Acute Exudative Arthritis in Leprosy—Rheumatoid-arthritis-like Syndrome in Association with Erythema Nodosum Leprosum

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Erythema nodosum leprosum is a fairly common complication of lepromatous leprosy and is variously reported to occur in 30 to 40% of all patients with lepromatous leprosy on sulphone treatment (Buu Hoi and Basset, 1963; Cochrane, 1964; Job et al., 1964). As yet there is no satisfactory explanation of the mechanism of production of erythema nodosum leprosum. Among the many hypotheses postulated, the concept of an immunological reaction as the fundamental basis of this rather dramatic complication is generally accepted (Aguas, 1963; Skinsnes and Tsang, 1963; Cochrane, 1964; Job et al., 1964). There is some evidence to link up this phenomenon with autoimmunity, such as the presence of lupus erythematosus cell and rheumatoid factor in the sera of a proportion of these patients (Cathcart et al., 1961; Bonomo et al., 1965; Matthews and Trautman, 1965; Karat et al., 1966). Pain in the joints (arthralgia) is a common and well-documented feature of erythema nodosum leprosum (Cochrane, 1964; Job et al., 1964). Lele et al. (1965) described five cases of leprosy presenting as rheumatoid arthritis. Except for Case 4, none of their patients had erythema nodosum. The synovial biopsy was done in four out of the five cases, and the main histopathological finding was infiltration by round cells, epithelioid cells, and occasional giant cells. In the patient with erythema nodosum synovial biopsy did not reveal any significant change.

In the past two years at Schieffelin Leprosy Research Sanatorium we have seen 10 patients with lepromatous leprosy who developed acute painful exudative polyarthritis clinically similar to acute rheumatoid arthritis during the course of erythema nodosum leprosum. The polyarthritis cleared up completely when erythema nodosum subsided, leaving no residual signs of rheumatoid arthritis, clinical or radiological.

We present the case reports of two of these patients who, during the course of erythema nodosum leprosum, developed acute exudative polyarthritis clinically simulating acute rheumatoid arthritis; in both of them synovial biopsies were carried out during the acute phase. The nearest to the description of this condition we can find is that of Davison (1961) and of Wheate (1962). Wheate gives the case report of one patient who had a unilateral small effusion into the knee joint and "ganglion-like swelling of the synovia of both wrists on the dorsal aspects."

Case 1

A man aged 30 was admitted to hospital with a history of recurrent attacks of erythema nodosum leprosum for one year while on dapsone. He had had leprosy for four years. During the last two attacks of erythema nodosum leprosum he had noticed swelling of the small joints of the hands, knees, and ankles.

On examination he was seen to be ill with diffuse infiltration of the skin over the trunk, limbs, and face; slight enlargement of the ears; thinning of eyebrows; a normal nose; a large number of erythema nodosum leprosum lesions over the face, trunk, and limbs; and bilateral ulnar and lateral popliteal nerve enlargement. There was no motor paralysis, but sensory loss over the feet.

He had spindling of the proximal interphalangeal and metacarpophalangeal joints of the right hand and swelling of the right wrist,

![Fig. 1.—Case 1. Swelling of metacarpophalangeal and proximal interphalangeal joints of the right hand. Swelling of right wrist is also shown.](image1)

with palpable thickening of synovium (Fig. 1), and effusion into both knees (Fig. 2) and both ankle joints. All the affected joints were tender and there was painful limitation of movements of these joints.

**Investigations.**—Haemoglobin 9 g./100 ml.; W.B.C. 21,000/cu. mm. (polymorphs 87%); erythrocyte sedimentation rate (Westergren) 32 mm. in first hour, 63 mm. in second hour; C-reactive protein four plus; antistreptolysin titre 333; Rose–Waaler test for
rheumatoid factor (D.A.T.) 1:4; skin smears for acid-fast bacilli 1+ (Wade's method 0–6 scale); total plasma protein 7.3 g./100 ml. (gammaglobulin 1.6 g.); L.E. cells negative. X-ray examination of hands, wrists, knees, and ankles showed generalised osteoporosis. No subarticular erosions were seen. Synovial fluid: protein 1.8 g./100 ml. (globulin 0.78 g.); sugar 50 mg./100 ml.; W.B.C. 22/cu. mm. (polymorphs 75%). Direct smear: no organisms seen with Gram's stain and Ziehl–Neelsen stain. Synovial fluid was sterile on routine and acid-fast bacillus culture.

Synovial Biopsy from Left Ankle.—On exploration of the ankle synovial membrane was found to be congested and thickened. There was villous hypertrophy. Clear straw-coloured fluid in the joint was aspirated and a synovial biopsy was taken. Histological examination showed numerous proliferating capillaries surrounded by inflammatory cells consisting of plasma cells and lymphocytes. There were focal collections of histiocytes and diffuse polymorphonuclear leucocytic infiltration. Acid-fast stain showed no bacilli (Figs. 3 and 4).

**Case 2**

A man aged 24 had had lepromatous leprosy for four years. He had been treated with dapsone for two years and during that time had had recurrent attacks of erythema nodosum leprosum. In the present attack he developed painful swelling of the metacarpophalangeal and interphalangeal joints of the hands, knees, ankles, and left elbow.

Examination revealed diffuse infiltration of the skin over the face, trunk, and limbs; erythema nodosum leprosum over trunk and face; loss of eyebrows; deformity of ears; partial collapse of the nose; enlargement of ulnar and lateral popliteal nerves on both sides with slight tenderness. There was no motor paralysis, but symmetrical loss of sensation in the feet.

He had spindling of proximal interphalangeal joints of fingers, and swelling of metacarpophalangeal joints, all of which were tender (Fig. 5); bilateral swelling of the knees, the right more pronounced than the left (Fig. 6); effusion into both the knee joints; painful limitation of movements of the knees; and painful swelling of and effusion into the right ankle joint (Fig. 7).

