A REVIEW OF THE BEHAVIOUR OF CHONDROSARCOMA OF BONE

N. G. SANERKIN, P. GALLAGHER

From the Departments of Osteo-articular Pathology and Orthopaedic Surgery, Bristol Royal Infirmary, and the Bristol Bone Tumour Registry

Sixty-two cases of chondrosarcoma of bone were reviewed and histologically graded as low, medium or high-grade tumours. After excluding patients dead from unrelated causes or lost to follow-up, forty cases were available for ten-year follow-up and fifty-eight for five-year follow-up. The rates of survival, recurrence and metastasis were analysed according to the histological grading. Recurrence was further analysed according to the adequacy of treatment. The results were compared with those previously reported in the literature.

There was a ten-year survival rate of 58 per cent. Recurrence developed in 58 per cent and was uncontrollable in 29 per cent. The recurrence rate was 87 per cent with inadequate treatment and 15 per cent with adequate treatment. Recurrences outside the limb bones usually proved uncontrollable; recurrences in the limb bones were amenable to further, and if necessary repeated, operations. High-grade chondrosarcoma had a metastatic risk of 75 per cent and eventual mortality of 88 per cent. Medium-grade chondrosarcoma had a metastatic risk of 14 per cent and a mortality of 60 per cent. Low-grade chondrosarcoma had a metastatic risk of 5 per cent and a mortality of 29 per cent.

Previous reviews of chondrosarcoma of bone, in particular the large series of Dahlin and Henderson (1956) and Henderson and Dahlin (1963), have firmly established the role of uncontrolled local growth in the fatal outcome of this tumour. They have also shown its usually lengthy progression and emphasised the importance of adequate primary surgical treatment in its management. The adverse effects on the prognosis of the higher grades of chondrosarcoma have also been referred to in a number of studies (O’Neal and Ackerman 1952; Dahlin and Henderson 1956; Lindborg, Söderberg and Spjut 1961; Marcove and Huvos 1971; Marcove et al. 1972). However, only a recent review of seventy-one cases (Evans, Ayala and Romsdahl 1977) has provided a detailed analysis of the behaviour of this tumour, particularly of its metastatic potential and prognosis, according to its histological grading. A review, essentially along similar lines, has been in progress at the Bristol Bone Tumour Registry, and its findings will be reported herein and compared with those of other series.

MATERIAL AND METHODS

In the records of the Bristol Bone Tumour Registry between 1946 and 1973 there were sixty-two cases of chondrosarcoma of bone, forty-nine before 1968 and thirteen between 1968 and 1973. Of these sixty-two cases, after excluding those who died from unrelated causes or were lost to follow-up, forty were available for ten-year follow-up and fifty-eight for five-year follow-up.

The histological sections were studied and the tumours subdivided into three groups designated as low, medium and high-grade chondrosarcoma, roughly equivalent to Grades I, II and III of other workers (Dahlin and Henderson 1956; Marcove and Huvos 1971; Marcove et al. 1972; Evans et al. 1977). The histological criteria used for the diagnosis and grading in this study have already been presented in a separate paper on the pathology of chondrosarcoma of bone (Sanerkin 1979). Briefly, low-grade chondrosarcoma may superficially resemble juvenile chondroma in its cellular composition (Lichtenstein and Jaffe 1943) but is invariably identifiable by its invasive activity in relation to the host bone. High-grade chondrosarcoma shows unmistakable features of anaplasia and has a relatively

N. G. Sanerkin, M.D., F.R.C.P.Ed., Department of Osteo-articular Pathology
P. Gallagher, F.R.C.S., Senior Registrar, Department of Orthopaedic Surgery
Bristol Royal Infirmary, Bristol BS2 8HW, England.

