SYPHILITIC JUXTA-ARTICULAR NODES*

BY

T. PUTKONEN, H. TEIR, and K. PYÖRÄLÄ

From the Kumpula State Hospital for Venereal Diseases, Helsinki, and the Department of Legal Medicine, University of Helsinki, Finland

Juxta-articular nodes (Lutz, 1891; Jeanselme, 1924) have usually been reported from tropical countries where yaws and syphilis are endemic. Kalz and Newton (1943) state that only about 200 cases have been reported from non-tropical regions. In the Scandinavian literature only one report of such nodes (Fex, 1927) has come to our knowledge and we therefore wish to present four cases observed at the Kumpula Hospital.

Case Reports

Case 1.—A motor-car driver aged 54 was treated in hospital from May 28 to July 12, 1951, for meningo-vascular cerebrospinal syphilis.

History.—In 1918 he had had a hard-edged ulcer on the lip for 3 weeks. Later the same year he was forced to sleep for several months on a stone floor; nodes then appeared in the region of the hips, knees, and right elbow, and within a few years reached their present size. The nodes had occasionally suppurated during the first few years but they had never been tender. Since December, 1950, he had suffered from severe headache and attacks of vertigo. He had never had anti-syphilitic treatment.

Examination.—Clinical and x-ray examination of heart revealed no abnormality. X rays of legs showed traces of periostitis. Nervous system also appeared normal.

The following subcutaneous nodes were found:

- (1) about 5 cm. in diameter, 5 cm. distal to the right elbow;
- (2) the size of a goose's egg, in the region of the great trochanter on both sides;
- (3) about 3 cm. in diameter, below both knees, about 5 cm. from the lower margin of the patella;
- (4) a flat node on the left patella, covering its lateral half (Fig. 1).

The nodes felt cartilaginous, non-tender, and to some extent mobile upon the underlying tissue. Four scars were present on the node on the left patella; all other nodes showed only one such scar. The skin over the nodes could be moved freely everywhere except in the area of the scars.

Histological Examination.—A biopsy specimen from the node in the area of the left great trochanter showed

three zones (Fig. 2, overleaf). The outer zone consisted of a coarsely fibrous area, poor in cells. Further inward was granulation tissue with numerous dilated blood vessels in which endothelial thickening appeared in places. Plasma cells and lymphocytes, showing perivascular arrangement in some places, predominated. The centre stained rather uniformly, and, with higher magnification, a large number of thin fibres in network-like arrangement could be distinguished. Plasma cells and mononuclear macrophages were present here and there in the network. Macrophages were particularly abundant in the outer parts of this central zone.

FIG. 1.—Case 1, juxta-articular nodes and scars below both knees and on left patella.

Laboratory Studies.—Wassermann reaction positive (1:32), cholesterol Wassermann positive (1:64), Kahn test positive, sitolipin positive.

Cerebrospinal fluid showed a protein content of 77 mg./100 ml., cell count 1440/3, mastic test 3444210000, Wassermann positive in 0.5 and 1.0 ml., cholesterol Wassermann positive in 0.5 and 1.0 ml.

Therapy.—After 7.2 million units procaine penicillin with aluminium monostearate (P.A.M.) given between July 12 and 28, 1951, all the nodes regressed. One week after the last penicillin injection the nodes over both great trochanters had completely disappeared and the others had diminished.

* Received for publication November 5, 1952.

FIG. 2.—Case 1, photomicrograph of juxta-articular node. The outer zone (on left) consists of coarse collagenic fibres, the intermediate zone shows granulation tissue, and the inner zone shows necrosis. $\times 300$.

Follow-up.—On December 12, 1951, the node below the right knee had disappeared (Fig. 3) while those below the left knee and on the left patella had diminished to about half their previous size. The node distal to the right elbow had decreased to the size of a little-finger tip; it was removed surgically on April 2, 1952. Histological examination (Fig. 4) showed that the zone-like structure was no longer so distinct as it had been. The most conspicuous change, however, was in the resolution of the inflammation. The zone of granula-

tion tissue could no longer be distinguished, and the fibrous structure of the central zone had almost disappeared. Structureless debris surrounded by a slight inflammatory reaction was observed in places. The outer, fibrous layer had also altered in structure: the fibrous arrangement was no longer quite distinct and there were some granuloma formations with giant cells and also solitary multi-nucleated cells resembling the giant cells of Langhans; the nuclei in these were located at the periphery (Fig. 5).

FIG. 3.—Case 1, same nodes as in Fig. 1, 5 months after penicillin therapy; that below the right knee has disappeared, the others have diminished.

