CHONDROMYXOID FIBROMA OF BONE
Report of a Case

J. Hutchison and W. W. Park, Dundee, Scotland

From the Departments of Orthopaedics and Pathology,
University of St Andrews, Queen’s College, Dundee

Chondromyxoid fibroma, a benign neoplasm of bone, has a histological appearance that suggests something much more malignant. Indeed, this entity, named by Jaffe and Lichtenstein (1948), was recognised by them during a restudy of their own material filed as chondrosarcoma. Until their description and definition of this lesion, there is little doubt that many a patient suffered unnecessarily radical treatment. A recent report of six cases (Iwata and Coley 1958) brings the total so far recorded to thirty-six. None of these was reported in the British literature.

The clinical and pathological features of the lesion were fully described by Jaffe and Lichtenstein in their original paper; more recent accounts are those of Lichtenstein (1952) and Dahlin (1956). The patient complains of pain over the affected area which is nearly always in the lower limb (thirty-two out of thirty-six cases), especially at the upper end of tibia or lower end of femur. The lesion, arising apparently in close relation to the epiphysial line, is oval or rounded and may be up to five centimetres in greatest diameter at the time of diagnosis. Radiologically it shows rarefaction with trabeculation and, sometimes, condensation around its margin; surgical exploration reveals a cavity in the bone, filled with firm white almost avascular tissue. Curettage of the cavity, sometimes with cauterisation of the walls and packing with bone chips, appears to be adequate treatment, but local resection has proved satisfactory when the lesion has been in the fibula, ulna, rib or metatarsal bone. In their original article Jaffe and Lichtenstein stated that, even if removal of the neoplastic tissue was incomplete, spontaneous regression of the remnants followed. However, in four of the thirty-six cases so far recorded, and in our own patient, local recurrence occurred. In one of these four cases (Case 5 of Iwata and Coley) the recurrent tissue at the proximal end of the fibula was regarded histologically as a low-grade chondrosarcoma and amputation was performed: the patient was well thirteen months later. Metastasis has never been reported.

CASE REPORT

The patient, a girl aged eleven when first seen in 1953, presented with a swelling of the upper end of the tibia which had been noticed seven weeks previously. She complained of slight discomfort and of pain on minor trauma to the swelling. Her general health was good and she had not suffered from any previous illness of significance. The family history was likewise negative.

On examination, the swelling was diffuse, firm, and painful only on pressure or percussion. It extended from the joint line on the antero-medial aspect of the knee downwards for a distance of eight centimetres. General examination revealed no other abnormality, and routine investigations were negative.

Radiographic examination—Radiographs showed an area of rarefaction in the antero-medial part of the upper tibial metaphysis traversed by a few coarse trabeculae which gave the lesion a multilocular appearance. A marked defect was present in the adjacent tibial cortex, at the lower limit of which was subperiosteal new bone formation (Fig. 1).

Pre-operative diagnosis—A provisional diagnosis of a tumour of cartilaginous origin was made; but the erosion of cortex and the extension of the process into the soft tissues raised the
question of malignancy. It was therefore decided to explore the swelling, and if it appeared to be simple, to curette the cavity and pack it with bone chips.

First operation (September 1953)—Exploration revealed a poorly encapsulated, lobulated tumour which had extruded through a defect in the tibial cortex and extended upwards to the joint line underneath the deep fascia. The mass was white and firm. It was friable on handling and removal in one piece was not possible. The cavity in the tibia had several thick bony...
septa dividing it into compartments the walls of which seemed to consist of relatively compact bone. An attempt was made to remove all the abnormal tissue with a curette. When this was completed it was found that part of the undersurface of the upper tibial epiphyseal plate formed the roof of the space. The cavity was not packed because the lesion was not obviously benign.

**Progress**—When histological examination showed the tumour to be a chondromyxoid fibroma a search of the literature was made and revealed records of only thirteen cases at that time. The patients previously reported had been cured by such simple measures as those already applied in our patient. The similarity of the clinical and radiological appearances of the case in question was so striking that it was decided not to undertake further operation.

The patient was kept under observation and radiographs were taken at six-monthly intervals. These appeared to show that the cavity was being slowly obliterated. However, two and a half years after operation some small cystic areas which had persisted began to increase in size. Bone growth in the interval had resulted in these lesions becoming more remote from the epiphyseal plate (Fig. 2). It was felt therefore that a more radical approach could now be made to the problem without the risk of damaging the plate.

**Second operation** (September 1956)—The antero-medial aspect of the upper end of tibia was exposed and two of the small cysts were found to have penetrated the cortex. When these were excised, together with some of the surrounding healthy bone, two further cavities were revealed which were dealt with likewise. The resultant bone defect was filled with cancellous chips from the bone bank.

**Later progress**—Subsequent observations seem to indicate complete eradication of the tumour. There is no clinical or radiological evidence of recurrence three years after the second operation (Fig. 3).