Requests for reprints should be sent to Dr N. G. Sanerkin.
high mitotic rate—mitoses are readily found; it must be distinguished from chondroblastic osteosarcoma by the absence of alkaline phosphatase or tumour osteoid. Medium-grade chondrosarcoma forms an intermediate group; the diagnosis of chondrosarcoma is immediately obvious from its cellular composition, but it shows no anaplastic features and its mitotic activity is decidedly low—mitoses, if found, must be diligently searched for.

The following clinical information was analysed: age, sex, site, associated abnormalities, treatment and follow-up data. For the purposes of this study, adequate surgical treatment was taken as the complete removal of the tumour with a clear margin of normal tissue without exposing the tumour, together with the previous biopsy wound. The rates of survival, recurrence and metastasis were determined in relation to the grading of the tumour and the adequacy or otherwise of treatment. The statistical significance of the observed differences was determined by the chi-square test.

**Table I. Age distribution in the three grades**

<table>
<thead>
<tr>
<th>Age range (years)</th>
<th>Mean age (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-grade tumours</td>
<td>19–77</td>
</tr>
<tr>
<td>Medium-grade tumours</td>
<td>25–78</td>
</tr>
<tr>
<td>High-grade tumours</td>
<td>19–73</td>
</tr>
</tbody>
</table>

**RESULTS**

The age distribution of the sixty-two patients is given in Figure 1. There was a peak in the fifth decade, and the mean age was fifty-one. The two youngest patients were both aged nineteen. The age distribution and the mean age did not differ in the three grades (Table I). In the ten chondrosarcomata of all grades which metastasised, the age of the patients ranged from thirty-eight to seventy-three, and the mean age was fifty-five.

There were twenty-nine men and thirty-three women. This sex distribution is different from that reported in previous series, in which there has been almost invariably a male preponderance.

**Site of the tumour.** The anatomical site of the sixty-two chondrosarcomata is given in Figure 2. This distribution differed from that given in previous reviews, in which the pelvis had been the commonest site. The femur (thirteen cases) was a slightly more frequent site than the pelvis (eleven cases) and, significantly, six chondrosarcomata occurred in the hand (nearly 10 per cent of all cases).

**Associated abnormalities.** Three patients had multiple enchondromata and four multiple osteochondromata. At least two patients had proven antecedent solitary enchondroma, but the precise incidence of pre-existing enchondroma was impossible to determine with any confidence.

**Grading of tumours.** Thirty-nine tumours were of low

**Table II. The frequency of the various grades at different sites**

<table>
<thead>
<tr>
<th>Site</th>
<th>Low-grade</th>
<th>Medium-grade</th>
<th>High-grade</th>
<th>All grades</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femur</td>
<td>7</td>
<td>3</td>
<td>3</td>
<td>13</td>
</tr>
<tr>
<td>Pelvis and sacrum</td>
<td>7</td>
<td>4</td>
<td>1</td>
<td>12</td>
</tr>
<tr>
<td>Scapula, sternum and ribs</td>
<td>7</td>
<td>2</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>Hand and foot</td>
<td>7</td>
<td>1</td>
<td>—</td>
<td>8</td>
</tr>
<tr>
<td>Skull</td>
<td>6</td>
<td>—</td>
<td>—</td>
<td>6</td>
</tr>
<tr>
<td>Humerus</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Spine</td>
<td>2</td>
<td>—</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Tibia</td>
<td>1</td>
<td>1</td>
<td>—</td>
<td>2</td>
</tr>
<tr>
<td>Larynx</td>
<td>—</td>
<td>1</td>
<td>—</td>
<td>1</td>
</tr>
<tr>
<td>All sites</td>
<td>39</td>
<td>14</td>
<td>9</td>
<td>62</td>
</tr>
</tbody>
</table>
grade (63 per cent), fourteen of medium grade (23 per cent) and nine of high grade (14 per cent). Three of the high-grade chondrosarcomata arose in tumours of lower grade: two progressed from the lower to the higher grade and the third arose by fibrosarcomatous "dedifferentiation" (Dahlin and Beabout 1971). The frequency of the various grades at different sites is shown in Table II. In view of the small numbers involved, the forequarter amputation in 1975. Five died from unrelated diseases, one was lost to follow-up, fifteen remain alive and well.

