CHONDROSARCOMA OF THE SOFT TISSUES

TWO DIFFERENT SUB-GROUPS

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Chondrosarcomas arising from soft tissues are rare. Two different varieties are described, myxoid and mesenchymal. We have collected nine cases of the tumour, five myxoid and four mesenchymal, from a review of 513 cases of chondrosarcoma seen between 1904 and 1988. We report the principal clinical, radiographical and histological differences between the two varieties and discuss their surgical treatment and prognosis.

Extraskeletal chondrosarcomas are much less common than those in bone. Tumours arising from the soft tissues are not attached to bone, periosteum or cartilage (Stout and Verner 1953; Goldenberg, Cohen and Steinlauf 1967; Amir et al 1985). They can be divided into two histological varieties: myxoid and mesenchymal. The aim of this paper is to define these two entities.

PATIENTS AND METHODS

At the Bone Tumour Centre of the Rizzoli Institute, Bologna, 513 cases of chondrosarcoma were seen between 1904 and 1988 and have been reviewed clinically, radiographically and histologically. Only in nine patients was the diagnosis of soft-tissue chondrosarcoma confirmed (1.7%). Of these, five were myxoid and four were mesenchymal.

Clinical findings. Clinical details are reported in Table I for the seven women and two men aged 32 to 62 years. Eight tumours were in a lower limb and only one in an upper limb. Pain and tenderness were the main symptoms. The duration of symptoms ranged from three to 24 months (average, 12 months: 17 for myxoid, nine for mesenchymal chondrosarcoma).

Imaging. In myxoid chondrosarcoma the radiographs were normal (case 3) or showed only a soft-tissue mass...
Table 1. Clinical details of nine patients with soft-tissue chondrosarcoma

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (yr)</th>
<th>Site</th>
<th>Stage</th>
<th>Treatment</th>
<th>Time to metastasis (mth)</th>
<th>Follow-up (mth)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>62 F</td>
<td>Vastus medialis</td>
<td>IA</td>
<td>Wide excision</td>
<td>-</td>
<td>19</td>
<td>Tumour free</td>
</tr>
<tr>
<td>2</td>
<td>32 F</td>
<td>Deltoid</td>
<td>IA</td>
<td>Wide excision</td>
<td>-</td>
<td>36</td>
<td>Tumour free</td>
</tr>
<tr>
<td>3</td>
<td>45 F</td>
<td>Vastus medialis</td>
<td>IA</td>
<td>Wide excision</td>
<td>-</td>
<td>60</td>
<td>Tumour free</td>
</tr>
<tr>
<td>4</td>
<td>48 F</td>
<td>Triceps surae</td>
<td>IB</td>
<td>Marginal excision*</td>
<td>-</td>
<td>108</td>
<td>Tumour free†</td>
</tr>
<tr>
<td>5</td>
<td>46 M</td>
<td>Vastus medialis</td>
<td>IA</td>
<td>Marginal excision*</td>
<td>-</td>
<td>132</td>
<td>Tumour free†</td>
</tr>
<tr>
<td>6</td>
<td>28 F</td>
<td>Leg</td>
<td>IIB</td>
<td>Marginal excision*</td>
<td>21</td>
<td>33</td>
<td>Died</td>
</tr>
<tr>
<td>7</td>
<td>37 F</td>
<td>Buttock</td>
<td>IIIB</td>
<td>Hindquarter amputation (wide)</td>
<td>0</td>
<td>13</td>
<td>Has metastases</td>
</tr>
<tr>
<td>8</td>
<td>55 M</td>
<td>Leg</td>
<td>IIB</td>
<td>Marginal excision</td>
<td>6</td>
<td>48</td>
<td>Died</td>
</tr>
<tr>
<td>9</td>
<td>27 F</td>
<td>Buttock</td>
<td>IIB</td>
<td>Marginal excision</td>
<td>15</td>
<td>87</td>
<td>Died</td>
</tr>
</tbody>
</table>

* local recurrence; see text for details
† free of tumour after excision of local recurrence

with no distinctive features (cases 1, 4 and 5). In one patient (case 2) minute stippled calcifications were seen (Fig. 1).

In mesenchymal chondrosarcoma the most frequent radiographic finding was an ovoid mass, with numerous irregular calcifications (cases 6, 8 and 9, Fig. 2). In case 7 the lesion was ill-defined, with blurred margins and thin, cobweb-like calcification (Fig. 3).

