THE QUESTION OF A MIXED INFECTION FROM SYPHILIS AND TUBERCULOSIS.

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[THE following formed part of a paper read before the American Dermatological Association at Richfield Springs, N. Y., in September, 1890. It was not published at the time, partly because some further investigations in the same line were contemplated, and partly because the coming of tuberculin promised an easy and definite solution of the question at issue. Tuberculin, however, has proved disappointing, not only from a therapeutic, but also from a diagnostic standpoint, for although it has been shown to have a relative diagnostic value, it cannot be relied upon as an absolute test. It has been thought proper, therefore, to put upon record the experimental studies embodied in this paper, which, although few in number, may serve a purpose in connection with others of a similar nature. Since the paper was written a short *résumé* of a dissertation on this subject by Leppendorf, Würzburg, has come to my notice. The material was offered by a case of lichen syphiliticus, in which signs of tuberculous infection also were present. No tubercle bacilli were found in the tissue excised. A papule of the lichenoid eruption was inserted in the eye of a rabbit, but failed to produce tuberculosis.]

The histological characters of tubercle were, as is well known, considered for some time to be pathognomonic of this affection. The Langhans giant cell with its peripherally arranged nuclei, necrotic centre and protruding processes, was considered when taken in connection with the other characteristics of the so-called Wagner-Schüppel tubercle to make up a picture found only in true tuberculosis. Later, doubt was thrown on this view by the discovery of typical Langhans cells in other conditions.

Baumgarten, who has interested himself especially in this subject, published a series of papers, showing that he had found Langhans cells in gummatous nodules of the liver, in gummatous lesions of the dura, and in the tissue about vessel ligatures. Of six cases of gummatous orchitis, three were found to contain Langhans cells in large numbers. Hence, he concludes that Langhans giant cells can no longer be considered typical of tuberculosis. In 1884, however, in a paper published in Virchow's *Archiv*, Bd. 97, Baumgarten declares that he has modified his previous view somewhat, and that he regards those cases of syphilis where Langhans cells and the Wagner-Schüppel tubercle structure are present, as mixed forms of syphilis and tuberculosis. For the support of this view he adduces the following reasons:

(1) It appears improbable, from his own observations and those of others, that any other process besides tuberculosis that is developed spontaneously in the human body, possesses the power of producing Langhans giant cells or the structure of the Wagner-Schüppel tubercle.

(2) The subjects who present gummata in which the Langhans cells and the type of the Wagner-Schüppel tubercle are found, almost always shows unmistakable signs of a present or past tubercular infection.

(3) The gummata of syphilitic subjects who can be positively demonstrated to be free from tubercular complication, are never found to contain Langhans cells or the tubercle structure.

(4) The initial lesion of syphilis, as it is caused by the direct action of the syphilitic virus, and must be looked upon as the type of the specific affection of the tissues, never contains Langhans cells or a typical tubercular structure, but accords histologically with the pure gummata of skin, periosteum and internal organs.

In 1889, the subject was taken up anew by Michelson, who published an interesting article in Virchow's *Archiv*, entitled, "Is lichen syphiliticus the product of a mixed infection of syphilis and tuberculosis?" He publishes a sequence of three cases of small papular, lichenoid eruption in members of the same family, which proved to be examples of syphilitic lichen. Papules excised from two of these cases showed in the corium a typical Wagner-Schüppel tubercle structure, with Langhans giant cells. This accords with the anatomical researches of Griffini, who in 1875 described the papule of lichen syphiliticus as made up of nodules of tubercular structure immediately below the papillary layer, containing giant cells more or less branched and with peripheral nuclei, surrounded by a mass of epithelioid and lymphoid cells.

Neumann also has described and pictured giant cells in these papules of lichen syphiliticus that accord pretty well with the Langhans type.

Michelson, therefore, considers that there are grounds for questioning whether the syphilitic lichen be not a complication of syphilis and tuberculosis, as Baumgarten had suggested for those gummatous lesions where Langhans cells are found. This view he finds supported by the fact that the lichenoid syphilide is found in cachectic or tubercular subjects, and that it is especially obstinate and often relapses. His attempts to find tubercle bacilli in the excised papules, were, however, totally unsuccessful.

My attention having been called to the structure of the lichenoid syphilide by this article of Michelson's, an opportunity to study it was offered by what was to all clinical appearances, a typical instance of this form of specific eruption, which I will briefly describe.

CASE A. T. D., male, nineteen, May, 1890.

Of good family history, had been well, with the exception of an abscess in the axilla a year and a half ago. Date of infection uncertain. Six weeks ago the eruption appeared on the back of the neck extending downward. Now presents a grouped, lichenoid eruption of trunk, arms and legs with a few large papules interspersed. The glands behind the ear are enlarged, and a long chain of epitroclear glands can be felt. Glands in groin not especially altered. No alopecia. Nothing abnormal found on physical examination of the chest.

The patient was treated with mercury by inunction and appeared ten days later with an iritis, whereas the cutaneous lesions had diminished.

July 8th. Eruption had practically disappeared, leaving only a few spots of pigment. Iritis much improved.

No possible doubt can be entertained, from the clinical appearances, and from the result of treatment, that this was a typical instance of lichen syphiliticus. No symptoms of tuberculosis could be found. The patient's appearance was, as is so customary in this form of syphilis, somewhat cachectic, but his general health improved rapidly as the eruption disappeared.