Case 2.—A farmer aged 31 was treated in hospital from September 29 to November 5, 1951, for meningo-vascular cerebrospinal syphilis. In December, 1950, an ulcer had appeared on the glans penis. In March, 1950, the patient had had a sore throat and noticed loss of hair, and wart-like formations around the anus. During the last year a non-tender node had developed on both hips. The patient had not received anti-syphilitic treatment. His wife had asymptomatic, sero-positive syphilis.

Examination.—A round, pale scar was observed on the glans, and scars of condylomata around the anus. Small, irregular pupils reacting normally to light, and diffuse choroido-retinitis in both eyes. Clinical and x-ray examination of the heart showed no abnormality. There was a non-tender node over the great trochanter on each side. These nodes were the size of the tip of the thumb and almost cartilaginous. They were mobile upon the underlying tissue and the skin over them could be moved freely and was entirely normal in appearance.

FIG. 4.—Case 1, photomicrograph of juxta-articular node 8 months after penicillin treatment. The zone-like structure is no longer clear. The most conspicuous change is the resolution of inflammation. In places there are granuloma formations with giant cells. $\times 300$.

FIG. 5.—Case 1, same specimen as in Fig. 4, solitary multinuclear cell resembling a giant cell of Langhans. $\times 1000$

FIG. 6.—Case 2, photomicrograph of juxta-articular node. The zone-like structure resembles that in Fig. 2, but the inflammatory changes are less pronounced. $\times 300$.

Histological Examination.—The right-sided node which was removed *in toto* showed an outer zone consisting of a coarsely fibrous tissue, rather poor in cells (Fig. 6). In the centre was a fairly oedematous, densely fibrous area poor in cells, and cords of granulation and scar tissue projected into it. This old granulation tissue was fairly abundant in the specimen, but in many other places there were large numbers of dilated blood vessels with endothelial thickening and perivascular infiltration by inflammatory cells. The majority of these inflammatory cells were lymphocytes but plasma cells were also present. There were some indistinct granuloma formations without giant cells.

Laboratory Studies.—Wassermann reaction positive (1 : 16), cholesterol Wassermann positive (1 : 16), Kahn test positive (1 : 16), sitolipin positive (1 : 256).

Cerebrospinal fluid study showed a protein content of 56 mg./100 ml., cell count 627/3, mastic test 3210000000, Wassermann positive in 0.5 and 1.0 ml., cholesterol Wassermann positive in 0.5 and 1.0 ml.

Therapy.—After therapeutic malaria and 9 million units procaine penicillin between November 18 and December 12, 1951, the remaining node disappeared entirely.

Case 3.—A workman aged 55 was treated in hospital from November 24 to December 12, 1951, for tabes dorsalis.

For the last 2 years the patient had had intermittent pain in the lower extremities, especially at night and during bad weather. In the same period a node had appeared on each hip causing tenderness when lying on the side. The patient had never been treated for syphilis. Sero-positive, asymptomatic syphilis had been diagnosed in his wife.

Examination.—Oval scar on the glans, Argyll Robertson pupils, and slightly ataxic gait. Knee and ankle jerks were absent and the sense of vibration was lost in both lower extremities. Clinical and x-ray examination of the heart revealed no abnormality. Slightly tender subcutaneous nodes were present over the great trochanter on each side. The nodes felt almost cartilaginous, were freely mobile upon the underlying tissue, and were unattached to the skin (Fig. 7). The node on the right side, which appeared bilobular on palpation, measured 3 by 3.5 cm., and that on the left 2.5 by 3 cm. The surface of both nodes was uneven. The covering skin was normal.

FIG. 7.—Case 3, juxta-articular node in area of right great trochanter.

FIG. 8.—Case 3, photomicrograph of juxta-articular node. Far advanced fibrosis in places with granulation tissue containing large numbers of inflammatory cells. $\times 300$.

Histological Examination of the node removed from the left hip showed far advanced fibrosis in places, and granulation tissue rich in inflammatory cells (Fig. 8), chiefly lymphocytes but also plasma cells. No clear division into zones was observed in the node. Fibroblast activity was moderate everywhere. There were no granulomata and no giant cells, no typical perivascular collections of inflammatory cells, and no endothelial thickening.

Laboratory Studies.—Wassermann reaction positive (1 : 16), cholesterol Wassermann positive (1 : 32), Kahn test positive (1 : 2), sitolipin positive (1 : 320).

