RADIOThERAPY FOR OSTEOGENIC SARCOMA

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The purpose of this paper is to consider the contributions of radiotherapy to the curative treatment of osteogenic sarcoma, in the light of the experience gained by the Bristol Bone Tumour Registry.

MATERIAL AND METHODS

Between 1942 and 1946 nine tumours have been treated radically by radiation—that is, by doses of 5,500–8,000 rads given with the object of permanent cure. Over the same period fifty-one amputations were done for tumours without demonstrable metastases.

The nine patients reported here are not all of those submitted to elective radiotherapy: in all, forty-one patients were so treated, but thirty-two are excluded because they received only palliative doses of under 5,000–5,500 rads. The tumours were classified histologically into three grades according to the percentage of cells in mitosis. For this work it is essential to have the services of a histologist specially experienced in this field. He must be able to separate the Grade 1 osteogenic sarcoma from other conditions malignant and benign such as chondrosarcoma, chondroblastoma, osteogenic fibroma, fibrous dysplasia, simple periosteal reactions, infection and exuberant callus.

RESULTS

In Table I the results obtained from the treatment of sixty tumours are classified according to their histological grading. The Table includes both cures and failures, and the results both of amputation and radiation. The numbers are small and some of the cases have been observed for not more than three years. Sixteen patients (26 per cent) were alive three or more years after treatment. If the twenty-eight patients with advanced disease seen during the same period are added to the failures the rate of survival falls to 17 per cent.

It will be seen how important the histological grading is: nine out of thirteen patients with tumours of Grade 1 treated by both methods are still alive, though one of them has pulmonary metastases. Only seven out of thirty-two patients with tumours of Grade 2 survive, and not a single patient out of fifteen with Grade 3 tumours is alive.
The successes after amputation—Five out of seven patients with tumours of Grade 1 survived after amputation (Table II). In this group there was frequently some uncertainty of diagnosis in the early stages. In three of these five the original histology was inconclusive or atypical. Radiological appearances were typical in three, but clinical histories were often long.

### TABLE II

**SURVIVORS AFTER AMPUTATION—GRADE 1 (FIVE PATIENTS)**

<table>
<thead>
<tr>
<th>Number</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Date of operation</th>
<th>Clinical features</th>
<th>Pathological features</th>
<th>Radiological features</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>18</td>
<td>January 1942</td>
<td>Typical</td>
<td>Inconclusive originally; confirmed after amputation</td>
<td>Typical</td>
</tr>
<tr>
<td>2</td>
<td>Female</td>
<td>14</td>
<td>October 1944</td>
<td>Typical</td>
<td>Typical osteoblastic</td>
<td>Typical</td>
</tr>
<tr>
<td>3</td>
<td>Male</td>
<td>21</td>
<td>February 1944</td>
<td>Long history and slow development</td>
<td>Debatable at first, Bristol Tumour Registry confirmed sarcoma</td>
<td>None special</td>
</tr>
<tr>
<td>4</td>
<td>Female</td>
<td>23</td>
<td>July 1953</td>
<td>Diagnosed and treated as osteoclastoma 1951; tumour extended until 1953, then amputation</td>
<td>Classified as sarcoma in osteoclastoma. Never typical</td>
<td>Cystic lesion, not typical</td>
</tr>
<tr>
<td>5</td>
<td>Male</td>
<td>8</td>
<td>October 1952</td>
<td>Swelling with little pain</td>
<td>Fairly typical but hint of synovioma</td>
<td>Typical</td>
</tr>
</tbody>
</table>

