OSTEOGENIC SARCOMA IN FOUR SIBLINGS

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In 1935 Roberts and Roberts reported the occurrence of osteogenic sarcoma in non-identical siblings (one brother and two sisters) with no previous chronic bone disorder. In this report fibrosarcoma and osteogenic sarcoma were included: one tumour was diagnosed as fibrosarcoma, one as sclerosing osteogenic sarcoma, and one as round-cell osteogenic sarcoma. A year later the occurrence of osteogenic sarcoma in two sisters was reported by Pohle, Stovall and Boyer (1936). The two cases were diagnosed pathologically as osteolytic osteogenic sarcoma. Before this Werner (1930) reported osteogenic sarcoma developing in three members of a family whose members were prone to multiple fractures. Barry (1961) reported osteogenic sarcoma arising in members of the same family in association with Paget’s disease. Roberts and Roberts suggested a genetic origin for these tumours, but this is not generally accepted. This paper reports the occurrence of osteogenic sarcoma in four siblings.

The family consisted of normal parents and eight siblings, four of whom have not so far shown any evidence of malignant disease. The only history of malignant disease in the family was in a paternal uncle and the paternal grandmother, both of whom died of metastatic cancer, but the primary sites are not known. The case histories of the four affected siblings follow.

CASE REPORTS

Case 1 (Dr F. E. Wait’s case)—A fifteen-year-old boy seen in 1948 had had a minor injury to the right knee in October 1947, with development of a small non-tender lump on the medial aspect of the knee. Two months later he noticed discomfort in the knee. The swelling increased in size, became painful and spread to involve the lateral, anterior and popliteal areas, with limitation of extension and consequent limp.

The patient was admitted to hospital in February 1948. Physical examination revealed a hard, exquisitely tender, diffuse swelling of the right leg extending from the medial condyle of the tibia to the junction of the lowest and middle thirds of the femur. There were no skin changes. The circumference of the lower right thigh was two and a half inches greater than that of the left, and that at knee level was one inch greater on the right than on the left.

Radiographs showed marked irregularity of the lower six inches of the diaphysis of the right femur (Fig. 1). Bone destruction and extensive new bone formation with soft-tissue extension was evident. The chest showed no evidence of metastases. A biopsy specimen taken from the lateral side of the mass was reported to show malignant cells on frozen section. On the basis of this the right lower limb was amputated through the hip joint.

Pathology (Dr Henry J. Block)—The lower end of the femur was swollen in a fusiform manner. On section it contained bony rays and the marrow was replaced by firm yellow tissue. Histological examination (Fig. 2) showed extensive new bone formation with tumour cells somewhat compressed by abundant osteoid matrix. Other areas showed spindle-shaped cells forming interbranching bundles. Frequent mitotic figures were seen, but there was no blood-vessel involvement.

The patient’s condition after the operation was good and recovery was uneventful. Four months later he was free from symptoms, but a radiograph of the chest showed extensive metastases. He died a year after the first onset of symptoms.
Comment—This was a typical case of osteogenic sarcoma of the lower end of femur which in spite of prompt radical treatment progressed rapidly to a fatal outcome with pulmonary metastases.

Fig. 1
Case 1—Radiological appearances: note the lesion in the lower part of the right femoral shaft.

Fig. 2
Case 1—Histological appearances: interlacing bundles of spindle cells are seen, together with an area of osteoid tissue and malignant osteoblasts. (Haematoxylin and eosin, × 41.)

Case 2 (Dr F. E. Wait’s case)—A twenty-year-old man came at the end of 1948 with a history of minor injury to his left ankle, some months previously, followed by several episodes of twisting of the ankle. Three weeks before his admission to hospital he noticed swelling and tenderness over the back of the ankle and for two weeks had had stiffness and pain on walking.
On his admission to hospital, examination revealed a hard, tender swelling of the lower end of the left tibia, with blue discoloration of the overlying skin. The left ankle showed a decreased range of movement. There were no palpable popliteal or inguinal lymph nodes.

Radiographs showed a lesion involving the lower tibial diaphysis with destruction of bone and with radiating formation of new bone extending into the soft tissues (Fig. 3). The chest showed no evidence of metastases.

A biopsy specimen taken from the medial aspect of the lesion just above the malleolus showed sarcomatous tissue on frozen section. On the basis of this finding supracondylar amputation was done.

Pathology (Dr Henry J. Block)—A moderately firm mass three inches in diameter protruded from the posterior aspect of the tibia. Its surface was irregular and nodular, and on section it showed as a yellow-pink tissue filling the marrow cavity. Histological examination showed tumour cells arranged in masses and whorls supported on varying types of stroma, including fibrous, osteoid and atypical osseous tissue (Fig. 4). The tumour cells were large with
disproportionately large, darkly staining nucleoli. Tumour giant cells were present. Sections through blood vessels, fibula and proximal tibia showed no apparent extension.