Cerebrospinal fluid study showed protein content 86 mg./100 ml., cell count 778/3, mastic test 3355432100, Wassermann reaction positive in 0.5 and 1.0 ml., cholesterol Wassermann positive in 0.5 and 1.0 ml.

Therapy.—After 9 million units procaine penicillin given between December 4 and 17, 1951, the remaining node had regressed to about half its previous size and had divided into three separate parts. Tenderness had wholly disappeared.

Follow-up.—On April 23, 1952, only two pea-sized nodules remained (Fig. 9).

Case 4.—A farmer's wife, aged 36, 6 months pregnant, was treated in hospital from April 21 to May 5, 1952, for tertiary syphilis.

History.—Some 10 years before, a plum-sized tumour, which had developed in the course of one year, had been removed from the area of the right elbow. Soon afterwards the node began to grow again in the same place and in about 2 years had reached its present size. The patient had noticed skin lesions in the region of the right elbow

FIG. 9.—Case 3, same node as in Fig. 7, 4 months after penicillin treatment.

a few weeks before admission. She had never had anti-syphilitic treatment. Her husband had neurosyphilis.

Examination.—Heart and nervous system normal. The fundus uteri could be felt about four finger-breadths above the umbilicus and foetal movements were present.

A subcutaneous node measuring 3×1 cm. was observed some 4 cm. distal to the right elbow; it was to some extent mobile upon the underlying tissue and beneath the overlying skin. It had a rubbery consistency and the surface felt nodular. The covering skin was slightly red and showed an old operation scar.

FIG. 10.—Case 4, juxta-articular node distal to right elbow; tuberoserpiginous syphilids are seen close to the node.

Slightly radial and distal to the node there was a crescent-shaped area of tuberoserpiginous lesions 4 cm. long (Fig. 10), and a few centimetres distal to this a similar ring-shaped area, 2 cm. in diameter.

Histological Examination.—Three separate zones were distinguished. The outer zone was fibrous, consisting of coarse collagenic fibres with hyaline degeneration in the inner parts. Further inward was a zone of granulation tissue with lymphocytes and plasma cells situated perivascularly in many places. Granuloma formations were seen here and there. The vessel walls were thickened and hyalinized in places. The inner zone was a fairly structureless area of necrosis in which practically no cells were observed.

A specimen from the area of the tuberoserpiginous lesions was most suggestive of syphilitic inflammation.

Laboratory Studies.—Wassermann reaction positive (1:16), cholesterol Wassermann positive (1:16), Kahn test positive (1:8), sitilipin positive (1:320). The spinal fluid was normal.

Therapy.—After 7.2 million units procaine penicillin given between April 25 and May 5, 1952, it was observed that the node was only 0.4 cm. high and was of softer consistency. The tuberoserpiginous lesions also showed distinct improvement.

Discussion

These four patients all had untreated syphilis and all presented subcutaneous nodes in the vicinity of

the large joints which corresponded clinically with the descriptions of syphilitic juxta-articular nodes found in the literature (Jessner, 1926; Sweitzer and Winer, 1942; Kalz and Newton, 1943). The regions of the elbow and knee are reported to be the most usual sites in that order, and the ankle, hip, and wrist to be much less common sites. It is interesting that three of our patients, all with neurosyphilis, had a node in the region of the great trochanter on each side, and that, in two of these cases, this was the only site where nodes occurred. Suppuration of all nodes, as in Case 1, is unusual (Jessner, 1926), and tenderness of the nodes, as observed in Case 3, is also exceptional.

In three cases, the interval between the onset of syphilitic infection and the appearance of nodes could be estimated. In Cases 1 and 2 they had begun to develop within one year of the supposed primary lesion. In Case 3 the date of infection could not be established, but, in view of the fact that the patient had tabes and had had the nodes for only 2 years, they had certainly not appeared until the late stages of the disease. From the literature, the period between the onset of infection and the appearance of nodes seems to vary from 3 months to 29 years. However, juxta-articular nodes are regarded generally as late manifestations of syphilis.

Jeanselme (1924) described juxta-articular nodes histologically as having three separate zones: an outer connective tissue zone containing inflammatory changes, a narrow, intermediate, fibrous zone composed partially of degenerated connective tissue, and a central necrotic zone. In three of our patients (Cases 1, 2, and 4), a clear division into three zones was observed. The outer layer, however, was fibrous and was made up of coarse collagenic fibres. The intermediate zone consisted of granulation tissue and the inner zone of necrosis. In Case 3, such distinct zones were not present, and the histological appearance was entirely non-specific. Even though three of our cases presented a very similar histological picture we consider that this alone does not permit a diagnosis of syphilis. Staining by Levaditi's method showed no spirochaetes. However, the great similarity of the histological picture in these cases indicates a common aetiology. Jessner reported cases which resemble histologically our Cases 1, 2, and 4, and he took the same cautious view with regard to histological diagnosis.

