PRIMARY RETICULO-SARCOMA OF BONE

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Although Oberling and Raileanu (1932), after an extensive study of the histology of Ewing's tumour, concluded that it was to be regarded as a reticulo-sarcoma arising in the bone marrow it was not until 1939 that Parker and Jackson published the first paper on this subject recording seventeen cases collected from their own material, and from the Registry of Bone Sarcomas. From that time there have been numerous papers in the American literature recording further series of cases, but British publications have been limited to a paper by Valls et al. (1952) and one case reported by Fripp and Sissons (1954). This paper is concerned with reporting seven cases of reticulo-sarcoma of bone and considering the relationship between this tumour and Ewing's sarcoma.

In 1921 Ewing described a tumour which he called a diffuse endothelioma of bone. It occurred particularly in children, was often multifocal in the skeleton and rapidly fatal with generalised metastases. This paper was followed, from then until now, by a spate of papers on the subject, many of them describing isolated cases with inadequate pathological reports and usually no necropsy records. In 1933 Colville and Willis published the first critical paper on the subject. They reported the case of a child, found to have a neuroblastoma at necropsy, which presented in life the clinical picture of Ewing's syndrome. Willis (1940) reported a similar case and suggested that it was very likely that all cases of Ewing's tumour could be explained in this way. Although there can be no doubt that this view was true of many of the published cases the passage of time and the publication of series of cases in the American literature with adequate necropsy reports makes it clear that there is a primary tumour of bone which many still call Ewing's tumour. Willis (1953), while rightly pointing out that many of the cases presenting the clinical and pathological picture of Ewing's syndrome are metastatic neuroblastosomas if occurring in children and adolescents, and metastatic carcinomas if occurring in adults, accepted the fact that primary reticulo-sarcoma of bone accounts for a minority of such cases.

During the past ten years there have been several important reviews of Ewing's tumour in the American literature. Lichtenstein and Jaffe (1947) reported seventeen cases, four of which came to necropsy. Coley et al. (1948) based their study on ninety-one cases, and Geschickter and Copeland (1949) reviewed a series of 167 cases with necropsy reports on twelve. McCormack et al. (1952) reviewed all the bone tumours seen at the Mayo clinic between 1907 and 1949. They found eighty cases which they regarded as Ewing's tumour. In all these papers Ewing's tumour is regarded as an entity distinct from reticulo-sarcoma of bone.

Since Parker and Jackson's paper in 1939 there have been a number of papers reviewing large series of cases of reticulo-sarcoma of bone. Ivins and Dahlin (1953) reviewed all the available material in the period 1905–52. They found forty-nine cases of reticulo-sarcoma of bone and over eighty cases of Ewing's tumour. Of the forty-nine cases of reticulo-sarcoma thirty-two had already been reported by McCormack et al. (1952). Francis et al. (1954) reported forty-four cases of reticulo-sarcoma of bone and smaller series have been recorded by Simmons (1939), Chan Szutu and Chih-Kuang Hsieh (1942), Sherman and Snyder (1947), Khanolkar (1948), Uehlinger et al. (1948) and Fruhling et al. (1954).

Although in most papers in the American literature Ewing's tumour and reticulo-sarcoma are regarded as separate entities, there has been a tendency in recent years to stress the difficulty of separating them, and Geschickter and Copeland (1949) described reticulo-sarcoma of bone
as atypical Ewing's sarcoma. In the case of Ewing's tumour the main features are said to be the youth of the patient, the rather characteristic radiographic picture, the radiosensitivity of the tumour, the very bad prognosis, and the uniform histological appearance. In the case of reticulo-sarcoma of bone the main features are their occurrence in an older age group, the relatively good prognosis, and the pleomorphic histological picture with the emphasis on the presence of reticulin fibre between the tumour cells (Table I).

**TABLE I**

**SUMMARY OF MAIN DIFFERENCES BETWEEN EWING'S TUMOUR AND RETICULO-SARCOMA OF BONE**

<table>
<thead>
<tr>
<th></th>
<th>Ewing's sarcoma</th>
<th>Reticulo-sarcoma of bone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>Early life (41-25 years)</td>
<td>Later life (20-40 years). Extremes 10-59 (Parker and Jackson)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td>Male : Female = 2 : 1</td>
<td>Male : Female = 2 : 1</td>
</tr>
<tr>
<td><strong>Site</strong></td>
<td>Shaft of long bones. 40 per cent in femur or tibia</td>
<td>Flat bones, trunk, metaphysis of long bones extending to shaft</td>
</tr>
<tr>
<td><strong>Onset</strong></td>
<td>6 weeks to 2 years; average 9 months (McCormack et al.)</td>
<td>6 months to 8 years; average 1-2 years</td>
</tr>
<tr>
<td><strong>First symptom</strong></td>
<td>Pain or swelling</td>
<td>Pain or swelling</td>
</tr>
<tr>
<td><strong>Fever</strong></td>
<td>Present in 30 per cent</td>
<td>Infrequent</td>
</tr>
<tr>
<td><strong>Radiology</strong></td>
<td>Not diagnostic: early stages new bone formed—later stages osteolytic</td>
<td>Not diagnostic: usually osteolytic</td>
</tr>
<tr>
<td><strong>Radiotherapy</strong></td>
<td>Sensitive—reappearance of normal-looking bone</td>
<td>Sensitive—forms more dense bone after treatment</td>
</tr>
<tr>
<td><strong>Prognosis</strong></td>
<td>Poor. Five-year survival 10-15 per cent</td>
<td>More favourable. Five-year survival 35-45 per cent</td>
</tr>
<tr>
<td><strong>Gross specimen</strong></td>
<td>Bulk of tumour subperiosteal: often reactive new bone in medulla</td>
<td>Tends to be localised in area of metaphysis</td>
</tr>
<tr>
<td><strong>Microscopy</strong></td>
<td>Uniform cell masses separated by trabeculae of collagen. No reticulin fibre in cell masses</td>
<td>More pleomorphic histology. Reticulin fibre between cells</td>
</tr>
</tbody>
</table>