**Pathological examination**—The material filling the cavity in the bone was solid and of a firm, slightly elastic consistency. It glistened but was not of a glairy character, and, apart from small areas of blood staining, was uniformly white. Representative portions were fixed in formol-sublimate, and stained initially with haematoxylin and eosin.

In previously reported cases relatively little study has been given to the histological behaviour of this neoplasm. It therefore seemed to us appropriate to try to define some of its histological characters and so provide a "specification" against which other examples could be compared. Differences in histological or histochemical behaviour, for example, might be found to be correlated with differences in clinical behaviour and so help in defining prognosis.

**Haematoxylin and eosin staining**—The neoplasm consisted essentially of wide sheets of stellate cells embedded in an abundant stroma of finely granular, rather translucent appearance— the myxoid element of the neoplasm (Figs. 4 and 5). The general pattern of the neoplasm—large fields of uniform myxoid tissue—was disturbed in places by areas of extravasated blood and small deposits of iron-containing pigment: otherwise the tissue was remarkably avascular. Occasional multinucleated giant cells of osteoclastic type were present.

The stellate cells were distributed uniformly throughout the myxoid sheets but were more thickly crowded at the edges where they merged with zones of fibrous tissue; cellular proliferation appeared to be at its maximum in these areas. These bands of cellular condensation gave the neoplasm a somewhat lobular histological pattern. Occasional mitotic figures and atypically large cells could be seen in these areas. It is the presence of highly cellular, proliferative areas of this kind that gives the neoplasm its superficially ominous histological character. Individual cells have an oval or stellate, deeply and uniformly basophilic nucleus, and abundant cytoplasm, nearly always in the form of many long, tapering processes.

In a few small but diagnostically significant areas the cells showed a distinctly cartilaginous appearance—the chondroid element of the neoplasm (Fig. 6). The interstitial tissue in such areas was morphologically similar to that elsewhere but the cells themselves were now rounded and relatively sharply demarcated, and wholly without cytoplasmic processes. No foci of calcification were present in any of the sections.
The edge of a sheet of myxoid tissue where it becomes more highly cellular and merges with a strand of fibrous tissue. A single giant cell is present near the top of the field. (H. and E., × 240.)

At higher magnification the stellate shape of the cells, and the finely granular character of the myxoid stromal tissue, are evident. (H. and E., × 630.)
Trichrome (Gomori) and van Gieson staining—These preparations revealed occasional relatively very small areas of collagenous tissue—the fibrous element of the neoplasm. The collagen occurred in the form of thin fibres, not condensed sheets, and was seen most prominently as a background to the marginal zones of cellular condensation. Taking the neoplasm as a whole, not more than 5 per cent of its area contained collagen as demonstrated by these stains. Reticulin staining (Slidders, Fraser and Lendrum 1958)—As might be expected, the amount of reticulin formation varied with the degree of differentiation of the neoplasm. Where the structure resembled fibrous tissue, pericellular reticulin was plentiful; where it resembled cartilage, reticulin was absent. Since the amount of tissue resembling fibrous tissue was relatively small, reticulin formation was inconspicuous.

Further staining methods were used to investigate the nature and reactions of the intercellular stroma, namely, the mucicarmine, P.A.S., dialysed iron, toluidin blue and alcian green procedures. These were applied to sections of tissue after incubation at 37 degrees Centigrade in 1) water, 2) a solution of Hyalase* (1milligram/millilitre) for three hours, 3) the same solution for twenty hours, and to ordinary untreated sections. The results are summarised in Table I.

In order to compare the reactions of the myxoid stroma with those of epithelial mucin a section of intestinal mucosa was at all times processed in parallel with a section of the neoplasm.

Mucicarmine (Southgate's)—According to Jaffe and Lichtenstein (loc. cit.) the stroma of the chondromyxoid fibroma gives a negative reaction with this stain. In our case the reaction was positive, though less strongly so than that given by intestinal mucin. The positive reaction

* Bengers Laboratories Ltd., Holmes Chapel, Cheshire.
TABLE I
THE STAINING REACTIONS OF THE NEOPLASTIC (CONNECTIVE TISSUE) MUCIN COMPARED WITH THOSE OF INTESTINAL (EPITHELIAL) MUCIN

<table>
<thead>
<tr>
<th>Staining method</th>
<th>Neoplastic tissue</th>
<th></th>
<th>Intestinal mucin</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Untreated</td>
<td>Hyalase 3 hours</td>
<td>Hyalase 20 hours</td>
<td>Untreated</td>
</tr>
<tr>
<td>Mucicarmine</td>
<td>+ + + +</td>
<td>+</td>
<td>+</td>
<td>+ + + +</td>
</tr>
<tr>
<td>Toluidin blue (metachromasia)</td>
<td>+ + + +</td>
<td>+</td>
<td></td>
<td>+ + + +</td>
</tr>
<tr>
<td>Alcian green</td>
<td>+ + + +</td>
<td></td>
<td>+</td>
<td>+ + + +</td>
</tr>
<tr>
<td>Dialysed iron</td>
<td>+ + + +</td>
<td></td>
<td>+</td>
<td>+ + + +</td>
</tr>
<tr>
<td>Periodic Acid-Schiff</td>
<td>+ + + +</td>
<td></td>
<td>+</td>
<td>+ + + +</td>
</tr>
</tbody>
</table>

In the stroma was almost completely abolished by pre-treatment with Hyalase, whether for three or for twenty hours. The epithelial mucin, on the other hand, suffered little reduction in its affinity for the stain even after twenty hours' incubation.

