells are plainly arranged in knots and around the vessels, whose walls are seen to be thickened. The small veins would seem in particular to be involved. On staining for acid-fast bacilli small, short intracellular rods are to be seen, scattered and in small groups. Acid-fast bacilli are also to be seen in the walls of the vessels. Thus the picture is one of a curious nodular, periarteritic and periphlebitic process in the skin. In a specially stained section no definite relationship to nerve fibers is to be seen.

Diagnosis: Leprosy (a periarteritic and periphlebitic process). Signed: Prof. Erik Waaler, M.D., Dr. F. G. Gade's Pathological-Anatomical Laboratory, Bergen.

The histological examination of this rash which developed during a lepra reaction presents a curious picture, with numerous leprosy bacilli. It may be assumed that during lepra reaction a hematogenous spread of the bacilli takes place, with a severe reaction on the part of the organism.

No conclusions regarding the effectiveness of corticotropin

in controlling lepra reaction can, of course, be drawn from a single case. It is impossible to conclude whether the effects observed after the institution of the treatment were due to the drug, or if it coincided accidentally with a spontaneous remission of the reactional process. It is also possible that a psychic factor may have played a part, for it took us several days to obtain the cortropin, about which the patient had been told and for which he had waited in tense excitement as a "marvellous medicine."

This case is nevertheless published because it so very well supports the observations of Roche and associates (1). I did not, however, see their article till several months after my own observation had been made. In this Norwegian case the effects were apparently more lasting, and were achieved with a considerably smaller dosage.

SUMMARY

A case is recorded of lepra reaction with an apparent favorable response to cortropin. No conclusion can be drawn, but the result is in accord with those reported by Roche and associates in Venezuela, the beneficial effects apparently more lasting.

ADDENDUM. After this article was submitted for publication this patient had another reaction episode, in November 1951, he having remained afebrile until then. After about two weeks he was again treated with corticotropin, first with a long-stored lot obtained from Holland, which had less effect than was obtained during his previous episode, and then with a new Norwegian product under which the patient became afebrile within a week. Since then (until the time of writing, April 1952) he has remained perfectly well; there has been no skin eruption, and the sedimentation rate went down from 100 to 25. Also since this article was written, we have had two other cases of lepra reaction.

RESÚMEN

Se reporta un caso de reacción leprosa, el primero en Noruega desde el 1931, en un paciente que había estado bajo tratamiento con promina por cerca de cuatro meses. El paciente desarrolló nuevas lesiones en la cara y las extremidades, acompañadas por fiebre y dolores neuríticos agudos. No hubo mejora alguna con el tratamiento dado, (sedativos y una droga antihistamínica); el paciente guardó cama y se tornó demacrado. A los 40 días de haberse desarrollado la reacción, se empezó a administrar corticotropina, pero por error en dosis muy pequeñas, 1 mgm. cuatro veces al

día durante los primeros 8 días y aún menos durante los subsiguientes 15 días; también se continuaron las drogas administradas previamente.

La fiebre desapareció durante el segundo día de tratamiento, y el paciente mejoró rápidamente en su estado general. La mejora obtenida continuó después de haberse descontinuado, la corticotropina, aunque aparecieron por algún tiempo nuevas infiltraciones en las extremidades. Se incluye el resultado de una biopsia de una de las lesiones.

No se puede derivar conclusión alguna con un caso solamente, y hasta es posible que el resultado obtenido fué coincidencia y también que algún factor psíquico estuvo envuelto. No obstante, los resultados coinciden con aquellos reportados por Roche y sus asociados en Venezuela, y hasta aparentemente más prolongados. Esto indica que ahora tenemos a mano un remedio capaz de arrestar reacciones leprosas. Esto es confirmado por el resultado obtenido en una reacción subsiguiente.

REFERENCE

1. ROCHE, M., CONVIT, J., MEDINA, J. A. and BLOMENFELD, E. The effects of adrenocorticotropic hormone (ACTH) in lepromatous lepra reaction. Internat. J. Leprosy **19** (1951) 137-145.