ARTERITIS AND LOCALISED PERIOSTEAL NEW BONE FORMATION

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We report here three cases in which localised periosteal new bone formation was associated with periosteal arteritis or other occult evidence of systemic lupus erythematosus.

Case 1—A thirty-six-year-old fitter first noticed the gradual onset of swelling above the left ankle in 1956. Over the next year this gradually increased and he developed spontaneous pain in the left calf extending into the left ankle and heel. During that time he lost twenty pounds in weight and had slight general malaise, but no specific constitutional symptoms. He was

FIG. 1

Case 1—Periosteal new bone (*left*) and cellular foci in the thickened periosteum. (Haematoxylin and eosin, $\times 35$.)

first seen in 1958, when radiographs revealed slight periosteal new bone formation in the lowest third of the left tibia and fibula. A biopsy specimen of the affected tibia at that time (Fig. 1) was found to contain trabeculae of recently formed woven bone enclosing loosely fibrous spaces in which inflammatory cells were inconspicuous or absent. Attached to the bone was a layer of fibrous and fibro-fatty tissue several millimetres thick, which was the thickened periosteum, and in which there were numerous foci of chronic inflammatory cells, mainly lymphocytes. Serial sections showed that these were related to focal lesions of small arterioles (Figs. 2 and 3). Each lesion affected a short length of the vessel (about $500\ \mu$) but the whole circumference was involved. The essential change appeared to be a severe oedematous separation of the constituents of the media, and to a less extent the adventitia, with consequent loss of structural definition but without gross necrosis or the development of fibrinoid; the intima was swollen but recognisable except in severely affected vessels in which recent throm-

bosis had occurred. The larger arteries showed considerable fibrous intimal thickening but no inflammatory cellular infiltration. On the basis of these findings the patient was transferred to the Manchester Rheumatism Centre for further investigation.

On examination the lower end of the left leg was swollen and warm (Fig. 4). Over the left medial malleolus the skin was red and thin and ulcerated in places, the ulcers appearing to have developed from small haemorrhagic spots. The left tibia and fibula felt thickened and warm but were only slightly tender. The ankle and subtalar joints were limited to about a quarter of the normal range. The calf muscles were normal. The viscera were healthy, and neurological examination revealed no abnormality.

The urine contained neither albumin nor sugar. The haemoglobin was 12.1 grammes per cent, the white cell count 12,100 per cubic millimetre, and the sedimentation rate was 57 millimetres in the first hour. The blood urea was 21 milligrams per cent; serum albumen was

FIG. 2

FIG. 3

Case 1—The same periosteal arteriole at different levels of section. In Figure 2 there is recent thrombosis, adventitial oedema and inflammatory infiltration in the surrounding fibrous tissue. In Figure 3 the necrotic arteriolar wall and the thrombus contain degenerate nuclei; the oedematous adventitia and the surrounding fibrous tissue contain swollen fibroblasts, scattered lymphocytes and occasional polymorphs. (Haematoxylin and eosin, $\times 200$.)

FIG. 4

FIG. 5

Case 1—Figure 4 shows the swollen left ankle and Figure 5 the periosteal new bone.

4.7 and serum globulin 2.8 grammes per cent. The blood Wassermann reaction and the sheep cell agglutination test for rheumatoid factor were negative. Radiographs of the chest were normal, but those of the left ankle showed periosteal new bone formation on the lowest third of both tibiae and fibulae (Fig. 5).

The patient was considered to have a granulomatous lesion and was treated with prednisolone in an initial daily dose of 20 milligrams. The left leg promptly became painless and much less swollen and red, and he began to gain weight. The sedimentation rate fell to 5 millimetres in the first hour after one month. Over the course of a year the ulcers healed and steroid therapy was gradually reduced and then discontinued. In 1961 he again developed an ulcer over the medial malleolus which again responded to steroid therapy.

FIG. 6

Case 2—Shows the periosteal new bone formation of the left tibia.

Case 2—A sixty-three-year-old man was first seen in 1960 complaining of swelling and slight aching of the left leg just below the knee. The swelling had been present for three months but had not interfered with walking, and generally he had felt well. On examination there was a slightly tender and oedematous thickening over the left tibia just below the knee. The right leg was normal. The veins of both legs were healthy. The blood pressure was 230/130 millimetres of mercury and there was some cardiac enlargement, but otherwise no abnormality was detected in the viscera. Radiographs of the affected leg revealed periosteal new bone formation in the middle and uppermost two-thirds of the antero-lateral aspect of the tibia (Fig. 6).