Oberling (1928) and Oberling and Raileanu (1932) went exhaustively into the histogenesis of Ewing's tumour and concluded that it was a reticulo-sarcoma with a variable histological picture similar to that seen in reticulo-sarcomas arising in lymph nodes. Sternberg (1935) regarded it as an undifferentiated sarcoma, and Stout (1943), in an excellent critical paper on the subject, found himself unable to separate the two tumours on histological grounds. Willis (1953) accepted the existence of a reticulo-sarcoma of bone and stated: "whether there does indeed exist a primary tumour of bone, other than reticulum-cell sarcoma, capable of giving Ewing's syndrome is, I think, still uncertain." Lichtenstein and Jaffe (1947) and Lichtenstein (1952), however, while accepting that Ewing's tumour arises from the reticulo-endothelial elements in the bone marrow, regarded it as a separate entity from reticulo-sarcoma of bone.

**CASE REPORTS**

**Case 1**—Man aged thirty-one years. Laboratory assistant.

**History**—This man was first seen in June 1953 complaining of pain in his back for eighteen months. The pain came on after helping to move a piano. It persisted throughout 1952, but became more intense and "girdle" in character during February 1953. A radiograph taken at that time was thought to show a crush fracture of a vertebra.

**On examination,** he looked ill and there was spastic paralysis of the lower limbs. The level of
FIG. 1
Case 1—Initial radiographs of spine.

FIG. 2
Case 1—Sternal, with adjacent soft-tissue shadow seen before radiotherapy (left) and after radiotherapy (right).
anaesthesia extended up to T.11. The spinous process of this vertebra was tender, and movement at this level was limited. There was no fever. The sternum was the site of a large hard swelling in the manubrium. This was not tender.

**FIG. 3**
Case 1—The pleomorphic pattern of the tumour is well seen. (×650.)

**FIG. 4**
Case 1—A silver impregnation to show the fairly well developed reticulin fibre network in the tumour. (×450.)

Radiographs showed wedge-collapse of the vertebral body, with condensation of bone (Fig. 1). The disc spaces were intact. For some months this was considered to be a crush fracture. The clue to the diagnosis is to be seen in the antero-posterior radiograph in which a paravertebral soft-tissue...
swelling was visible. The radiograph of the sternum showed some bone destruction and a large soft-tissue swelling (Fig. 2).

Investigations—The urine contained no Bence-Jones protein. Blood examination showed: alkaline phosphatase 4·5 King-Armstrong units 100 millilitres; acid phosphatase 1·0 King-Armstrong units 100 millilitres; haemoglobin 16·3 grammes per 100 millilitres; white blood cells 5,800 per cubic millimetre.

Biopsy—The specimen consisted of several irregular fragments of firm white tissue, the largest measuring 1·0 centimetres in diameter, together with a small fragment of cancellous bone. Sections showed a somewhat pleomorphic picture (Fig. 3). The predominant cell resembled a reticulum cell but there were all gradations in size to lymphocytes. There was an occasional multinucleate cell. The nuclear pattern was variable and mitoses were infrequent. There was a rich reticulin fibre content (Fig. 4). The tumour was not unduly vascular. Conclusion: the histological picture was that of a polymorphic reticulo-sarcoma.

Fig. 5
Case 2—Initial radiograph of spine.

Operation (June 5, 1953)—Costo-transversectomy. A large mass of soft tumour was found in the mediastinum surrounding the vertebral body. A limited antero-lateral decompression was performed and material was removed for examination.

Post-operative radiotherapy—1,400 r in one week at 180 kilovolts to the sternum. 1,800 r in two and a half weeks at 220 kilovolts to the vertebra.

Progress—Five months after operation the patient returned to work wearing a spinal brace and walking with two sticks. Three months later he was short of breath, the abdomen was distended, and enlarged lymph nodes were present in the axillae and groins. Radiographs of the chest showed metastatic deposits in the right lung. The patient died in April 1954. Necropsy was not performed.

