HYPERPLASTIC CALLUS FORMATION IN OSTEONEogenesis IMPERFECTA

Report of a Case and Review of the Literature

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Hyperplastic callus in osteogenesis imperfecta is rare. I have been able to find only fifteen reported cases. The condition manifests itself by the formation of enormous masses of callus which may follow a fracture or a simple contusion or which may arise spontaneously without any preceding injury. Baker (1946) gave a classical account of the pathology and Fairbank (1948) gave an equally comprehensive picture of the clinical features. The first case report is by Battle and Shatlock (1908) who described "a remarkable case of diffuse cancellous osteoma," the description and illustration of which leave no doubt that it was a case of hyperplastic callus formation.

Treatment is difficult and uncertain. One patient was subjected to amputation because the disease was mistaken for sarcoma. For the same reason another patient was treated by deep x-ray therapy but this was not effective. A further patient treated by deep x-ray responded favourably (Hilton 1934). In the case reported here, I had the opportunity of observing the early development of the condition in several bones at different times. I believed that any treatment could be effective only if given in the earliest stage of callus formation when its growth is most rapid and mitosis at its height.

CASE REPORT

An eleven-years-old girl had been under observation in the orthopaedic department of Alder Hey Children's Hospital under the care of Mr F. C. Dwyer, and had been treated altogether for six fractures. No member of her family had blue sclerotics or fragile bones. Her mother stated that she had no illness during pregnancy. Delivery was normal.

The patient sustained a mild head injury when seven months old and this was followed by a large swelling of the skull, but the radiographs did not show any bone injury. The swelling subsided after two weeks. She broke her right clavicle at the age of ten months, her right elbow at two and a half years and again at four, the left calcaneum at six years, the left clavicle at six and a half, and the left elbow at eight. The fractures of her elbows united with cubitus varus.

A radiograph of the spine showed mild flattening of the thoracic vertebral bodies such as is commonly seen in osteogenesis imperfecta. A radiograph of the pelvis showed small bony outgrowths of the iliac bones just above the acetabula.

When she was nine years old she noticed a lump in her right thigh. There was no history of injury. The radiograph showed a large bony excrescence of the upper part of the right femoral shaft (Fig. 1). A later radiograph of the forearms showed several small spiculated bony excrescences of the interosseous borders of the radius and ulna and a dislocation of the head of the left radius (Figs. 2 and 3). More recently the radiographs show hyperostotic ridges on the humeri and the upper end of the radius. These were first noted in the supracondylar region and subsequently they spread up the shaft, where their outline was wavy.

At the age of ten years she had a mild injury to her left thigh but was able to walk about for two weeks. After this she developed a limp and complained of pain in the thigh. Two weeks later marked tenderness of the lower third of the left femur was observed and
a vague thickening could be felt. She was admitted to hospital and her leg was immobilised by skin traction. **Investigations**—The blood sedimentation rate, blood count, serum calcium, inorganic phosphates, alkaline phosphatase and serum proteins were normal; the Mantoux test 1:10,000 was positive; the Wassermann reaction was negative. A radiograph at that time did not show any abnormality.

**Progress**—The next weeks were marked by a steadily increasing swelling of her left thigh. This was exquisitely tender and the superficial veins were enlarged. The temperature varied between 100 and 102 degrees, the sedimentation rate rose to 78 millimetres in the first hour and the white cell count to 11,000 cells per cubic millimetre. There was no material change in the blood chemistry apart from a rise of the alkaline phosphatase to 26.5 King Armstrong units. Because of the pyrexia and extreme tenderness the diagnosis of osteomyelitis was considered, but when the swelling continued to increase sarcoma was suspected although hyperplastic callus formation was believed to be the most likely diagnosis.

A radiograph taken two months after the onset of pain showed periosteal elevation with marked new bone formation around the lower half of the femoral diaphysis (Fig. 5). There was no radiological evidence of bone destruction, but the dense new bone was deposited in the shape of "sun ray spicules."

**Biopsy**—On the same day Mr F. C. Dwyer removed a deep wedge for histological examination. The histological report confirmed the diagnosis of hyperplastic callus formation. **Macrosopically** the specimen consisted of a wedge of tissue 4.5 centimetres long, 2 centimetres deep and 1 centimetre wide at its superficial margin. The surface was slightly nodular and covered with a thin layer of fibrous tissue. Beneath this there was a firm gelatinous greyish-white zone grading more deeply into a whiter, more cartilaginous tissue. Both these zones varied in thickness from two to five millimetres. Superficially they were avascular; but more deeply,
The swelling of the left thigh four weeks before it reached its peak.

Figure 5—Radiograph of the left femur five weeks after the onset of the hyperplastic callus formation. Figure 6—Hyperplastic callus formation at its height.
minute vessels could be seen running in a radial fashion. The inner part of the biopsy consisted of cancellous bone with a few small islands of cartilage. Microscopically the superficial part of the biopsy consisted of a zone of oedematous and fragmented connective tissue in which there were small haemorrhages and perivascular accumulations of lymphocytes and plasma cells. Deep to this there was a narrow zone of proliferation of fusiform and stellate fibroblasts, which changed gradually to a fibro-chondroid tissue arranged in irregular trabeculae separated by a loose vascular fibrous stroma. The deeper part of this zone showed calcification and true cartilage formation in the chondroid tissue with osteoclastic resorption at the margin of the trabeculae. Woven bone was being formed, and the deepest part of the biopsy consisted of trabeculae of woven bone and calcified cartilage with occasional central islands of uncalcified cartilage.