Radiographs of the chest showed left ventricular enlargement but no lung disease. The leg was treated with supportive dressings, but four months later the swelling was still present and

there was a mild pyrexia. The patient was admitted to hospital and given a course of penicillin, streptomycin and achromycin lasting a month, but the swelling of the leg and the pyrexia remained unchanged. The tibia was then exposed at operation revealing very oedematous and thickened periosteal soft tissues but no obvious pus. Two pieces of the tibial cortex and subjacent marrow, about three inches by one-quarter of an inch in size, were removed for histological examination and culture. No organisms were seen and the culture remained sterile. Sections (Figs. 7 and 8) confirmed the presence of periosteal new bone deposition and revealed a chronic periostitis featuring numerous arterial lesions similar to those of Case 1, except that arterial thrombosis was not seen and plasma cells were present in some arterial lesions; in addition scanty eosinophils were scattered throughout the periosteum. It is noteworthy that in spite of considerable periosteal new bone formation there was no bone sclerosis or new bone formation in the underlying cortex, changes which would be expected in the presence of cortical bone abscess or osteoid osteoma. Post-operative investigations revealed a normal urine, a serum albumen of 2.5 grammes per cent and a serum globulin of 3 grammes per cent, numerous lupus erythematosus cells in the blood smear and a negative Hyland test for rheumatoid factor. Three weeks after operation the wound had healed satisfactorily but there was still a mild pyrexia. Six months later a course of betamethasone was given, and though this produced no dramatic effect the swelling and tenderness of the leg gradually diminished. During the subsequent two years he has remained well with no further trouble in the leg, which clinically appears to have resolved completely and, to a less extent, radiologically. In 1962, eighteen months after operation, the blood was negative for lupus

FIG. 7

FIG. 8

Case 2. Figure 7 is a section of the tibial cortex from which the periosteum has been removed, showing periosteal new bone (*above*) and healthy compact and cancellous cortical bone (*below*). (Haematoxylin and eosin, $\times 20$.) Figure 8 shows periosteal arteriolitis. There is subintimal swelling and the oedematous wall and adventitial tissues are infiltrated mainly with lymphocytes. (Haematoxylin and eosin, $\times 250$.)

erythematous cells and the serum albumen and globulin were 4.2 and 2 grammes per cent respectively.

Case 3—A fifty-eight-year-old man was seen in 1962 because of a painful swollen left ankle. In 1953 he consulted an orthopaedic surgeon because of a painful swollen left knee. On examination, the knee was crepitant, painful, and limited in movement and contained a sterile effusion; the sedimentation rate was 15 millimetres in the first hour. A diagnosis of osteoarthritis was made and he was treated with manipulation and physiotherapy, but with no lasting benefit. In 1960 he first noticed swelling of the left ankle. During the next two years the ankle became increasingly stiff and painful and the swelling persisted in spite of wearing an elastic stocking. During this time the right ankle also became slightly swollen but was neither painful nor limited in motion; his general health had been excellent and there was no history of skin rash, Raynaud's phenomenon or any systemic disturbance. On examination, in 1962, he appeared to be fit with a normal pulse and blood pressure and no visceral abnormalities. There was a brawny swelling of the left leg below the mid-thigh with some pitting oedema. The calf muscles felt wooden; the left tarsus, ankle and knee joints were limited in motion and the tissues around them were thickened and warm. Similar, but much less marked, changes were present in the right tarsus and ankle. Radiographs (Figs. 9 and 10) revealed periosteal new bone formation at the lower end of both the right and left tibiae and fibulae and erosion and periosteal new bone formation around the knee.

The sedimentation rate was 20 millimetres in the first hour. The haemoglobin was 14 grammes per cent and the white cell count 7,400 per cubic millimetre. The Wassermann reaction and sheep cell agglutination test were negative and no lupus erythematosus cells were found in the blood. The serum albumen was 4.1 grammes per cent and the serum globulin 4.1 grammes per cent with a small increase in the gamma fraction. The serum alkaline phosphatase was 12.5 King-Armstrong units. An electromyograph showed no myopathic

FIG. 9

FIG. 10

FIGS. 9 and 10

Case 3—Radiographs showing, in Figure 9, periosteal new bone formation in the right and left tibiae and fibulae and, in Figure 10, erosion and new bone formation around the knee joint.