*Toluidin blue* (Martinotti's method. See Lee (1946), para. 385)—Metachromasia was marked in the stroma of the neoplasm, and was severely reduced by three hours', and abolished by twenty hours', incubation in Hyalase. Metachromasia was much less intense in the untreated section of intestinal epithelium, and relatively less inhibited by pre-treatment with Hyalase. These findings suggest that the ground substance was of acid mucopolysaccharide nature, either chondroitin sulphate, such as is found in hyaline cartilage, or hyaluronic acid, such as occurs in synovial tissues. The hyaluronidase lability, however, does not distinguish between these.

*Alcian green* (Attwood 1958)—Stromal tissue of the neoplasm in the untreated section showed a strongly positive reaction, though less intense than that shown by the intestinal epithelium. Incubation in Hyalase markedly reduced and, after twenty hours, finally abolished the reaction in the neoplasm whereas the intensity of the reaction in the intestinal mucin was not affected at all. These results further support the view that the ground substance is of the nature of an acid mucopolysaccharide but again cannot distinguish between chondroitin sulphate and hyaluronic acid.

*Dialysed iron* (Hale 1946)—The two tissues gave an equally strongly positive reaction. That of the stromal tissue of the neoplasm was slightly reduced in intensity by Hyalase (no more so after twenty than after three hours), that of the intestinal epithelium not at all reduced by Hyalase. This result, incidentally, confirms the view of Pearse (1953) that the dialysed iron method is of low specificity as a stain for acid mucopolysaccharides.

*Periodic acid-Schiff sequence* (using the alcoholic periodic acid solution of Hotchkiss (1948); and the SO₂-prepared Schiff solution of Itikawa and Ogura (1954)—Both the intestinal epithelium and, rather surprisingly, the stromal tissue of the neoplasm showed strong fuchsinophilia. In neither case was the intensity of the staining reduced by Hyalase. It is difficult to explain why the ground substance should stain so well with P.A.S., even after pre-treatment with Hyalase, in view of the fact that acid mucopolysaccharides do not usually stain satisfactorily with this procedure.

The neoplastic tissue removed at the second operation showed essentially the same histological features.

COMMENT

According to Lichtenstein's *(loc. cit.*) classification of neoplasms of bone, chondromyxoid fibromas, benign chondroblastomas, and osteocartilaginous exostoses form a group of cartilage-forming neoplasms of connective tissue origin. It certainly seems clear that the
first two, at any rate, are closely related pathologically, for the neoplasms in three of Dahlin’s eleven cases of chondromyxoid fibroma, and others quoted by him, showed areas with the typical histological structure of benign chondroblastoma. However, this similarity did not appear in our case. None of the many sections of tissue examined showed the foci of calcification, swollen cells and collagenous plaques which characterise benign chondroblastoma: in fact, the morphological characters corresponded almost exactly with those described originally by Jaffe and Lichtenstein, and later by Lichtenstein, as characteristic of a pure chondromyxoid fibroma. The histochemical characters, on the other hand, differed in that the stromal tissue gave a strongly positive reaction with mucicarmine. Whether this difference is due merely to differences in fixation or staining techniques, or whether it means that this is a feature of those chondromyxoid fibromas that are particularly prone to recur, is a question that can only be answered by a study of further cases. It does not, at any rate, necessarily imply a poor long-term prognosis because the outcome in our patient has so far been highly satisfactory.

SUMMARY
1. A case of chondromyxoid fibroma of the tibia is reported.
2. Initial removal by curettage was followed by regrowth of residual foci; these were removed by a second curettage three years later. Re-examination after a further three years shows no evidence of regrowth, and suggests that cure has been achieved.
3. Some histological features of the neoplasm are briefly described.

We wish to thank Professor A. C. Lendrum for many helpful comments, and Mr Douglas Fraser of the Department of Pathology, Dundee Royal Infirmary, for a great deal of technical assistance with the histology.

REFERENCES
JAFFE, H. L., and LICHTENSTEIN, L. (1948): Chondromyxoid Fibroma of Bone; a Distinctive Benign Tumor Likely to be Mistaken Especially for Chondrosarcoma. Archives of Pathology, 45, 541.