The patient made an uneventful recovery from the operation and remains alive and well sixteen years later (February 1965).

Comment—Although the outcome in this case has been unusually favourable for osteogenic sarcoma, radiological and pathological appearances of the lesion leave no doubt of the diagnosis of sarcoma of bone. The peripheral position of the lesion may help to explain the favourable outcome.

Case 3 (Dr J. L. Gulley's case)—A girl of eleven gave a history of a minor injury to her upper left tibia in December 1956, with development of a persistent swelling with pain and tenderness. On admission to hospital three months later she was pale and looked ill. Physical examination was essentially negative except for the left lower limb, where there was an acutely tender swollen area over the upper end of the left tibia. There was no skin change and no evidence of lymphadenopathy. All the joints of the left leg had a good range of movements.

Radiographs showed patchy sclerosis of the lateral aspect of the upper tibial metaphysis, with some bone destruction. There was extension of new bone laterally into the soft tissue with involvement also of the fibula. The appearances of the chest were within normal limits.

Before biopsy a single exposure of 800 r was given with the cobalt unit. Figure 5 shows a radiograph of the lesion with the markers outlining the proposed radiotherapy fields. Biopsy of the lesion was done in March 1957, at which time the periosteum was found to be thickened over soft tumour-like tissue. Histological examination showed cartilage and bone within a malignant stroma (Fig. 6). Malignant osteoblasts were present with complete loss of polarity and variation in size, shape and staining qualities of the nuclei. Mitotic figures were seen. The diagnosis was osteolytic osteogenic sarcoma.

After biopsy the patient received a central tumour dose of 5,000 r in twenty-five daily treatments from the cobalt unit. Six weeks after biopsy the limb was amputated through the thigh. Histological examination (Dr Peter W. Davey) of the tumour at this time showed
relatively acellular connective tissue with spicules of bone, occasional leucocytes, and remains of necrotic tumour cells. There was also necrosis of osteocytes in the adjacent normal canaliculi with little inflammatory reaction.

The patient made an uneventful recovery from the operation. Eight years later (February 1965) she remains well with no evidence of metastases or recurrence of the disease. A radiograph of the chest taken in September 1964 showed no evidence of disease.

Comment—Although the outcome in this case too is unusual, the radiological and histological appearances of the lesion were typical of osteogenic sarcoma.

Case 4 (Dr D. W. Denny’s case)—A twenty-two-year-old man came having sustained a minor injury to his left leg just below the knee in December 1960. Aching in the injured area followed, and progressed to pain severe enough to make analgesics necessary. Later a swelling appeared over the upper part of the tibia, the knee became stiff after exhaustive use and the patient...
began to limp. At the time of admission physical examination showed a warm, tender, swollen left lower leg whose circumference was one inch greater than that of the right. The skin was blue over the medial aspect of this swelling. Flexion and extension of the knee were limited by pain.

Radiographs showed two areas of bone destruction in the medial cortex of the upper left tibia with some intervening sclerosis (Fig. 7). There was no expansion of the shaft or periosteal reaction. A skeletal survey and radiograph of the chest showed no evidence of metastases.

In February 1961 a biopsy specimen was taken from the medial aspect of the upper tibia. Histological examination indicated endosteo-fibrosarcoma: accordingly, a mid-thigh amputation was performed three weeks later.

Pathology (Dr H. K. Fidler)—There was a raised, firm area on the anterior surface of the upper metaphysis of the tibia measuring five by two centimetres. On section this was seen to consist of soft, thick, grey tumour-like tissue which filled the entire marrow space, but did not extend into the cortex. Histological examination showed an anaplastic tumour of mesenchymal origin with scattered spicules of necrotic bone (Fig. 8). The nuclei were mostly fibroblastic, in association with a good deal of fairly mature collagen. Small amounts of osteoid tissue were seen.

The patient made an uneventful recovery after operation and was well until nearly a year later when he developed pain in and swelling of the left anterior chest wall. Radiographs taken ten months after operation showed extensive pulmonary metastases. These steadily progressed in spite of treatment with Procytox. He died twenty months after the first appearance of symptoms.

Comment—This case showed the features typical of a malignant tumour of bone. Some features of the histological examination suggested a fibrosarcoma but the presence of abnormal osteoid tissue established the diagnosis of osteogenic sarcoma.

SUMMARY

1. The case histories of four siblings affected by osteogenic sarcoma are described.
2. The lesions appeared over a period of twelve years. The ages of the patients at the onset of symptoms were fifteen, twenty, eleven and twenty-two years.
3. The diagnosis of osteogenic sarcoma was in each case established by radiological and histological methods.
4. Two patients survived for eight and sixteen years after treatment and both are still alive and well.

REFERENCES