Case 2—Girl aged seventeen years. Shop assistant.

History—In December 1949 she fell from her bicycle and felt pain in the lower part of the back. After a week’s rest she was able to return to work. In February 1950 the pain returned and she spent two weeks in bed. In March 1950 she noticed increasing weakness of her legs and difficulty with micturition.

On examination, there was a flaccid paralysis of the lower limbs and retention of urine. No local tenderness of the spine could be found.

Radiographs (Fig. 5) showed extreme collapse of the twelfth thoracic vertebra. The remains of the
Case 2—The pleomorphic cytology is well shown, several small multinucleated giant cells being present in the centre. (×170.)

Case 2—Showing the considerable fibrous stroma. (×170.)
vertebral body were seen as a dense shadow resembling Calvé's disease. In the antero-posterior film a paravertebral shadow was visible. There were deposits of growth in the tarsal bones of the left foot. *Investigations*—The urine contained no Bence-Jones protein. Albumen was present, and there was infection with staphylococcus aureus and pyocyanus. The blood showed: haemoglobin 13.3 grammes per 100 millilitres; white blood cells 13,200 per cubic millimetre; erythrocyte sedimentation rate (Westergren) 1 millimetre in 1 hour. Marrow puncture showed no neoplastic cells. *Biopsy*—The specimen consisted of numerous small irregular fragments of pale brown opaque tissue in which there were a few yellow streaks. Sections showed a pleomorphic picture similar to that seen in polymorphic reticulo-sarcomas arising in soft tissue (Figs. 6 and 7). The growth had considerable fibrous stroma and was rich in reticulin fibre. *Operation* (March 24, 1950)—Antero-lateral decompression was followed by little improvement of her condition. *Post-operative radiotherapy*—3,200 r in two weeks at 180 kilovolts to the spine. 2,000 r in ten days at 180 kilovolts to the foot. *Progress*—Two months after operation there were widespread deposits in the lungs. The patient died in June 1950.

**Necropsy**—The striking feature was the extent of involvement of the skeleton by metastatic growth. Secondary deposits were present in all the thoracic and lumbar vertebrae and in most of the ribs. There were also extensive deposits in the head and upper part of the shaft of the left femur and in the right middle and lateral cuneiform bones. The primary tumour (Fig. 8) had completely replaced the twelfth thoracic vertebra and growth extended into the spinal theca, compressing the spinal cord. There was no mediastinal mass and no suggestion that this tumour had arisen primarily from the adjacent soft tissue. There were extensive secondary deposits in the lungs and pleurae (Fig. 9). Everywhere the growth was firm in consistency and whitish in colour. No growth was found in any groups of lymph nodes except small deposits in the tracheo-bronchial lymph nodes. Careful search was made throughout the body for any small primary carcinoma, but none could be found and the suprarenals were normal. The histological picture in all sites of growth was similar to that seen in the original biopsy of the primary growth.

**Case 3**—Girl aged seventeen years. Shop assistant. *History*—This patient was first seen in October 1951 complaining of swelling of her left thigh. The swelling had been present for two months and had rapidly increased in size. Pain was absent except for an occasional ache. *On examination*, there was a firm swelling of the lower third of the left thigh which encircled the bone.
(Fig. 10). It was not tender and there was no enlargement of lymph nodes. Considerable fever was present.

Radiographs showed slight elevation of the periosteum with new bone formation (Fig. 11). This might well have been caused by infection. Six weeks later there was a large periosteal soft-tissue mass containing "sunray" spicules of new bone (Fig. 12). The radiological appearance was that of an osteogenic sarcoma.

Investigations—The urine contained no albumen or Bence-Jones protein. The blood showed: haemoglobin 10.7 grammes per 100 millilitres; white blood cells normal count; erythrocyte sedimentation rate (Westergren) 26 millimetres in 1 hour.

Biopsy—The specimen consisted of an irregular piece of soft friable tissue and a lymph node 1.0 centimetres in diameter. Section showed a very necrotic growth. In surviving areas the tumour was seen to be composed of a reticulum type of cell tending to be arranged around blood vessels (Fig. 13). The nuclei were large and hyperchromatic and mitotic figures were numerous. Little or no stroma was present. Section of the lymph node showed no evidence of tumour. Conclusion: a syncytial reticulo-sarcoma.

Radiotherapy—2,700 r in three weeks at 220 kilovolts.

Progress—After treatment the tumour was much reduced in size and the patient gained weight. Radiographs showed that the new bone formation was circumscribed and of increased density (Fig. 14). The patient remained well for fourteen months but then complained of pain in her left thigh. On further examination in January 1953 a soft-tissue recurrence was found in the site of the biopsy scar. The histology of a further biopsy was like that of the primary lesion. The recurrence was treated by radiotherapy, 2,900 r in one week at 220 kilovolts.

Operation (February 1953)—Disarticulation at the left hip.