The appearances resembled those described by Baker (1946) in cases of hyperplasia of callus in fragilitas ossium. Later progress—The left thigh, from groin to below the knee, increased relentlessly, attaining a circumference of twenty-one inches six months after the onset as compared with the thirteen inches circumference of the right thigh at the same level (Figs. 4 and 6). During the next few months there was slight but steady shrinkage (Fig. 7). The temperature returned to normal and the blood sedimentation rate dropped to 13 millimetres in the first hour.

Five months later a swelling of the right thigh was observed; this had appeared without any injury while she was confined to bed in hospital. The radiograph and the rapid increase of the right thigh made it clear that this was also hyperplastic callus formation. She was given A.C.T.H. in the hope that this drug might cause cessation of the callus formation like its reported inhibition of granulation tissue (Howes et al. 1950). The swelling was unaffected (Fig. 7). In three months the girth of the right thigh reached its peak of twenty-two inches and thereafter diminished gradually. After the A.C.T.H. therapy there was considerable generalised osteoporosis and marked biconcavity of the vertebral bodies. The hyperplastic callus of both femora took part in the generalised osteoporosis and there was slipping of the right upper femoral epiphysis.

A month later a new focus of callus appeared spontaneously at the upper end of the left ulna (Fig. 8). At the suggestion of Dr S. E. Keidan and with the kind collaboration of Dr P. Haslam a single dose of deep x-ray therapy (K.V. 240, H.V.L. 3-0 millimetres Cu) was given to the affected area a few days later. This was given through two parallel and opposed fields giving a tumour dose of 500 r. After this the callus did not increase further and the circumference of the forearm became normal within five weeks. A radiograph taken four months later showed only a trace of the callus.

Soon after the swelling of the left ulna appeared it was also noticed that the left thigh, which had been slowly diminishing, was again rapidly swelling. With the encouragement of the favourable response of the ulna to x-ray therapy, a single dose of 500 r was given to the left thigh which also soon began to diminish.

Soon afterwards a spontaneous swelling of the left tibia occurred. A radiograph showed hyperplastic callus at the mid-tibia and an apparently unconnected spontaneous
fracture of the upper end of the tibia without any callus formation (Fig. 9). The tibia was similarly irradiated and again there followed steady diminution of the swelling.

**Comments**—The notable features of this case are: 1) Mild fragilitas ossium of the post-natal, non-familial type with absence of blue sclerotics. 2) Enormous hyperplastic callus formation of the left femur after a mild injury without a demonstrable fracture, and similar callus formations of the right femur, left ulna and right tibia without any injury; these developed while the patient was in hospital and on an adequate vitamin C intake. This fact is of interest in view of the suggestion made by Brailsford (1943) that scurvy plays a part in the causation of this condition. 3) A.C.T.H. had no effect on the callus formation of the right femur, but a single dose of deep x-ray apparently arrested callus formation on the three occasions when it was tried. 4) Bony excrescences of the right femur, the interosseous borders of the forearm bones and the ilia, not associated with injuries; I believe that the dislocation of the head of the radius is due to the excrescences which meet in the interosseous space and thus push the radius outwards and forwards. 5) Hyperostotic ridges most marked in the supracondylar region of the humeri; these have formed only recently and are perhaps a special form of bony excrescences. 6) Prolonged pyrexia while the hyperplastic callus was forming. 7) Normal blood chemistry, with the exception of the high serum alkaline phosphatase.

**REVIEW OF THE LITERATURE**

Altogether fifteen cases have been reported of hyperplastic callus formation in one or several bones. Some of the cases have been described by several authors at different times. All except three occurred in childhood. Nine patients were male, six female. In seven patients only one bone was involved, in three patients two bones were involved, in two
patients three bones were involved, in one patient four bones were involved and in two patients five bones were involved. Of the thirty-three affected bones twenty-two were femora, six were humeri, three were tibiae, one was the ulna and one was the radius. There was a preceding fracture in twelve instances, there was no preceding fracture in thirteen instances, there were doubtful fractures in three instances, there was no mention of a fracture in five instances.

Hyperplastic callus formation has usually attained its peak after two to six months. Thereafter the affected limb diminished, but usually some permanent enlargement remained. No patient is reported to have died except one (Brailsford 1943) whose tibia became the seat of a sarcoma. Pyrexia was marked in two cases. Bony excrescences were present in eight of the fifteen cases. There was dislocation of the head of the radius in three cases, separation of the upper femoral epiphysis in two cases. Hyperostotic ridges were present in five patients and were a prominent feature in Hilton’s case. Only two patients are reported to have had blue sclerotics and only one had a family history of osteogenesis imperfecta. The brother of the patient reported by Battle and Shattock suffered from the same condition, but no mention was made of underlying fragilitas ossium in either. In Hilton’s case there was no osteogenesis imperfecta but the familial incidence was striking.

SUMMARY

A case of hyperplastic callus formation is reported in a girl of eleven; several bones were affected. There were no associated fractures. She is believed to be suffering from a mild non-familial type of osteogenesis imperfecta without blue sclerotics and presents multiple bony excrescences unassociated with injury. The relevant literature is reviewed. The effect of a trial of treatment with A.C.T.H. and with deep x-ray is reported.

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REFERENCES