### TABLE III

**SURVIVORS AFTER AMPUTATION—GRADE 2 (SIX PATIENTS)**

<table>
<thead>
<tr>
<th>Number</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Date of operation</th>
<th>Site</th>
<th>Clinical features</th>
<th>Pathological features</th>
<th>Radiological features</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>38</td>
<td>1949</td>
<td>Lower femur</td>
<td>Typical</td>
<td>Typical osteoblastic</td>
<td>Atypical, osteoblastoma or fibrosarcoma suggested</td>
</tr>
<tr>
<td>2</td>
<td>Female</td>
<td>36</td>
<td>January 1951</td>
<td>Lower femur</td>
<td>Typical, but sixteen months' history</td>
<td>Typical pleomorphic, osteolytic</td>
<td>Typical osteolytic</td>
</tr>
<tr>
<td>3</td>
<td>Female</td>
<td>76</td>
<td>September 1952</td>
<td>Lower femur</td>
<td>Pathological fracture presenting symptoms</td>
<td>Sarcoma in Paget's disease</td>
<td>Paget's disease and sarcoma</td>
</tr>
<tr>
<td>4</td>
<td>Female</td>
<td>53</td>
<td>May 1953</td>
<td>Tibia</td>
<td>Typical, with Paget's disease</td>
<td>Typical osteolytic</td>
<td>Typical</td>
</tr>
<tr>
<td>5</td>
<td>Female</td>
<td>36</td>
<td>May 1955</td>
<td>Upper tibia</td>
<td>Typical</td>
<td>Typical</td>
<td>Typical osteolytic</td>
</tr>
<tr>
<td>6</td>
<td>Male</td>
<td>22</td>
<td>September 1956</td>
<td>Upper tibia</td>
<td>Typical, but pain slight</td>
<td>Osteolytic with tendency to chondrosarcoma</td>
<td>Osteolytic with tendency to chondrosarcoma</td>
</tr>
</tbody>
</table>

Six out of thirty patients with tumours of Grade 2 survived after amputation (Table III). In most cases the histology was typical from the first.

The successes after radiotherapy—Five out of the nine patients treated by radiation survived (Table IV). The first three were treated with deep x-rays; the last two by cobalt beam. Four tumours were of Grade 1 and one was of Grade 2. The three earliest were tumours of the humerus, and the first two of these were only diagnosed after some time. The first tumour was not discovered until biopsy was repeated; the second was treated as osteomyelitis for

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some time until the diagnosis was revealed by biopsy. Both tumours received high doses of radiation, and both patients suffered local necrosis of bone as a result, but retained the arm and a useful hand.

THE IMPORTANCE OF HISTOLOGICAL GRADING

Diagnosis—Diagnosis is more difficult in all Grade I cases either by clinical, radiological or histological means. It was not possible to determine which tumours would be better treated by amputation or by radiation.

Prognosis—Histological grading is the best indication of prognosis. A Grade I case will probably do well with either method of treatment. The choice of therapy must be made on other grounds than chances of survival.

CASE REPORTS

Case 1—A boy aged twelve complained of pain and swelling of the right elbow in April 1945. In November 1945, in Ceylon, a biopsy was done but the section showed signs only of “osteitis fibrosa.” This section is not now available. Symptoms increased and a second biopsy was taken in January 1946. A diagnosis of osteogenic sarcoma was made from this. The tumour was classified as Grade I (Fig. 1).

FIG 1
Case 1—Histology of second biopsy specimen, showing appearances of Grade I osteogenic sarcoma. (225.)
Over five weeks in February and March 1946 a dose of 6,700 rads of deep x-rays was given. Up to February 1960 there has been no sign of recurrence of the tumour, but in October 1946 the boy suffered a pathological fracture of the upper end of the ulna caused by radionecrosis. This fracture in due course healed. The radiation also caused fibrosis of soft tissues and consequent stiffness of the elbow, though the hand retained excellent function. The radiological appearances before and after treatment are shown in Figures 2 and 3: the external appearance in 1949 is shown in Figures 4 and 5.
Case 2—A girl of nine complained of pain in the right shoulder in July 1948. The initial diagnosis by the orthopaedic surgeon was osteomyelitis of the upper end of the humerus. By May 1949, however, progress was clearly not as good as it should have been and biopsy was done (Fig. 6). The histological diagnosis of osteogenic sarcoma was accepted by the
Bone Tumour Registry, and the tumour was classified as Grade I. The upper arm was given a dose of 8,500 rads of deep x-rays over a period of three months from June to September 1949. There has been no recurrence of the tumour, but in 1951 pathological fracture was caused by radionecrosis. The necrotic bone was then removed by local resection and replaced by a bone graft. Sections of this necrotic bone showed no evidence of recurrence of the tumour (Fig. 7).

Improvement has continued since, with no signs of recurrence or metastases, though there is some restriction of movement at the shoulder. The radiological appearances before and after treatment are shown in Figures 8 and 9.