Histological Examination.—Several papules were removed from the back. The horny layer somewhat

thickened. In the centre of each papule examined, could be seen the follicular opening, enlarged and filled more or less completely with horny matter. The papule is seen to be caused by an infiltration of cells around the follicle in the upper part of the corium. The papillæ over this cell infiltration are effaced. The infiltration is made up of epithelioid and round cells with very numerous Langhans giant cells. There was no cheesy degeneration or suppurative change.

Sections from two different papules were examined for the tubercle bacillus by Ehrlich's method with much care. Forty-four sections from one papule and twenty-nine from another were searched with an absolutely negative result.

Inoculation Experiment.—May 21, 1890, two more papules were removed antiseptically and after being crushed and mixed with sterilized water, were injected into the abdominal cavities of two rabbits.

July 9th. The two rabbits, who had remained apparently healthy, were killed. Examination showed nothing abnormal, with the exception of some foci with a necrotic centre in the liver of one of the rabbits. The amount of fibrous growth at the periphery suggested a not very recent process, and there was nothing in their histological appearances to warrant the diagnosis of a tubercular process, nor could the bacillus of tuberculosis be detected.

This case, while it accords with the descriptions of Griffini, Neumann and Michelson as to the histological structure of the lichenoid syphilide—showing it to be made up of a cell structure that cannot be differentiated from that of tubercle—brings no support to the theory that this form is a combination of syphilis and tuberculosis. There were no tubercular symptoms, no bacilli were found, and inoculation experiments failed in two instances to produce tuberculosis.

Another instance of the presence of Langhans giant cells in a presumably syphilitic tissue was found in the following case:

CASE B. E. H., male, age thirty-five, May, 1890. No history of previous troubles. For three years has had an affection of the scrotum which has repeatedly broken down into ulcerations. Was operated on in March, 1888, when he says a part of the right testicle was removed, and that the wound never healed entirely. He now presents an ulceration of nearly the whole scrotum, without apparent implication of the testicles, with somewhat indurated edges. In places are islets of firm, cicatricial tissue.

Patient was treated with iodide of potash in ten-grain doses three times a day, and the ulcers dressed with boracic acid ointment. In a week a great improvement had taken place, and at the end of three weeks the ulceration had entirely healed.

Histological Examination.—Pieces of tissue excised showed beneath the ulcerated surface, in the lower layers of the corium, a granulation tissue, and in almost every section one or more typical Langhans giant cells. No arrangement of the cell growth in clusters, such as is seen in the typical Wagner-Schüppel tubercle, was found in this case. Examination by Ehrlich's method of a small number of sections failed to detect a single tubercle bacillus.

Inoculation Experiment.—May 21, 1890, secretion and pieces of tissue were taken from the ulcer of the scrotum, were mixed with sterilized water, and injected into the peritoneal cavity of two rabbits. July 9th, the rabbits, who had appeared healthy, were killed,

and post-mortem examination revealed nothing abnormal.

The diagnosis of syphilis, which could not be positively made from the clinical appearances, was rendered pretty clear by the result of treatment with the iodide of potash. The histological examination on the other hand was able to throw little light, as appearances were found that have been by some considered characteristic of tuberculosis. The failure to find the tubercle bacillus, and the result of the inoculation experiments, while they offer no conclusive proof that the affection was not of a tuberculous nature, may be accepted as negative evidence of considerable weight. There can be little doubt that the ulcer was a syphilitic gumma, and the presence of the Langhans cells accord with the reports of those who have observed these cells before in lesions of this nature. The negative result of the bacteriological search and of the inoculation experiments, brings no support to the view that there was a complication of syphilis and tuberculosis.

It may, then, be positively asserted, that, in certain syphilitic lesions, namely, in gummata and in the lichenoid syphilide, the histological appearances are not to be differentiated from those of true tubercle. Moreover, Neumann asserts that giant cells are to be found in disseminated papules, in the pustular and lichenoid forms, in tubercula cutanea, and in subcutaneous gummata. He is not, however, always careful to show that he means cells of the Langhans type, a point of the utmost importance, inasmuch as the term giant has been applied to large cells with several nuclei, which are found in a variety of conditions, and which bear little or no resemblance to the Langhans type. He speaks, however, in his paragraph on giant cells in such a way as to lead us to infer that he always has in mind the Langhans type, and this is besides shown in some of his illustrations.

In pathological conditions other than syphilis, however, there is as yet,¹ so far as I am aware, no record of the discovery of Langhans cells or of the Wagner-Schüppel tubercle structure, with the exception of a case of Baumgarten, where these appearances were found in a sarcoma of the tibia, the subject of which finally died with generalized abdominal tumors, so that the case was regarded as unique.

The theory that in these cases we have to do with a mixed infection of syphilis and tuberculosis has not as yet received other support than that offered by the histological appearances. No tubercle bacillus has been found, and, so far as I am aware, there are no records of inoculation experiments besides those above mentioned, which proved negative. Still it must be admitted that this is merely negative evidence, and of value only if repeatedly verified.

It may be asked, of what significance in a doubtful cutaneous lesion, is the demonstration of Langhans cells and of the tubercular structure? With our present data we may say that we know of but two affections, syphilis and tuberculosis, where the cutaneous lesions may offer these appearances, but that in cases where the search for tubercle bacilli is not made, or proves negative, we are seldom justified in making a differential diagnosis from the histological structure alone.

¹ Since the above was written an article has appeared in the *Annales de Derm. et de Syph.*, by Barthélemy, describing a peculiar affection termed *acutis*, in which giant cells of the Langhans type were found by M. Darier.