Pathology—A longitudinal section through the femur and soft tissue (Fig. 15) showed the bone marrow to be soft and red in the head, neck and upper part of the shaft, and soft and yellow in the mid-shaft. The marrow cavity in the lower third of the femur was replaced by dense bone. On the lateral surface of the femur in this region the periosteum was raised by a small area of soft growth containing spicules of bone. On the medial aspect of the femur there was a subperiosteal mass of growth extending

Fig. 10
Case 3. Figure 10—Photograph showing the swelling of the thigh. Figure 11—Initial radiograph. Figure 12—Six weeks later.
FIG. 13
Case 3—Several blood vessels surrounded by growth of a uniform cell pattern. (× 170.)

FIG. 14
Case 3—Radiographs of femur after radiotherapy.
down to the medial condyle and about half-way round the circumference of the shaft. Its cut surface was white and the consistency soft. Six lymph nodes were present in the inguinal fat. Section of the marrow cavity in the lower third of the femur showed masses of new bone and no tumour tissue. Sections of the main subperiosteal mass showed a very similar picture to that seen in the biopsy but, in some sections, the cell pattern tended to be considerably more pleomorphic. There was still no reticulin fibre present. There was no suggestion of osteoid tissue or other evidence of bone formation on the part of the tumour. Sections of the lymph nodes showed no evidence of metastasis.

Progress—Three months after amputation she complained of pain in the back. Radiographs showed collapse of the eleventh thoracic vertebra. She developed swellings in the skull, frontal and occipital regions with radiological evidence of growth (osteolytic). There was cerebral compression, proptosis and papilloedema. The patient died in June 1953. Necropsy was not undertaken.

Case 4—Man aged thirty-nine. Window cleaner.

History—This patient complained of periodic attacks of pain and swelling in the upper end of the right tibia for four years. The swelling first arose while he was in India and was described as painful "red spots." These were thought to be inflammatory and were treated with fomentations. They soon disappeared but six weeks later came back and again got better with rest and compresses. There had been no injury. Over the next two years recurrences became more frequent, and in July 1946 he returned to the United Kingdom and entered hospital. A diagnosis of osteomyelitis was made. Treatment given was penicillin and poultries.

On examination (January 1948), there was a diffuse red swelling over the subcutaneous border of the upper third of the right tibia, measuring two and a half inches by one and a half inches. The swelling was tender, firm and lobulated. The inguinal lymph nodes were palpable and tender. Radiographs (report only available) showed diffuse osteoporosis of the upper tibia, with periostitis of the tibia and fibula. No other radiological changes were present in the skeleton.

Investigations—The blood showed: haemoglobin 12·7 grammes per 100 millilitres; white blood cells
10,900 per cubic millimetre; Wassermann reaction negative. Biopsy of an inguinal lymph node showed "non-specific inflammation."

Biopsy of tumour—Sections of the tumour tissue removed from the centre of the bone and from the subperiosteal region showed the histological picture of a trabeculated reticulo-sarcoma (Fig. 16). The subperiosteal tumour showed no striking evidence of recent rapid growth—mitotic figures were sparse and many of the vessels in the fibrous tissue showed obliterative endarteritis. The tumour tissue from the marrow cavity, however, was much more vascular and showed numerous mitotic figures. There was practically no reticulin fibre in the tumour cell masses.

Treatment—Radiotherapy 3,200 r in two weeks at 180 kilovolts to the tibia. Two weeks later, above-knee amputation (March 1948).

Pathology—On dissection the only abnormality was a slight fusiform enlargement of the upper third of the shaft of the tibia. One small lymph node was present in the popliteal space. On sawing through the tibia longitudinally two areas of soft haemorrhagic tumour tissue were found in the medullary cavity (Fig. 17). The uppermost was 9·0 centimetres in length and corresponded to the external fusiform enlargement which was due to thickened cortical bone. The second was at the lower end of the shaft and was circular, measuring 1·0 centimetres in diameter. The cortical bone overlying the upper growth was being infiltrated. Sections from the tumour mass at the upper end of the medullary cavity showed much of the growth to be destroyed by radiotherapy and replaced by fibrous tissue, but considerable areas of viable growth were still recognisable. Section from the other area of growth showed a more pleomorphic picture than that seen in the original biopsy. While there was still little stroma and no reticulin fibre the cells varied in size and shape and the nuclear pattern was much less constant. Section of the lymph node showed no abnormality.

Progress—Six years after amputation the patient was alive and well, working as a lift attendant.

Case 5—Married woman aged twenty-eight, with four children.

History—She complained of swelling of the outer side of the left lower leg of seven months duration. Size increasing, with some pain.

On examination, there was a swelling, three inches by two inches, situated in the middle third of the fibula, fixed to bone, tender, but not hot. There was no fever, and no enlargement of lymph nodes. Radiographs showed an osteolytic lesion of the fibula (Fig. 18). In some areas there was a suggestion of expansion of the cortex. The extent of the radiological lesion should be compared with that seen in the pathological specimen (Fig. 19).
Investigations—Blood examination showed: haemoglobin 11·9 grammes per 100 millilitres; white blood cells 11,000 per cubic millimetre.