CT scans were performed in six cases, showing a soft-tissue mass in the patient with normal radiographs and contributing to pre-operative staging by demonstrating different densities of tumour and surrounding soft tissue and the relationship to bone and neurovascular bundles. Usually the tumour was distant from the bone but in two patients (cases 6 and 7) the mass was in contact with bone, without any erosion or penetration (Fig. 4).

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**Fig. 2**

Case 6. Mesenchymal chondrosarcoma showing a large ovoid mass with irregular calcification between tibia and fibula.

**Fig. 3**

Case 7. Mesenchymal chondrosarcoma of the buttock showing net-like calcification within a mass with ill-defined margins.
Bone-seeking isotope scans, available in seven cases, showed uptake in all patients. There was increased activity within the lesions showing calcification. In the two cases where tumour extended to the periosteum, isotope scans also showed a reactive uptake in the adjacent bone.

**Gross findings.** The five cases of myxoid chondrosarcoma presented as ovoid, soft, nodular masses, well circumscribed by a distinct pseudocapsule. On section the surface appeared translucent, gelatinous, and grey to brown in colour with large haemorrhagic and sometimes necrotic areas. The size of the tumours ranged from 5 to 8 cm.

The mesenchymal chondrosarcomas, were multilobulated and circumscribed, firm in consistency with no well-defined pseudocapsule. Cut sections of specimens showed a pale grey, fleshy surface with scattered cartilaginous foci, which creaked on cutting. Areas of necrosis were abundant while haemorrhagic zones were scanty. The tumour size ranged from 10 to 20 cm.

**Histological findings.** Myxoid chondrosarcomas were multilobular and well circumscribed by a condensed connective tissue capsule, which had resulted from the expansile growth of the tumour. Fibrous septae of variable thickness with a few small blood vessels extended in from the pseudocapsule. Within the lobules, the cells were small, uniform, round or slightly elongated. There was a narrow rim of deeply eosinophilic and sometimes vacuolated cytoplasm around the small, ovoid, hyperchromatic nucleus. Typically the cells were arranged in fine anastomosing strands and small nests giving the tumour a lace-like appearance. These cells were separated by variable amounts of mucoid ground substance which was weakly basophilic with haematoxylin and eosin, but sometimes contained small droplets of homogeneous eosinophilic material (Fig. 5).

In case 2 there were cells in clusters or whorls with scanty myxoid ground substance. Anaplasia and pleomorphism were rare and mitotic figures were absent. We observed no differentiated chondrocytes within distinct lacunae. Mucoid material was abundant in three patients and in two, the typical texture of myxoid chondrosarcoma was disturbed by large haemorrhagic and necrotic areas and occasional calcification. Silver stains showed a few haphazardly arranged reticulin fibres and some granular argyrophilic material within the myxoid matrix. PAS stain was always positive, probably due to the presence of glycogen in the cytoplasm.

**Mesenchymal chondrosarcoma** showed a characteris-
tic pattern of two basic cellular elements: undifferentiated round or spindle-shaped cells and small nodules of well-differentiated tumour cartilage. In cases 8 and 9, the mesenchymal component showed the histological pattern of haemangioepicytoma (Fig. 6). Case 7 showed many areas of dense cellularity reminiscent of Ewing’s sarcoma, and in case 6 there were round cells arranged like a lymphoma. Mesenchymal cells had ovoid or elongated hyperchromatic nuclei and scanty, poorly outlined cytoplasm. In all cases there were numerous atypical mitotic figures and dilated vascular clefts.

Cartilaginous foci were present in all tumours, but abundant in only two. These nodules were well defined in two cases while in another two they had ill-defined margins that blended with the mesenchymal areas. In three cases they followed lobules of low-grade malignancy (grade 1 to 2). Haemorrhagic areas were rare but in three cases there were large necrotic zones. PAS stain was always negative. Silver stains showed a well-defined pattern of reticulin fibres around small groups of undifferentiated cells and vessels.

TREATMENT
Three cases of myxoid chondrosarcoma were treated by wide excision. All these patients are alive and free of tumour after an average of 38 months (19 to 60). In case 4 a marginal excision had been performed elsewhere and at 12 months a local recurrence in the popliteal fossa required amputation. This patient is alive and disease-free at nine years.