The effect of the adequacy of the initial treatment on survival is given in Figure 5. The survival rate is 67 per cent with adequate treatment and 50 per cent with inadequate treatment. The difference is not statistically significant.

![Figure 3](image1.png)

**Figure 3**—Survival in fifty-eight cases of chondrosarcoma followed up for five years. Figure 4—Survival in forty cases of chondrosarcoma followed up for ten years. The graph for high-grade chondrosarcoma shows a rather misleadingly high survival, because one exceptional patient died after the tenth year (the only one to do so in this series). In fact, only one high-grade chondrosarcoma eventually survived.

![Figure 4](image2.png)

![Figure 5](image3.png)

**Figure 5**

Survival according to adequacy or otherwise of the initial treatment. Recurrent chondrosarcoma in the limb bones are usually amenable to further surgical treatment, with consequent favourable effect on survival of patients initially treated inadequately.

Relative frequency cannot be assessed reliably. However, there is a higher percentage of low-grade tumours in the skull and the hands and feet.

**Survival**. The survival rates are given in Figures 3 and 4. The five-year survival (Fig. 3) was 78 per cent overall, with 89 per cent in low-grade, 71 per cent in medium-grade, and 38 per cent in high-grade tumours. The ten-year survival (Fig. 4) was 58 per cent overall, with 71 per cent in low-grade, 40 per cent in medium-grade, and 33 per cent in high-grade tumours. The difference in survival between the high-grade tumours and the rest is statistically significant ($P<0.01$).

Of the seventeen deaths in the ten-year follow-up, thirteen (76 per cent) occurred in the first five years and four (24 per cent) between the fifth and tenth years.

Twenty-three patients survived beyond ten years, all but two of them were free of recurrences and apparently cured. One of the two patients with recurrences died in the sixteenth year with metastases from fibrosarcomatous "dedifferentiation" of his chondrosarcoma. The other had a low-grade chondrosarcoma of the humerus with multiple recurrences over thirty years, and he remains alive and well after a
Recurrence. In this analysis only the first recurrence has been taken into consideration. High-grade tumours have not been included, because with them the major problem is metastasis rather than local recurrence. In no instance did the first recurrence take place after the fifth year and we believe the use of the five-year period of follow-up to be valid for analysis of recurrences.

The rate of recurrence (Fig. 6) was 58 per cent overall, with 50 per cent in low-grade, and 78 per cent in medium-grade tumours. These differences are not statistically significant.

Figure 7 sets out the rate of recurrence according to the adequacy of treatment. Inadequate treatment resulted in a recurrence rate of 90 per cent in medium-grade and 85 per cent in low-grade tumours; with adequate treatment, the corresponding figures were 50 per cent for medium-grade and 6 per cent for low-grade tumours. The differences due to treatment are statistically significant with low-grade tumours ($P<0.01$) but not with medium-grade tumours. Uncontrolled recurrence, not amenable to further surgical treatment and leading to the patient's death, occurred in 29 per cent of the patients overall, and in 17 per cent of low-grade and 42 per cent of medium-grade tumours. These figures indicate that about half of the recurrences, mainly in the limb bones, were amenable to subsequent surgical control.

The pelvis and the thoracic region account for most of the deaths from uncontrolled local disease. Taking into account those cases with a ten-year follow-up, of twenty cases with pelvic or thoracic tumours eleven (55 per cent) died from local disease; of fourteen chondrosarcomata in the limbs (including three in the hands and feet) only two (14 per cent) led to death from local disease, in both by direct extension from proximal tumours into the pelvis or thorax. These differences are statistically significant ($P<0.1$) and a logical reflection of the fact that tumours of the trunk are less amenable to local control than those in the limbs.