Operation (February 1947)—Excision of the mid-shaft of the fibula together with adherent muscles into which the growth was infiltrating.

Pathology—The specimen (Fig. 19) consisted of a portion of fibula measuring 13·0 centimetres. For the most of its length it was enveloped by a fusiform mass to which muscle was attached. The fibula was fractured about the centre of the specimen. On cutting the bone and tumour through longitudinally most of the bone was seen to be destroyed and replaced by a firm fleshy tumour which had invaded the periosteum and infiltrated the adjacent muscle. It extended up and down the marrow cavity to the ends of the specimen. In some areas the tumour was haemorrhagic but for the most part it was yellowish in colour. Sections showed the growth to consist of masses of cells consisting almost entirely of nucleus, there being little cytoplasm and the cell boundaries being difficult or almost impossible to define (Fig. 20). The nuclei were pale and vesiculated: mitotic figures were infrequent. The cell masses were separated by large blood sinuses, many of which had no lining apart from tumour cells (Fig. 21). There was no necrosis. The growth had practically no supporting stroma and little or no reticulin fibre was present. Conclusion: a syncytial reticulo-sarcoma arising in the bone marrow. This growth was likely to be very radiosensitive.

Post-operative radiotherapy—2,150 r in two and a half weeks at 180 kilovolts to the operation site.

Progress—When seen seven and three-quarters years after operation this patient was well. She has had another child since the operation.

Case 6—Married woman aged thirty-eight.

History—This patient complained of a lump in the sternum increasing in size for two years. At first it was painful, but latterly not so. In July 1952 a biopsy of the sternal swelling was carried out, and the histological report suggested "chronic infection."

On examination (December 1952), there was a hard tumour projecting from the sternum, and measuring two inches by two inches. A retrosternal swelling could be felt in the suprasternal notch.

Investigations—Blood examination showed: haemoglobin 12·1 grammes per 100 millilitres; white blood cells 7,000 per cubic millimetre; erythrocyte sedimentation rate (Westergren) 6 millimetres in 1 hour. Wassermann reaction negative.

Radiographs (Fig. 22) showed an osteolytic lesion in the sternum with a large soft-tissue mass (compare with Case 1, Figure 2). Intravenous pyelography showed normal kidneys. The chest radiographs were normal.

Biopsy—Sections showed tumour masses separated by irregular trabeculae of collagen. The tumour
Fig. 21
Case 5—Showing a large blood space entirely surrounded by tumour cells. (×110.)

Fig. 22
Case 6—Radiographs of sternum before radiotherapy (left) and after radiotherapy (right).
FIG. 23
Case 6—Section showing a pleomorphic structure like that seen in Case 1.

FIG. 24
Case 6—A silver impregnation showing the rich reticulin content of the tumour. (×170.)
FIG. 25
Case 7—Radiograph showing lesion in the acromion process.

showed a very pleomorphic picture (Fig. 23) which was very similar to that seen in a polymorphic reticulo-sarcoma arising in lymphoid tissue. It was very rich in reticulin fibre (Fig. 24). The histology was almost identical to that seen in Case 2.

Treatment—Radiotherapy only. 4,000 r in forty-two days to the sternum.

Progress—When seen two years after treatment the patient was well, and the swelling had disappeared.

TABLE II
SUMMARY OF MAIN CLINICAL FEATURES IN SEVEN CASES OF RETICULO-SARCOMA OF BONE

<table>
<thead>
<tr>
<th>Case</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site</td>
<td>Spine-sternum</td>
<td>Spine</td>
<td>Femur</td>
<td>Tibia</td>
<td>Fibula</td>
<td>Sternum</td>
<td>Acromion</td>
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<td>Age</td>
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<td>17</td>
<td>17</td>
<td>39</td>
<td>28</td>
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<td>Pain</td>
<td>Pain</td>
<td>Swelling</td>
<td>Pain and swelling</td>
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<td>Duration</td>
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<td>2 months</td>
<td>2 months</td>
<td>48 months</td>
<td>7 months</td>
<td>24 months</td>
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<tr>
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<td>Radiotherapy</td>
<td>Radiotherapy</td>
<td>Radiotherapy, Amputation</td>
<td>Radiotherapy, Amputation</td>
<td>Excision, Radiotherapy</td>
<td>Radiotherapy</td>
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<tr>
<td>Follow-up</td>
<td>Died 28 months</td>
<td>Died 7 months</td>
<td>Died 22 months</td>
<td>Alive 10 years</td>
<td>Alive 8 years</td>
<td>Alive 3½ years</td>
<td>Alive 3 years</td>
</tr>
<tr>
<td>Time since first symptom</td>
<td>28 months</td>
<td>7 months</td>
<td>22 months</td>
<td>11 years</td>
<td>8½ years</td>
<td>3½ years</td>
<td>3 years</td>
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<tr>
<td>Cause of death</td>
<td>Deposits in lungs</td>
<td>Multiple deposits (autopsy)</td>
<td>Multiple deposits, Skull, Spine</td>
<td>—</td>
<td>—</td>
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</table>
Case 7—Married woman aged twenty-two.