The fifth patient had a marginal excision elsewhere, with the diagnosis of ‘myxoma’ and five years later developed a local recurrence; biopsy then provided the correct diagnosis of myxoid chondrosarcoma and a wide excision was recommended. However, the excision was no more than marginal and in 1984 a further recurrence developed, again excised marginally. In 1986 the patient came under our care with a further large local recurrence in the thigh involving the femoral vessels. A wide excision was attempted with an arterial bypass. The surgical margins of this specimen were confirmed to be wide, but three years later a further small recurrence developed close to the bypass. A marginal excision was performed, followed by radiation therapy. The patient is alive and free of tumour at 11 years from the first operation and at six months from the last.

Of the four cases of mesenchymal chondrosarcoma, one was treated by hindquarter amputation with a wide surgical margin. This patient had a mass in the gluteal region, attached to the iliac wing and involving the anterior portion of the thigh. At the time of diagnosis, there was a single pulmonary metastasis. This was excised. Ten months later multiple pulmonary metastases developed; the patient was treated with chemotherapy and radiotherapy. He is still alive at 13 months.

The other three patients with mesenchymal chondrosarcoma had conservative surgery. The surgical margins were ‘marginal’ and a local recurrence developed in two cases at three and 12 months respectively. In case 6 radiation therapy was used in an unsuccessful attempt to control the local recurrence; finally an amputation was performed. In case 9 the recurrence was adherent to the periosteum of the iliac wing without involvement of the bone; wide excision with a partial resection of the iliac wing was performed. In these three cases metastases developed in lung, liver and bone and case 6 also had involvement of supraclavicular lymph nodes. These
patients died at 33, 48, 87 months from surgery. Chemotherapy has been used only in one patient (case 8) when metastases appeared in bone.

**DISCUSSION**

Extraskeletal chondrosarcoma is a quite rare tumour arising 'de novo', and not from a pre-existing chondroma of the soft tissues (Enzinger and Weiss 1983). Recently Enzinger and Shiraki (1972), Hajdu (1979) and Campanacci, Bertoni and Bacchini (1981) have distinguished two typical sub-groups.

**Clinical findings.** Myxoid chondrosarcoma occurs more frequently in young, deep to the fascia in muscular compartments (stage A) (Campanacci et al 1981; Enzinger and Weiss 1983). Mesenchymal chondrosarcoma may arise in any mesenchymal tissue (Guccione et al 1973; Hajdu 1979), sometimes in an irradiated area (Brenner and Garret 1963). When it is found in the extremities, it usually arises in the soft areolar extracompartamental tissues (stage B, Enneking 1983). Myxoid chondrosarcoma occurs more frequently in adult and elderly males (Uehara and Becker 1960; Enzinger and Shiraki 1972; Angerville, Enerbæk and Knutson 1973; Mehio and Ferency 1978; Campanacci et al 1981; Amir et al 1985) although in our series we observed a 4 to 1 female to male ratio. The mesenchymal variety occurs more often in young adult females (Salvador, Beabot and Dahlin 1971; Guccion et al 1973; Campanacci et al 1981; Enzinger and Weiss 1983; Nakashima et al 1986).

Pain and tenderness are the most frequent symptoms observed in both types of extraskeletal chondrosarcoma (Salvador et al 1971; Campanacci et al 1981; Enzinger and Weiss 1983; Amir et al 1985). In our patients the average duration of complaints was 17 months in myxoid and nine months in mesenchymal chondrosarcoma.

**Imaging.** A well-defined soft-tissue neoplasm, often speckled with calcification, is more indicative of a mesenchymal than a myxoid chondrosarcoma because in this second type there is no intratumoural calcification or only minor stippling (Uehara and Becker 1960; Enzinger and Shiraki 1972; Campanacci et al 1981; Amir et al 1985). In mesenchymal chondrosarcoma the flecks and flocules are different from the granular or 'popcorn' pattern typical of the osseous type of chondrosarcoma (Campanacci et al 1981; Bertoni et al 1983; Enneking 1983). In myxoid chondrosarcoma the lack of distinctive radiographic features does not allow a differential diagnosis from other soft-tissue sarcomas (Campanacci et al 1981; Enzinger and Weiss 1983).

