

ERYTHEMA NODOSUM LEPROTICUM

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The position of erythema nodosum seems to be shared by a good many skin diseases which, despite all attempts, are still difficult to classify according to their etiology. From the appearance of the lesions and from the course of the disease one feels rather inclined to believe in the probability of its being an infectious disease, though varied in its nature. These features are suggestive enough in the majority of the cases to permit the acceptance of this view as a possibility. That we are not dealing with a uniform etiology, however, is evident.

Whether we should accept an idiopathic and a symptomatic erythema nodosum is still an unsettled question. According to many investigators the so-called idiopathic erythema nodosum is a well defined clinical entity, and any deviation from the well known picture should not be designated simply as erythema nodosum but the respective etiological adjective should be added, as in erythema nodosum mycoticum, typhosum, etc.

Erythema nodosum idiopathicum is ushered in by constitutional disturbances (fever, rheumatoid joint pains) which are frequently preceded by tonsillitis. This is followed by the appearance of hazel- to walnut-sized subcutaneous nodes and nodosities which are symmetrically distributed over the extensor surfaces of the lower extremities, rarely on the upper extremities and extremely rarely on the trunk or the face. These lesions have a faintly outlined, rather edematous border, and are painful to touch. They have no tendency to extend peripherally or to become confluent, and rarely break down. The nodes do not preserve for long their original color, changes taking place in a few days similar to those which are observed in bruises; a bluish, brownish or greenish discoloration is produced, for which reason erythema nodosum is also called erythema contusiforme. After three to four weeks complete recovery takes place, without scar formation.

This is the classical appearance of erythema nodosum idiopathicum, which affects children most frequently but, in a slightly

modified form, also affects adults. While we are quite familiar with the characteristic clinical features of the condition, we are still not in a position to reach any definite opinion as to a uniform etiology. There are quite opposing conceptions, each of which is supported by reasonable and convincing arguments.

The view that erythema nodosum in children is caused by the tubercle bacillus in a majority of cases is, however, rapidly gaining place, and the hypothesis of rheumatic (streptococcal) etiology is gradually losing its supporters. But besides these etiological factors practically all infectious diseases play a causative role in the condition. Toxic lesions of similar nature have been also observed after medication with iodides, bromides, salicylates, phenactin and salvarsan. Infectious diseases which are mentioned most frequently as the cause of the condition are scarlatina, measles, typhoid fever, syphilis, gonorrhoea and lymphogranuloma inguinale. Moon and Strauss even described an entirely new organism, the *Corynebacterium cutis nodosae*, which seems to be identical with one described by Rosenow.

Leprosy is hardly ever mentioned as a cause of erythema nodosum. In the available literature I have found only two references. Burgos Cid observed two cases which developed leprosy during the course of the disease. Hayashi reported that 50 percent of his erythema nodosum cases started in young lepers, generally two years after the onset of the disease, and two to six years after the appearance of nodules. A relationship with treatment has been also noticed by him in that the condition appeared one year after treatment began in 48 percent of the cases and two years after it in 23 percent. The most frequent localization was the face and less frequently the forearm and thigh. During the attack leukocytosis, with decrease of erythrocytes and hemoglobin, were observed.

Because very little attention has hitherto been paid to this manifestation of cutaneous leprosy in the literature of that disease, and because the cases observed by Burgos Cid and Hayashi had a slightly different clinical course from ours, it is not without interest to report the following two cases:

CASE REPORTS

CASE 1.—Hsia Chin Chen, male, aged 29, policeman, O.P.D. No. 0620. *Symptoms:* Numbness over left clavicular regions for 5 years, and then of the right small toe and left middle toe two years ago. Swelling of legs accompanied by numbness one year ago. Later numbness of forearms hands and

lower trunk developed, one after another. *Examination* (January 5, 1935): Face swollen, with diffuse, hypoesthetic, oval, light yellowish macular eruptions the size of a twenty-cent piece to a dollar scattered over trunk and extremities. Anesthetic areas over trunk and extremities, more marked below knees. Ulnar nerves bilaterally thickened. *Laboratory findings:* (a) Total white count 11,200, with 76 percent polymorphonuclears, 16 percent large lymphocytes, 4 percent small lymphocytes and 4 percent eosinophiles. Erythrocyte count normal. (b) Blood Wassermann and Kahn tests negative. (c) Blood sedimentation 10 mm. (d) Leprolin test only slightly positive. (e) Nasal smears reveal numerous acid-fast bacilli. Treatment started on April 15, 1935, iodized chaulmoogra oil (Culion), 2 cc. intradermally three times a week, and 10 percent sodium thiosulphate, 10 cc. each time (started on May 17). The subjective feelings became much better. Macular eruptions were fading and anesthetic areas diminishing when examined on June 15th. The leprolin test, repeated on August 25th, showed a slightly positive reaction.