History—In May 1953 she complained of pain in the right shoulder of gradual onset for ten months. Pain was severe for the first three weeks, but afterwards only intermittent. On examination, the patient was four months pregnant. The acromion process was tender but there was no swelling. Movements of the shoulder were slightly limited and there was a little wasting of the deltoid and spinati muscles.

Radiographs showed mottling of the right acromion process (Fig. 25). No soft-tissue swelling was visible. The provisional diagnosis was "tuberculosis."

Investigations—The urine contained no albumen or Bence-Jones protein. Blood examination showed: haemoglobin 14·2 grammes per 100 millilitres; white blood cells 11,200 per cubic millimetre; erythrocyte sedimentation rate (Westergren) 15 millimetres in 1 hour.

Operation (June 1953)—Excision of acromion process.

Pathology—The terminal part of the acromion was expanded and a large amount of thickened fatty tissue was adherent to its surface. On cutting the acromion longitudinally it was seen that much of it was replaced by firm fleshy tumour tissue showing no necrosis. The growth did not appear to extend through the covering periostium. Sections showed the histological picture of a polymorphic reticulo-sarcoma. There was a rich reticulin fibre network between the cells of the growth.

Post-operative radiotherapy—1,300 r in two weeks at 180 kilovolts.

Progress—The patient was well one year after treatment.

CLINICAL FEATURES

Consideration of these seven cases emphasises certain points made by previous authors. The site of the tumours is shown in Figure 26. There were three tumours in the lower limbs, two in the spine, one in the sternum, and one in the acromion process. The latter is an unusual position. Of the patients with vertebral tumours, one had developed a sternal swelling before admission to hospital, but this was not until eighteen months after his first symptom in the spine. The insidious onset of the disease is well illustrated by these two spinal cases, in which backache has been present for several months, yet only when paraplegia became obvious did these patients seek hospital care. The first symptom was swelling in three cases and pain in three. One patient complained of both. The tumour of the femur (Case 3) was the only one to show a daily variation in size, which is mentioned in the literature as a feature of reticulo-sarcoma of bone.

The duration of symptoms varied between two and forty-eight months, the average being sixteen months. In the early stages the similarity to chronic bone infection was striking. This is well illustrated in the swelling of the tibia (Case 4) which had been treated as osteomyelitis for four years and in the sternal swelling (Case 6), the first biopsy of which was reported as showing "chronic infection."

Fever was present as an early symptom in only one patient (Case 3). In the late stages of the disease it was a result of urinary infection, when paraplegia had completed the picture (Cases 1 and 2). The good general health of these patients in relation to the size of the tumour is mentioned in the literature as a feature of reticulo-sarcoma. This was found to be true, and only when general dissemination had taken place did the patient begin to look ill or to lose weight. The same can be said in regard to lymph node involvement by the growth, as this was found in only one instance as a terminal event (Case 1).
RADIOLOGICAL FEATURES

Four facets of the radiological diagnosis will be considered: 1) The diagnosis of Ewing's tumour; 2) the diagnosis of reticulo-sarcoma; 3) the radiological appearances in the present series; and 4) how far can these tumours be distinguished by radiological means?

The diagnosis of Ewing's tumour—The appearances described in Ewing's tumour are extremely variable. It "can be confused with any lesion of bone from osteomyelitis to osteogenic sarcoma" (McCormack et al. 1952). Lysis, mottling, sclerosis, cyst formation and periosteal reaction are described. These authors were able to make a diagnosis in only twelve out of eighty cases on a radiological basis. The so-called characteristic features are the situation of the tumour in the shaft of a long bone, its extent, and the periosteal reaction. The well known laminated or "onion-peel" appearance of reactive bone is by no means a constant feature. When "sunray" spicules are present they suggest an osteogenic sarcoma. Expansion of the shaft is more commonly seen in Ewing's tumour (Coley 1948).

The diagnosis of reticulo-sarcoma—Typical radiological appearances of primary reticulo-sarcoma of bone are described in the literature. It is suggested that a diagnosis can be made upon radiological grounds alone in many cases (Sherman and Snyder 1947). The tumour is situated near the end of a long bone, but tends to extend towards the shaft. It originates in the medulla and is essentially osteolytic. The cortex is destroyed, but there is no expansion. Periosteal reaction is not a constant feature, and in fact some authors stress the absence of reactive new bone under the periosteum (Valls et al. 1952). A soft-tissue shadow is frequently seen in the radiograph. This contains no tumour pattern and is never calcified (Sherman and Snyder 1947), in contrast to the soft-tissue tumour shadow in osteogenic sarcoma, in which calcification is common.
The response to irradiation is characteristic. The soft-tissue shadow first disappears and this is followed by re-formation of the cortex. The medullary bone is repaired and assumes a density somewhat greater than that of normal bone.