Intrinsic radiopacities may suggest lesions which contain amorphous calcification, either benign tumours, such as angioma, synovial chondromatosis, or chondroma (Goldenberg et al 1967; Wilner 1982), or as tumoral calcinosis or soft-tissue calcification in secondary hyperparathyroidism (Bertoni et al 1983), or malignant as in extraskeletal fibrosarcoma (Goldenberg et al 1967; Enneking 1983), extraskeletal osteosarcoma (Bertoni et al 1983), or synovial sarcoma (Goldenberg et al 1967; Enzinger and Shiraki 1972; Wilner 1982; Bertoni et al 1983; Enneking 1983; Nakashima et al 1986).

Isotope scans show uptake in both types of tumour but is more pronounced in mesenchymal chondrosarcoma, sometimes with increased activity in the adjacent bone because the tumour was extended to the peristeum. In myxoid chondrosarcoma angiography delineates the mass and the reaction in the surrounding soft tissues and shows the relationship of the tumour with the adjacent neurovascular bundles. The tumour itself does not inject strongly because the interior of the mass is avascular in comparison with its peripheral reactive vascularisation (Enneking 1983). In contrast, angiography in mesenchymal chondrosarcoma shows a hypervascularisation of the neoplasm with many broadened capillaries (Campanacci et al 1981).

CT scans are necessary for surgical planning; they demonstrate differences in density in comparison with the adjacent soft tissues and with other soft tissue sarcomas (Enneking 1983). The myxoid variety has a very low fluid density due to the mucinous material, whereas mesenchymal chondrosarcoma shows a high density due to calcification. Only in a few reported cases is there evidence of erosion of the adjacent bone (Stout and Verner 1953; Goldenberg et al 1967; Steiner, Mirra and Bullough 1973; Amir et al 1985).

**Differential diagnosis.** Myxoid chondrosarcoma may be mistaken for other richly mucinous tumours such as myxoid liposarcoma, myxoma and chordoma. Myxoid liposarcoma has a plexiform vascular pattern, many lipoblasts and no stainable mucin after previous treatment of the sections with hyaluronidase (Campanacci et al 1981). Histologically, chordoma is very similar to myxoid chondrosarcoma because it also contains mucoid material with the same staining characteristics. However, the usual site (skull, spine and sacrum) and the presence of physaliferous cells, are useful for the differential diagnosis (Mehio and Ferency 1978). A myxoma can also be confused with a myxoid chondrosarcoma, but it has more scattered and less defined cells not arranged in cords, and the mucoid material has the same staining characteristics as myxoid liposarcoma (Enzinger and Shiraki 1972; Hajdu 1979; Campanacci et al 1981).

The differential diagnosis of mesenchymal chondrosarcoma is made from haemangiopericytoma, Ewing's sarcoma, lymphoma, rhabdomyosarcoma, synovial sarcoma, and high-grade liposarcoma. Mesenchymal chondrosarcoma may often be mistaken for a haemangiopericytoma because of its similar cellular pattern (Goldman 1967; Salvador et al 1971; Guccion et al 1973; Campanacci et al 1981; Bertoni et al 1983; Enzinger and Weiss 1983; Nakashima et al 1986), but it differs in its well-defined cartilaginous islands and the poor intercellular reticulum. Electron microscope studies (Steiner et al 1973; Fu and Kay 1974) show that in

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Table II. Differences between the two sub-groups of chondrosarcoma of the soft tissues

<table>
<thead>
<tr>
<th></th>
<th>Myxoid</th>
<th>Mesenchymal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>&gt;35</td>
<td>&lt;35</td>
</tr>
<tr>
<td>Clinical</td>
<td>Small mass</td>
<td>Large mass</td>
</tr>
<tr>
<td>Radiograph</td>
<td>Little or no calcification</td>
<td>Irregular calcification</td>
</tr>
<tr>
<td>CT scan</td>
<td>Low homogenous density</td>
<td>Irregular density</td>
</tr>
<tr>
<td>Bone scan</td>
<td>Faint uptake</td>
<td>High uptake</td>
</tr>
<tr>
<td>Angiography</td>
<td>Hypervascular margin</td>
<td>Avascular centre</td>
</tr>
<tr>
<td>Histology</td>
<td>Strands and cords of round cells within large amount of mucoid matrix</td>
<td>Undifferentiated mesenchymal cells and small islets of well-differentiated cartilage with central calcification</td>
</tr>
<tr>
<td></td>
<td>Slow growth</td>
<td>Quick invasive growth</td>
</tr>
<tr>
<td>Excision</td>
<td>Wide</td>
<td>Radical excision or amputation</td>
</tr>
<tr>
<td>Chemo/Radiotherapy</td>
<td>Useless</td>
<td>Probably useful</td>
</tr>
<tr>
<td>Local recurrence</td>
<td>Rare after wide excision</td>
<td>Frequent</td>
</tr>
<tr>
<td>Metastases</td>
<td>Rare and late</td>
<td>Common and early</td>
</tr>
<tr>
<td>Prognosis</td>
<td>Good</td>
<td>Bad</td>
</tr>
</tbody>
</table>