On September 13 the patient developed fever with reddish macular patches over the whole body, and swelling of the face, hands and feet. Some of the patches were around the sites of previous lesions where sodium thiosulphate and iodized chaulmoogra oil had been injected. Since that time he has received injections only at irregular intervals.

On February 2, 1936, the patient came back again with painful, hemorrhagic, subcutaneous nodes over the extensor aspects of the extremities, of one week's duration. Local smear negative, but one week later a second examination revealed the presence of acid-fast bacilli. Nasal smear negative. In addition to the hemorrhagic nodules, which varied from the size of a pea to that of a twenty-cent piece, there were also subcutaneous nodes covered by normal skin over the extensor surface of upper parts of legs, forearm and arms. *Laboratory examination:* Total white count 11,200, with 76 percent polymorphonuclears, 16 percent large lymphocytes, 4 percent small lymphocytes and 4 percent eosinophiles. Wassermann and Kahn negative. Some of the nodules became crusted, but by March 5 they had healed without the formation of a scar. *Histological examination:* The epidermis is thickened. In the cutis and subcutis, particularly surrounding the blood vessels and glands, there are patches of granulomatous change, which consists chiefly of round and spindle shaped mononuclear cells and foamy cells. Some of the patches show necrosis in the center, where fibrinous and leukocytic exudate is found. Several nerve trunks are found inside the necrotic part; the perineurium and endoneurium are infiltrated with cells and the nerve fibers are partly preserved in structure and partly degenerated. Sections reveal some acid-fast bacilli intracellularly in and around the necrotic part.

CASE 2.—Sun Tsai Pao, male, aged 15, student from Kiangyin, admitted March, 12, 1936. *Symptoms:* Anesthetic patch on left forearm for three years with alopecia and anhydrosis of the same duration. Numbness on right knee for about two and one-half years, and on left buttock for two years. Swelling of left face with patch of anesthesia, one year. The area of numbness on the right forearm and arm extended gradually. Examination reveals loss of eyebrows and infiltrations on both lower legs, forearms, right buttock and face. Both ulnar and both common peroneal nerves thickened. Touch sensation only slightly impaired over right buttock, sensation to pain and

heat and cold preserved. Slight muscular atrophy on left ulnar side and anhydrosis of left arm. Otherwise essentially negative. Family history and past history noncontributing. *Laboratory findings:* (a) Blood Wassermann and Kahn negative. (b) Nasal and skin smears positive. (c) Blood sedimentation 1 mm. in 30 minutes, 6 mm. in 40 minutes. (d) Urine normal. (e) Total white count 10,200, erythrocytes 5,204,000, hemoglobin 90 percent. On September 29 the total white count was 2,600, erythrocytes 3,360,000, hemoglobin 70 percent. (f) *Ascaris* eggs in stools.

Treatment started on March 14, consisting of biweekly intradermal injections of 2 cc. iodized chaulmoogra ethyl esters. On September 17 the patient complained of general body ache and headache, with malaise and slight fever (high, 100° F.). One week later the temperature rose to 101° F., with intense headache and chilly sensations, and on the next day reddish-brown nodular lesions developed on the extensor surfaces of the forearms and legs. These lesions faded gradually, leaving a greenish brown discoloration, while the temperature dropped by lysis.

Histological examination: Epidermis normal except for slight hyperkeratosis. Underneath the papillae are several foci of granulomatous tissue, composed chiefly of epithelioid cells and large mononuclear wandering cells, with a few polymorphonuclear leukocytes, lymphocytes, and here and there young fibrocytes. In the deeper layers of the cutis bordering the subcutaneous strata there are several large agglomerations of the same type of granulomatous tissue, more or less localized around the blood vessels. The endothelial cells of the vessels are rather swollen. In one of the nodes there is indication of giant-cell formation. Sections reveal some acid-fast bacilli.