Radiological appearances in the present series—In the two vertebral tumours (Cases 1 and 2) it is difficult to describe any special features. In both, collapse of the bodies had taken place before films were taken and the texture was that of condensed bone. A paravertebral soft-tissue shadow, together with collapsed vertebral body and intact intervertebral discs, suggested the diagnosis of a malignant tumour. The true nature of this tumour was not determined until a biopsy had been done.

The tumour of the femur (Case 3) is perhaps the most instructive. The early films showed the presence of periosteal new bone (Fig. 11) without cortical erosion. This might well have been of inflammatory origin. Six weeks later this new bone was still present above the medial femoral condyle, but there was now a large soft-tissue tumour which was ossifying with "sunray" bone spicules. These films suggested an osteogenic sarcoma (Fig. 12). The tumour proved to be radiosensitive and after treatment became circumscribed. The films should be compared with Figure 27, which shows the typical appearance of a Ewing's tumour with regard to its site, and lamination of the periosteum, but in which the histological diagnosis was that of an osteogenic sarcoma. Again, Figure 28 is a good example of laminated periostitis in a case of staphylococcal osteomyelitis.

The tumour of the fibula (Case 5) showed an osteolytic lesion with a suggestion of cortical expansion (Fig. 18). The cortex was destroyed in places but there was little reactive new bone. This film should be compared with the photograph of the specimen (Fig. 19). The radiograph does not indicate the true extent of the tumour, which occupies considerably more of the fibular shaft. On removal at operation the bone was divided through tumour tissue, yet the patient is alive more than eight years later. The radiological appearance was that of a Ewing's tumour.

The tumour of the sternum (Case 6) was an osteolytic bone lesion with destruction of the cortex, but no bone expansion. A soft-tissue mass was present (Fig. 22). The picture is almost identical with that seen in the secondary tumour of the sternum in Case 1 (Fig. 2). After radiotherapy the soft-tissue mass became smaller and there was reactive new bone in the sternum. The appearance is that of a reticulo-sarcoma.

The tumour of the acromion process showed mottled sclerosis and rarefaction. There was no periostitis and no soft-tissue mass (Fig. 25).

How far can these tumours be distinguished by radiological means?—Although they form too small a series from which to draw any sweeping conclusions, these seven cases illustrate the diversity of radiological changes, which do not conform to any one type. We are left with the impression that it is not possible to distinguish between a Ewing's tumour and a reticulo-sarcoma on radiological grounds.

Ancillary methods of investigation, which included erythrocyte sedimentation rates, blood picture and search for Bence-Jones protein in the urine, proved to be of no help in diagnosis. This must be based upon an interpretation of the history, clinical and radiological signs, and on the histological findings, the latter being of particular importance.

The differential diagnosis must include chronic osteomyelitis and periostitis, osteogenic sarcoma, secondary carcinoma, multiple myeloma, primary lymphosarcoma with bone involvement, and eosinophilic granuloma. The question of differential diagnosis between Ewing's tumour and reticulo-sarcoma will be discussed later.

PATHOLOGY

In our material it has not been possible to separate the tumours into two clear-cut groups on the clinical or radiological appearances, and the gross pathology and histological picture
also did not enable this to be done. Figure 26 shows the sites of the tumours in the seven cases. Three were in long bones (right tibia, lower third of femur and mid-shaft of fibula) and four were in short bones (two in vertebrae, right acromion and sternum).

The gross appearance of the tumours occurring in long bones did not differ remarkably from those seen in other primary osteolytic tumours. They appeared to arise either in the mid-shaft or in the metaphysis, and extended through the cortex with a variable degree of bone destruction, lifting up the periosteum and forming a subperiosteal mass which enveloped the bone (Figs. 15, 17 and 19). Although the tumours themselves were not osteogenic the periosteum might be stimulated to form bone, either in layers to produce the "onion-peel" appearance, or in a radial manner to produce the typical "sunray" appearance of a periosteal osteogenic sarcoma (Fig. 12). The growth tended to spread up and down the marrow cavity to a much greater extent than was revealed by radiology. Whilst the periosteum contained the growth for a very considerable time it might be infiltrated eventually and the surrounding soft tissues involved (Case 3, Fig. 15). The growths were reddish in colour and usually not unduly soft or necrotic unless there had been intensive recent x-ray therapy before amputation. In Case 3 (Fig. 15) the growth, present in the medullary cavity, had been almost completely replaced by new bone, but this was following intensive x-ray therapy.

When small bones such as vertebrae were involved the tumour rapidly destroyed the bone, which collapsed. The adjacent discs were not involved, but growth extended into the surrounding tissues to a varying degree to form a soft-tissue mass. When the growth arose in the acromion and in the sternum there was, however, no evidence of extension through the periosteum into the adjacent tissues. In the only case to come to necropsy (Case 2) the growth started in the twelfth thoracic vertebra. Despite radiotherapy, death took place three months from the time the diagnosis was made. At necropsy the twelfth thoracic vertebra was completely replaced by growth and there were extensive metastases in other parts of the skeleton and in the lungs. There was nothing to suggest a primary origin in lymph nodes and the suprarenals were normal. Whereas clinically this case behaved as a Ewing's tumour, histologically it would not have been accepted as such because its variable histological structure and rich reticulin fibre content classes it as a reticulo-sarcoma (Figs. 6 and 7).