mesenchymal chondrosarcoma the vascular features are the result of undifferentiated cells growing around vascular spaces; they do not have the characteristics of pericytes. Other malignant round cell tumours lack the foci of cartilaginous differentiation (Salvador et al 1971; Steiner et al 1973; Bertoni et al 1983; Nakshima et al 1986). An alveolar and haemangiopericytoma-like texture may also be observed in synovial sarcoma, but there is often a biphasic pattern, with a pseudoglandular appearance and proliferating spindle-shaped cells (Goldman 1967; Guccion et al 1973; Enzinger and Weiss 1983; Bertoni et al 1983; Nakshima et al 1986).

Treatment and prognosis. Staging studies are often omitted and tumours are treated by marginal or intralesional excision (Salvador et al 1971; Smith et al 1976; Enneking 1983; Amir et al 1985). The reported rate of local recurrence and metastasis, therefore, varies from 20% to 60% in soft-tissue chondrosarcomas (Stout and Verner 1953; Kauffman and Stout 1963; Goldenberg et al 1967; Guccion et al 1973; Wu, Collon and Guise 1980). In our series it occurred in 44% and was closely related to tissue margins at the first surgical treatment.

A marginal or intralesional excision has a high percentage of recurrence either in myxoid chondrosarcoma (30%, Enzinger and Shiraki 1972; 100%, in our series) or in the mesenchymal variety (33%, Salvador et al 1971; 40%, Guccion et al 1973; 66%, in our series). Wide surgical resection is the treatment of choice for the myxoid sub-type (Enzinger and Shiraki 1972; Campanacci et al 1981), whereas for the mesenchymal variety a radical excision is preferable (Salvador et al 1971; Campanacci et al 1981; Bertoni et al 1983; Enneking 1983; Enzinger and Weiss 1983; Nakshima et al 1986), because the tumour is frequently extracompartmental. For this reason, mesenchymal chondrosarcomas cannot often be treated by limb salvage surgery. Local recurrence of extraskeletal chondrosarcoma often requires an amputation (Salvador et al 1971; Enneking 1983).

There are no definitive data about the role of chemotherapy or radiotherapy in addition to an adequate surgical excision. Campanacci et al (1981), Bertoni et al (1983), and Enzinger and Weiss (1983) suggest the use of adjuvant therapy in mesenchymal chondrosarcoma.

In myxoid chondrosarcoma the rate of metastasis is lower (20%, Enzinger and Shiraki 1972) than in the mesenchymal variety (50%, Salvador et al 1971). We found a more striking difference: no metastasis compared with 100% respectively. When a metastasis is unique and well localised, the patient may be treated by pulmonary lobectomy or local excision, because of the slow growth of the tumour cells (Wu et al 1980). The patients must be followed up for a long time to evaluate correctly the survival and recovery, because soft-tissue chondrosarcoma may develop a recurrence or metastasis many years after surgical treatment (Wu et al 1980; Campanacci et al 1981).

From a study of all chondrosarcomas treated in our tumour centre (Mercuri et al 1988) central chondrosarcoma of bone is equally aggressive (31% of recurrences) as myxoid chondrosarcoma of soft tissue (40% of recurrences) but has a worse prognosis (39% of metastases as against no metastases). According to Enzinger and Shiraki (1972), Smith et al (1976), and Amir et al (1985), mesenchymal chondrosarcoma has a higher malignancy when it is localised in soft tissues: 14% recurrence and 71% metastasis in mesenchymal chondrosarcoma of bone as against 50% and 100% in the soft-tissue type. In our series, mesenchymal chondrosarcoma has a worse prognosis than both the myxoid variety and osseous chondrosarcomas.
Chondrosarcoma of soft tissues includes two histologically well defined and distinct sub-types, myxoid chondrosarcoma and mesenchymal chondrosarcoma (Table II). They differ in both clinical and radiographic features and in prognosis.

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REFERENCES


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