DISCUSSION

In both of the cases described the clinical picture, the course of the condition, and the histopathological changes are undoubtedly of such a nature as to bring these cases within the type of erythema nodosum. While in Case 1 the localization was not the classical one, and the lesions had a tendency to crust formation, the microscopic changes corresponded to the clinical findings, with slight difference. One could also consider in this case the possibility of a lepra reaction, as the eruptions developed during the treatment, a fact which plays the most important role in lepra reaction. However, the pure node-formation on the one hand, and the special localization on the other hand, differentiate this picture from the irregularly scattered old leprosy lesions which generally flare up in lepra reaction. In none of the cases was there rheumatic pain, or any involvement of the heart.

That we are dealing in both instances with a hematogenous metastatic dissemination of the leprosy bacilli is clearly shown by the histological changes in the cutis. The sites of the main attack are the vessels and the perivascular region. That the lesions are not produced by toxins but by the bacilli themselves has been

demonstrated in the sections and by repeated smears from the lesions. In Case 1 the bacilli disappeared after the resolution of the eruption, whereas in Case 2 they could be found in the site of the lesions for many weeks after the disappearance of the nodes. The possibility of a mixed tuberculosis infection has been ruled out by guinea-pig inoculation, and by further observations that no frank tuberculosis developed, as may occur as a sequel to erythema nodosum idiopathicum.

CONCLUSION

Two cases of erythema nodosum leproticum are reported, which give further evidence that erythema nodosum does not have a uniform etiology, but that we are dealing with a clinical syndrome in most of the cases. Erythema nodosum idiopathicum may be different, as it is clinically well defined, but in such cases the etiology is still uncertain.

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DESCRIPTION OF PLATES

PLATE 35

FIG. 1. Hypodermic nodules on both cheeks. Case 1.

FIG. 2. Several hazel-nut sized hypodermic nodules on the extensor surface of both forearms and hands. Case 1.

FIG. 3. Hazel- to walnut-sized hypodermic nodules on the extensor surface of both legs, in part with crusting. Case 1.

FIG. 4. Hazel- to walnut-sized hypodermic nodules on the extensor surface of the right forearm. Case 2.



PLATE 36

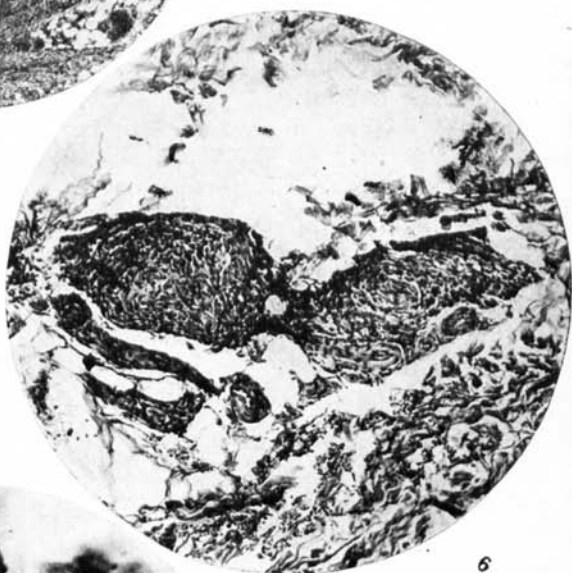
FIG. 5. Necrosis with fibrinous and leukocytic exudate. In the center the involvement of a nerve trunk. Case 1.

FIG. 6. Perivascular infiltration of epithelioid and large mononuclear wandering cells. Case. 2.

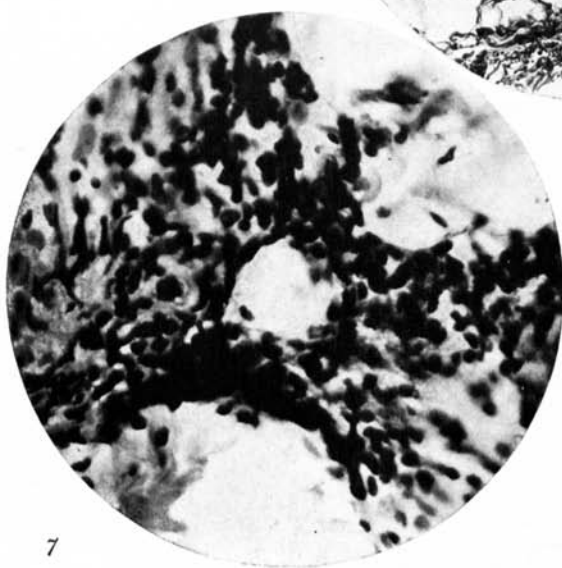
FIG. 7. High power magnification of a small lesion from the same section as Fig. 6.



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