In the seven cases studied the histological structure was variable. In some the emphasis was on solid masses of tumour cells separated by trabeculae of fibrous tissue and little or no reticulin between the tumour cells (Fig. 16), whereas in others the picture was more pleomorphic with considerable collagen and reticulin fibre present (Figs. 3 and 4). As in most malignant tumours the apparent constancy of the histological picture in any one case varied with the number of sections examined from different areas of the growth.

In those growths in which much of the tumour had a fairly uniform structure and conformed most closely to that described as typical of Ewing's tumour the masses of tumour cells showed no cell boundaries and their nuclei were large and vesiculated and had an average diameter of 8 microns. They were surrounded by only a small quantity of cytoplasm. Nucleoli were uncommon and mitoses not very frequent. There was little or no reticulin fibre in these masses of tumour cells. In more pleomorphic areas and in those growths which throughout had a much more variable structure there was a rich reticulin stroma. The tumour cells varied in size and shape from occasional multinucleate cells to cells the size and shape of lymphocytes, but the predominant cell was considerably larger than a lymphocyte with a round or oval nucleus. The cell boundary was surrounded by a varying quantity of cytoplasm, which was usually basophilic but occasionally acidophilic. Nucleoli were infrequent, but mitoses were quite numerous. In none of these cases were any structures resembling rosettes seen. In all seven cases the tumours had a rich blood supply. In one case (Case 5) there were many blood spaces lined by tumour cells (Fig. 21), yet this patient is alive and well more than eight years from the time the diagnosis was made. In no case was there any evidence of bone formation on the part of the tumour.
DISCUSSION

The impression gathered from the literature that the separation of Ewing's tumour and reticulo-sarcoma was an artificial one has been confirmed by a study of this small series of cases.

The age of our patients ranged from seventeen to thirty-nine years; five were females and two were males. There was no striking difference in the mode of onset of the disease or in the duration of symptoms from those described in the literature. Three tumours occurred in long bones and four in other parts of the skeleton. This series is, however, too small to draw any conclusions from these facts. In only one case was fever present early in the disease and in all the blood counts and urine were normal.

Radiologically these seven cases illustrate a diversity of changes which do not conform to any one type. The impression gained is that it is not possible to distinguish between a Ewing's tumour and a reticulo-sarcoma of bone on radiological grounds. When radiological and histological changes are considered together it will be seen that this distinction is even more difficult.

The gross appearance of the tumours was variable and might even resemble that of an osteogenic sarcoma. This was particularly so in long bones. The histological picture was inconstant and, in this respect, resembled that seen in reticulo-sarcomas arising in lymphoid tissue. In three cases the histology, on the whole, was that of a Ewing's tumour as described in the literature, yet two of these patients are alive and well eight and eleven years after their first symptoms. In four cases in which pleomorphism was marked and reticulin fibre content well developed two patients died rapidly.

The criticism could be made that all these cases were reticulo-sarcomas of lymphoid tissue with early manifestations in the skeleton. The clinical picture is against this because no lymph node enlargement was found except in one case as a terminal event when there were general metastases. Also, in no case was a mediastinal or retroperitoneal mass demonstrated at any time. Besides, involvement of the skeleton in reticulo-sarcomas arising in soft tissue is uncommon. Craver and Copeland (1934) investigated the incidence of involvement of bone in soft-tissue lymphosarcomas either directly or by haematogenous spread. In 164 cases only seventeen showed lesions in bone. Of these, all except one had lymph node involvement before there was evidence of a bone tumour.

Similarly the clinical course and pathological picture rules out the possibility that these cases were unusual examples of carcinomatosis or secondary neuroblastomas. While it is true that there was no necropsy on two of them, one patient was aged seventeen and the other aged thirty-one, and reference to their case histories and pathology will show that these assumptions are most unlikely.

We consider therefore that a case has been made out for the recognition of primary reticulo-sarcoma of bone as a clinical and pathological entity. We have found no evidence to support the conception that this tumour is an entity separate from Ewing's tumour. We believe that they are one and the same thing.

Reticulo-sarcoma of bone is not a common condition, only seven examples of it having been seen in eight years. Its recognition, however, is important because the prognosis may be good, five out of seven patients being alive and well, one for eight and another for eleven years. Two patients presented, on the whole, the accepted histological picture of a Ewing's tumour, yet these have survived the longest. Two patients showed histologically a pleomorphic picture with a rich reticulin fibre content, yet they died rapidly.

The tumours are radiosensitive, and the best treatment is probably a combination of radiotherapy with excision or amputation when this is possible.

SUMMARY

1. Seven new cases of primary reticulo-sarcoma of bone are recorded, including one in which a full necropsy was carried out.
2. The literature of Ewing's tumour and reticulo-sarcoma of bone has been examined and the conclusion reached that the separation of these two tumours is an artificial one.

3. The investigation of our cases confirms this observation.

REFERENCES