Metastasis. Metastases developed in ten cases (16 per cent): two in low-grade (5 per cent), two in medium-grade (14 per cent) and six in high-grade chondrosarcomata (75 per cent)*. The difference in the metastatic rate between the high-grade tumours and the others is statistically significant ($P<0.01$). In five cases metastases appeared early and the patients were dead within two years. In others metastases appeared later, between the third and eighth years, and in one exceptional case in the fifteenth year after "dedifferentiation" had occurred. Only one patient survived pulmonary metastasis and he remains alive and well, ten years after presentation and two years after thoracotomy for removal of the metastasis.

Four of the metastasising chondrosarcomata arose in the femur, and one each in the humerus, the scapula, the rib, the pelvis, the larynx and the hand. The apparent excess in the femur is not statistically significant.

Table III compares the results of the present study with those of previous series (Dahlin and Henderson 1956; Henderson and Dahlin 1963; Evans et al. 1977).

* Six out of eight cases; the ninth case died soon after diagnosis from postoperative complications.
**Table III.** A comparison of results (in percentages) in the present study with those in previous reviews

<table>
<thead>
<tr>
<th></th>
<th>Present series</th>
<th>Evans et al. (1977)*</th>
<th>Dahlin and Henderson (1956)</th>
<th>Henderson and Dahlin (1963)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Grading of tumours</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-grade (Grade I)</td>
<td>63</td>
<td>45</td>
<td>57</td>
<td>—</td>
</tr>
<tr>
<td>Medium-grade (Grade II)</td>
<td>23</td>
<td>30</td>
<td>37</td>
<td>—</td>
</tr>
<tr>
<td>High-grade (Grade III)</td>
<td>14</td>
<td>25</td>
<td>6</td>
<td>—</td>
</tr>
<tr>
<td><strong>Survival</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Five years</td>
<td>78</td>
<td>77</td>
<td>—</td>
<td>54</td>
</tr>
<tr>
<td>Ten years</td>
<td>58</td>
<td>67</td>
<td>—</td>
<td>38</td>
</tr>
<tr>
<td>When initial treatment was:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adequate</td>
<td>67</td>
<td>84</td>
<td>over 41</td>
<td>69</td>
</tr>
<tr>
<td>Inadequate</td>
<td>50†</td>
<td>79‡</td>
<td>27</td>
<td>19</td>
</tr>
<tr>
<td><strong>Recurrence</strong> (low and medium-grade tumours)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All cases</td>
<td>58</td>
<td>48</td>
<td>73</td>
<td>—</td>
</tr>
<tr>
<td>Uncontrolled</td>
<td>29</td>
<td>30</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>When initial treatment was:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adequate</td>
<td>15</td>
<td>16</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Inadequate</td>
<td>87</td>
<td>93</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td><strong>Metastasis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All cases</td>
<td>16</td>
<td>21</td>
<td>16</td>
<td>“Uncommon”</td>
</tr>
<tr>
<td>Low-grade (Grade I)</td>
<td>5</td>
<td>0</td>
<td>12</td>
<td>—</td>
</tr>
<tr>
<td>Medium-grade (Grade II)</td>
<td>14</td>
<td>10</td>
<td>18</td>
<td>—</td>
</tr>
<tr>
<td>High-grade (Grade III)</td>
<td>75</td>
<td>71</td>
<td>38</td>
<td>—</td>
</tr>
</tbody>
</table>

* Non-parametric estimation.
† Includes inoperable cases, biopsied only or partially removed.
‡ Excludes inoperable cases.

**DISCUSSION**

The results of this study are broadly in conformity with those of Evans et al. (1977) who dealt with seventy-one chondrosarcomata, including cases with less than a five-year follow-up, on a non-parametric estimate by the method of Kaplan and Meier (1958). We elected to deal with actual data on five-year and ten-year follow-up, because non-parametric analysis can at best give only an approximate estimate. Relatively few patients die after the tenth year, so that a ten-year follow-up provides a reasonable guide to survival. Few tumours recur for the first time after the fifth year, so that a five-year follow-up gives a fair assessment concerning local surgical control of the tumour.