Case 3—A man aged sixty complained in 1950 of pain in the right arm above the elbow. Radiographs (Fig. 10) showed extensive destruction of the lower end of the humerus. In January 1951 the swelling of the lower end of the humerus was subjected to biopsy. Sections showed a Grade 2 osteogenic sarcoma of osteolytic type arising in bone affected by Paget's disease (Fig. 11). The tumour was treated by deep x-rays, a dose of 6,000 rads being given over a period of two months up to April 1951.

At the end of 1955 there was recurrence of pain and swelling in the site of the tumour, and, recurrence being suspected, the arm was amputated in February 1956. Examination of the specimen showed radionecrosis of bone and only necrotic remnants of the tumour.

Case 3. Figure 11—Histological appearance of biopsy specimen. ( x 225.) Osteolytic type of osteogenic sarcoma, Grade 2. Figure 12—Histological appearance of necrotic bone five years after treatment. ( x 225.) Tumour cells dead and walled up in fibrous tissue.
hand could probably have been saved by local resection. The specimen taken five years after treatment showed no sign of tumour, except for a few degenerate cells apparently dead and walled up in fibrous tissue (Fig. 12). In most parts of the section only evidence of radionecrosis was to be seen.

Case 4—A woman of twenty-two complained in 1953 of pain and swelling in the line of the eleventh right rib. This was locally excised and found to be an osteogenic sarcoma of osteoblastic type. It was classified as Grade 1. The swelling recurred in 1955 and was again excised. The tumour was found to be invading the diaphragm and surrounding tissues and the removal was incomplete. Radiation was therefore given, 7,100 rads being administered by cobalt beam over eight weeks. Up to December 1959 there had been no local recurrence or trouble with necrosis, but secondaries appeared in the lungs in 1958 and the general condition was rapidly deteriorating in February 1960. It is possible that since the tumour itself was locally destroyed by irradiation, pulmonary metastasis might not have occurred had such treatment been given in 1953.

Case 5—A man of forty-seven complained in May 1955 of a pain in the region of the eleventh right rib. A swelling then developed which was locally excised in August 1955. Histological examination showed osteogenic sarcoma of osteoblastic type classified as Grade 1.

Radiotherapy to the area was started at once. A dose of 8,000 rads was given over ten weeks by the radio-cobalt unit. Up to December 1959 there has been no sign of recurrence of tumour or of damage to healthy tissues by the radiation, and the patient has remained very well.

DISCUSSION

It seems clear that many of the cases of osteogenic sarcoma which may be cured by any method of treatment are locally curable by heavy doses of radiation. However, the radiation needed is heavy enough to risk damage to normal tissues, such as excessive fibrosis and necrosis of bone. This necrosis of bone is less likely with Co60 or equivalent radiation, and the use of the cobalt beam or other supervoltage radiation is to be preferred.

The lower limb, if much damaged in this way, may be a considerable handicap to the patient, and may be so inefficient that a good artificial leg will be more useful. The hand, however, has never been adequately imitated, so it is better to retain the upper limb whenever possible, in spite of the possible local disability when radiotherapy is used, and in spite of the need for close follow-up to watch for local recurrence. At the first appearance of definite evidence of local recurrence the arm must be amputated. Further radiation is impossible. Radiation may be the only practicable method of treatment in many tumours of the axial skeleton, ribs and sternum.

If local necrosis of bone does occur the surgeon will need to resect the segment of bone, but may still save the limb. He may think local removal of the tumour a wise precaution in any case, when the reaction to radiation has settled.

It is suggested that many more cases of osteogenic sarcoma of the upper limb should be treated by radiotherapy. This should be done in any hospital where there is a radiotherapist who is prepared to give high doses with modern machinery, such as 7,000–8,000 rads in eight to nine weeks with Co60. Amputation is still the treatment of choice for sarcomata of the lower limb.

SUMMARY

1. Nine patients treated for osteogenic sarcoma by elective radical irradiation are reviewed. Five of the nine patients have survived for from three to fourteen years, but one patient has metastases.
2. These results are compared with those from primary amputation.
3. The importance of histological grading in prognosis is emphasised.
4. It is concluded that radical irradiation should be considered in place of primary amputation for osteogenic sarcoma in the upper limb.

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