**Investigations.**—Haemoglobin 8.25 g./100 ml.; W.B.C. 11,000/cu. mm. (polymorphs 74%); erythrocyte sedimentation rate (Westergren) 116 and 138 mm. (first and second hours); C-reactive protein five plus; Rose–Waaler test for rheumatoid factor (D.A.T.) 1:32; skin smears for acid-fast bacilli 1.25+ (Wade's method 0–6 scale); total plasma protein 8.6 g./100 ml.; serum gammaglobulin 4.8 g./100 ml. (by paper electrophoresis method). No L.E. cells found on repeated examination. X-ray examination of hands, knees, ankles, and feet showed generalized osteoporosis. No erosions seen. Synovial fluid: W.B.C. 270/cu. mm., of which 45% were polymorphs; direct smear on Gram's stain did not show any organisms; Ziehl–Neelsen stain showed a number of acid-fast bacilli, most of which were granular. Synovial fluid was sterile on culture for routine organisms and acid-fast bacilli.

'Synovial Biopsy from Right Knee.—On exploration of the right knee the synovial membrane appeared thickened and congested. The synovial fluid was dark straw-coloured and opalescent. Histological examination of synovial tissue showed fibro-fatty tissue with marked increase in vascularity and an exudate consisting of fibrin and
numerous polymorphonuclear leucocytes. There was marked tissue oedema. Acid-fast stain did not show any bacilli in the synovial tissue, but there were fragmented bacilli in a nerve present in the tissue. The entire appearance was typical of acute arthritis.

Clinical Course and Management

The clinical course correlated very well with that of erythema nodosum leprosum—the acute arthritis either coincided with the onset of crops of erythema nodosum leprosum or followed its appearance in 24 to 48 hours. The joint manifestations cleared up 7 to 14 days after the subsidence of erythema nodosum leprosum. The usual measures, such as intravenous administration of 1% potassium antimony tartrate and oral chloroquine, were adequate to deal with the erythema nodosum leprosum, as well as the arthritis, at each subsequent episode of recurrence.

During the acute phase of arthritis local heat in the form of wax baths to the hands was very helpful in relieving pain as well as increasing the range of movement. Except during these periods of active physiotherapeutic measures, the affected limbs were immobilized in functional splints and maintained in elevation. Active exercises were encouraged as soon as the acute phase of the arthritis cleared up, to prevent flexion deformity and stiffness of the fingers.

Comment

General.—Arthralgia has been well recognized as a clinical manifestation of "reaction" in leprosy (Cochrane, 1964; Job et al., 1964). An acute exudative polyarthritis occurring in association with these exacerbated phases has not been well documented. The clinical manifestations of this polyarthritis in leprosy closely simulate the acute phase of rheumatoid arthritis and may be mistaken for the latter. Unlike rheumatoid arthritis, the clinical manifestations in the joints clear up when the erythema nodosum leprosum resolves, without any residual damage or manifestations in the affected joints—as seen so far during a two-year follow-up of most of these patients. The synovial fluid, which had the biochemical features of a transudate, was sterile on culture, both for pyogenic organisms and for acid-fast bacilli. The Rose-Waaler test for rheumatoid factor was positive in one of the two cases described here and in 6 of the 10 patients we have so far observed. The joints most commonly affected were the small joints of the hands—the metacarpophalangeal and the proximal interphalangeal joints—the knees, and the ankles. Effusion into the knees and ankles was uncommon.

Age and Sex.—Both patients (Cases 1 and 2) were young men. We have seen this syndrome in 10 patients, of whom only one was female. This is in striking contrast with the usual higher incidence of rheumatoid arthritis among young women (Robinson, 1963). On the whole, erythema nodosum leprosum occurs less commonly in women and is usually not as severely disabling as in men (personal observation). This may explain the rarity of the syndrome among women leprosy patients.

Disease and Its Complications.—All the patients had lepromatous leprosy of longer than three years' duration. In all of them the "rheumatoid syndrome" occurred only after recurrent episodes of erythema nodosum leprosum. We have not seen this syndrome during a first attack, nor in association with mild erythema nodosum leprosum. In all the patients there was involvement of skin and the subcutaneous tissues in the erythema nodosum leprosum process. Every one of them had systemic manifestations of fever, anorexia, and general malaise.

Histopathology of the Synovium.—In the affected joints this is of considerable interest and helps to substantiate the suggestion that this acute exudative "leprosus" polyarthritis is different from acute rheumatoid arthritis. In this condition there is well-marked infiltration of the synovial membrane with polymorphonuclear leucocytes, and the joint cavity shows an exudate of fibrin with numerous polymorphs entangled in it. The acute inflammatory reaction in the synovial membrane is very similar to that seen in the coexistent erythema nodosum lesions found elsewhere in the body. This is in contrast with the lymphocytic and plasma cell infiltration of synovium which characterizes rheumatoid arthritis (Anderson, 1957).

It is interesting to note that none of our cases—the two reported here and the other eight cases we have so far observed—all had lepromatous erythema nodosum. Whether these joint manifestations are "autoimmune" is open to debate. It seems as though the pathogenesis of these acute joint manifestations is linked with that of erythema nodosum leprosum, and elucidation of one should help in the understanding of the other.

Summary

The clinicopathological features of exudative polyarthritis simulating acute rheumatoid arthritis occurring in two lepromatous leprosy patients in association with erythema nodosum leprosum is, so far as we are aware, described for the first time.

It is suggested that erythema nodosum leprosum and the exudative polyarthritis occurring together may be aetiologically determined by an immunological phenomenon.

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