The success of anti-syphilitic treatment, observed in all our cases, is the strongest evidence in favour of a syphilitic aetiology. This applies also to the therapeutic methods used before the introduction of penicillin (Jessner, 1926; Kalz and Newton, 1943). We agree fully with Jessner who says:

In studying the histological findings one would think it quite impossible that specific treatment could have any effect whatever on such tissue, and yet this is the case.

In Case 1 we were also able to obtain a biopsy specimen for histological study after treatment. The node had diminished considerably in size and granulomata with giant cells were noted. The most conspicuous changes in the histological picture included resolution of inflammation, weaker staining of collagenic fibres, and disappearance of fibres from the central necrotic area. Although this specimen was not from the same node as that studied before treatment, the findings throw some light on the changes occurring in these nodes during treatment.

Clinical differentiation of syphilitic juxta-articular nodes from rheumatic nodes is often impossible. It is true that, on histological examination, rheumatic and syphilitic nodes exhibit a similar division into three zones. In rheumatic nodes, however, the intermediate zone shows "peculiar and characteristically arranged large mononuclear cells arranged in radial fashion" (Dawson and Boots, 1930; Collins, 1937; Sweitzer and Winer, 1942). Our cases included only one (Case 1) in which large mononuclear cells were present, and these were not radially arranged, but situated round small areas of complete necrosis. The histological picture thus permits the conclusion that in our cases the nodes were not rheumatic.

As stated already, juxta-articular nodes are considered rare in non-tropical regions, but the cases here reported were collected among the patients treated in the course of one year at the Kumpula Hospital, Helsinki. During this time (May 28, 1951, to May 28, 1952) a total of 95 patients (21 men and 74 women) with previously untreated, acquired syphilis were admitted. This means that juxta-articular nodes occurred in about 4 per cent. of all our patients with untreated syphilis. In fact, the proportion may be higher still, as nodes were not routinely sought for in all patients. In our series, juxta-articular nodes were commoner in men (3 of 21) than in women (1 of 74). A possible explanation is that the women in our series were younger (average 37 years) than the men (average 45 years) and that in them the disease was consequently

at an earlier stage. Latent syphilis was also more frequent among the women patients (32 of 74) than among the men (5 of 21). It is interesting that three of our four patients had neurosyphilis; this suggests that juxta-articular nodes should perhaps be looked for particularly in patients with neurosyphilis, but the high proportion of neurosyphilis in this series from the Kumpula Hospital (44 of the total 95 patients) may explain the apparent association.

Summary

Four patients with juxta-articular nodes are reported. All had syphilis previously untreated, three had a node in the region of the great trochanter on both sides, and in two of them this was the only site of occurrence.

In three cases the histological picture was identical: an outer fibrous zone composed of coarse collagenic fibres, an intermediate zone of granulation tissue, a central area of necrosis. In the fourth case this division into zones was not present and the histological appearance was also in other respects non-specific. The syphilitic aetiology of these formations cannot be established on the basis of the histological picture alone.

The nodes were observed to regress or disappear in all cases after anti-syphilitic treatment. Three patients received only penicillin, while one had both therapeutic malaria and penicillin.

Syphilitic juxta-articular nodes are evidently not so unusual as is generally assumed. The four cases were noted in the course of one year among a total of 95 patients with previously untreated acquired syphilis. In this series there were 44 cases of neurosyphilis, but this apparent association of juxta-articular nodes and neurosyphilis may be merely coincidental.

REFERENCES

- Collins, D. H. (1937). *J. Path. Bact.*, **45**, 97.
Dawson, M. H., and Boots, R. H. (1930). *J. Amer. med. Ass.*, **95**, 1894.
Fex, J. (1927). *Svenska Läkt.*, **24**, 1069.
Jeanselme, E. (1924). *Paris méd.*, **51**, 242. Quoted by Jessner (1926).
Jessner, M. (1926). *Arch. Derm. Syph., Berl.*, **152**, 132.
Katz, F., and Newton, B. L. (1943). *Ibid.*, **48**, 626.
Lutz, A. (1891). *M. prakt. Derm.*, **13**, 488.
Sweitzer, S. E., and Winer, L. H. (1942). *Arch. Derm. Syph., Chicago* **45**, 315.