FIG. 11

FIG. 12

FIG. 13

Case 3—Figures 11 to 13 show three areas of the synovium of the knee joint with chronic inflammatory changes and the "haematoxylin bodies" indicated by arrows. (Haematoxylin and eosin, $\times 500$.)

potentials. A biopsy of the suprapatellar pouch of the left knee joint revealed chronic arthritis: the hypertrophied synovium (Figs. 11 to 13) was hyperaemic and infiltrated with lymphocytes and plasma cells; it also contained aggregates of Feulgen-positive material—"haematoxylin bodies"—which may be regarded as specific histological evidence of systemic lupus erythematosus. A biopsy of the medial head of gastrocnemius taken at the same time showed atrophy and degeneration of muscle fibres and a general oedema and diffuse fibrosis, but inflammatory cellular infiltration was scanty and limited to lymphocytic cuffing of small blood vessels; a destructive arteritis was not encountered in either muscle or synovium.

DISCUSSION

Generalised periosteal new bone formation is a feature of hypertrophic pulmonary osteoarthropathy, and juxta-articular periostitis may be seen in some forms of polyarthritis, particularly psoriatic arthropathy, Reiter's syndrome and Still's disease. Localised periosteal new bone formation may occur as a reaction to a variety of cortical or periosteal lesions, but, with the exclusion of trauma and malignant tumour, unilateral periosteal bone deposition in the tibia, the cause of which is not clear on clinical or radiological grounds, is most likely to be due to osteoid osteoma or a small cortical bone abscess. This at least has been our pathological experience. That localised periosteal bone deposition may be associated with arteritis of the periosteum does not appear to be widely appreciated. Saville (1956) and Serre, Simon and Mion (1961) reported isolated cases in which periostitis was the initial manifestation of polyarteritis nodosa. But in a detailed study of polyarteritis nodosa Rose (1957) encountered periostitis only twice in 111 patients. In these reported patients the periostitis was bilateral whereas in our patients the lesion was at first unilateral. It is not clear why periostitis should so rarely occur in polyarteritis nodosa. Subjects with rheumatoid arthritis may develop polyarteritis nodosa, and in such a case one of us (J. B.) has seen severe acute arteritis in the periosteal tissues around the knee unassociated with periosteal new bone deposition. It is possible that periosteal involvement in polyarteritis nodosa is infrequent or that the arterial lesions are transient as they sometimes are in other sites. The periosteal new bone formation in our patients presumably reflects a chronic but relatively mild inflammatory process; histologically the arteritis was less severe than that usually seen in polyarteritis nodosa in that fibrinoid necrosis did not occur, and on clinical and pathological grounds the process was slowly progressive rather than acute.

The albumin/globulin ratio was abnormal in two patients; in one of these, lupus erythematosus cells were found in the blood, and in the other there were haematoxylin bodies in the tissues. These findings, together with the satisfactory response to steroid therapy and the failure to establish another cause of the periosteal reaction, suggest that the lesion may be an unusual manifestation of systemic lupus erythematosus; the periosteal arteritis is consistent with this suggestion because vasculitis of various kinds is a well known feature of the pathology of systemic lupus erythematosus. The finding of haematoxylin bodies in Case 3 in the absence of lupus erythematosus cells in the blood was unexpected but, according to Worthington, Baggenstoss and Hargraves (1959) may occasionally occur. None of our patients appeared to be constitutionally ill, nor did they present the skin lesions or visceral abnormalities commonly associated with systemic lupus erythematosus. However, this syndrome frequently occurs in an incomplete form; and a considerable time may elapse between initial symptoms and the establishment of a firm diagnosis.

Bacterial culture was done only after the apparent failure of antibiotic therapy in one patient, and not at all in the other two. Nevertheless, bacterial osteomyelitis seems an unlikely diagnosis because it would not easily explain, first, the prompt response to steroid therapy alone in Cases 1 and 3, second, the chronic arthritis in Case 3, third, the presence of lupus erythematosus cells in Case 2, and finally, the haematoxylin bodies in Case 3.

SUMMARY

1. Three patients with localised periosteal new bone formation associated with periosteal arteritis and other evidence of systemic lupus erythematosus are described.
2. Systemic steroid therapy was valuable in the management of this condition.

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