The overall ten-year survival in the present series (58 per cent) is higher than the 38 per cent given by Henderson and Dahlin (1963) but lower than the rate of 67 per cent given by Evans et al. (1977). The reason for the small difference between our series and that of Evans et al. (1977) may possibly lie in the analytical methods employed. Nevertheless, both are significantly better than those of Henderson and Dahlin (1963). Perhaps, as suggested by Evans et al. (1977), this is due to the fact that Henderson and Dahlin’s series included many cases dating back to the earlier part of the century when surgical precepts and expertise in the treatment of chondrosarcoma may have been less well developed.

High-grade chondrosarcoma forms a relatively small proportion of cases (14 per cent) but is highly lethal, with a considerable risk of metastasis (75 per cent) and eventual mortality of 88 per cent. This metastatic risk is comparable with that for osteosarcoma...
over the age of twenty-five (Price and Jeffree 1973). It
may, therefore, be argued that in high-grade chon-
drosarcoma the primary operation should be augmented
with adjuvant chemotherapy as for osteosarcoma, in
the hope of controlling metastatic disease at an early stage.

With medium and low-grade chondrosarcoma,
the risk of metastasis is relatively low (14 per cent and 5
per cent respectively) and the main problem is the
control of local disease. Unless the initial surgical
operation is adequate—that is, the tumour is removed
completely without exposing any part of it, together with
the previous biopsy track—recurrence may be expected
in 90 per cent of medium-grade and 85 per cent of
low-grade chondrosarcoma and will prove uncontroll-
able in 42 per cent and 17 per cent respectively. Deaths
from uncontrolled local disease have mainly occurred in
patients with chondrosarcoma of the pelvis and thorax.
Recurrences in the limb bones are amenable to
further—if need be repeated—operations, unless they extend
from the proximal femoral or humeral tumours
to the pelvis or thorax, as happened in two of our cases.
The poor prognosis of chondrosarcoma of the pelvis
and thoracic cage is thus related to anatomical and
surgical problems rather than to any intrinsic aggressiv-
eness or metastatic potential. The percentage of
metastasising tumours at these sites was 13 per cent
compared with 20 per cent for tumours at all other sites.

Early adequate treatment of low-grade and
medium-grade chondrosarcoma is important, not only
for the prevention of uncontrollable recurrence, but to
forestall the possibility of “dedifferentiation” or pro-
gression to a high-grade tumour with its attendant high
metastatic risk. “Dedifferentiation” or progression
occurred in three of our cases and has also been noted in
most other series, with the exception of Evans et al.

There has been a general belief that, in chondrosar-
coma of bone, the younger the age of onset the worse
the prognosis, but this is not borne out by this study. The age
distribution of high-grade chondrosarcoma does not
differ in the slightest from that for all chondrosarcomata.
Indeed, patients with metastasising chondrosarcoma
had an age range of thirty-eight to seventy-three (mean
fifty-five), compared with nineteen to seventy-eight
(mean fifty-one) for the entire series. The current
misapprehension has presumably arisen from the frequent misdiagnosis of juvenile and adolescent chon-
droblastic osteosarcomata. The latter may show no
necrotic bone, either in the biopsy material or in the
entire tumour, and are then inappropriately diagnosed
as chondrosarcomata. The true nature of such osteoid-
deficient chondroblastic osteosarcomata can be estab-
lished by the demonstration of alkaline phosphatase in
the tumour cells.

We would like to thank the very numerous colleagues who have referred their cases to the Bristol Bone Tumour Registry with clinical, radiological and pathological material; to Messrs. Findlay, P. J. Hall and A. Wilson for technical and photographic assistance; and to Mrs. J. N. Nutt for secretarial help.

REFERENCES