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Fibrous dysplasia with locally aggressive malignant change

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Summary. This is a case report of a tumour which showed all the histological features of fibrous dysplasia without any features of high-grade malignancy, yet had become locally aggressive, causing cortical erosion and extension into soft tissue. Fibrous dysplasia is a well-recognised enitity that encompasses monostotic lesions, polyostotic involvement and Albright's syndrome [6, 8]. Lesions in bone usually spare the epiphysis before puberty, but often involve the epiphyseal area after maturity and can progress during adult life [3]. Unless cystic [6, 10] or malignant change [7, 10, 11] occurs, fibrous dysplasia usually remains contained within bone.

Case report

In September of 1987, a 26-year-old previously healthy woman first noticed an aching discomfort in her right shoulder with radiation towards the elbow; this was made worse by activity. She was examined and no abnormality of the shoulder or arm noted. Radiographs of the neck showed a small cervical rib on the right. Treatment consisted of physiotherapy.

Two years later she was seen again with a 6-month history of intermittent paraesthesia in the fingers of her right hand. The pain in her shoulder had become worse and movement was restricted. Clinical examination showed a fullness over the right shoulder anteriorly and wasting of the infraspinatus, spuraspinatus and deltoid posteriorly. An indistinct mass (8 cm × 3 cm) could be palpated deep to the deltoid, fixed to bone and with local tenderness. Shoulder range of motion showed abduction to 90°, flexion to 90°, full external rotation and internal rotation of 60°. Neurovascular function in the arm was unimpaired except for some wasting of the thenar eminence.

Haemoglobin, white cell count, erythrocyte sedimentation rate, alkaline phosphatase, calcium and phosphorus tests gave normal results. Electromyography of the right arm showed some T1 motor demyelination.

A radiograph of the shoulder revealed a lytic lesion involving the proximal 9 cm of the humerus (Fig. 1), with cortical expansion and extension into the soft tissues medially, the soft tissue component being largely demarcated by a calcific shell. A chest radiograph was normal. A bone scan showed increased uptake only over the lesion in the proximal humerus. Computerised tomography revealed expansion of bone and cortical destruction (Fig. 2). Magnetic resonance imaging demonstrated that the tumour has homogenous and separate from the vascular bundle with a low signal on T1-weighted images and progressively higher signal on T2-images (Fig. 3).

Management was by excisional biopsy and insertion of a custom prosthesis. The patient has remained well 15 months after surgery.

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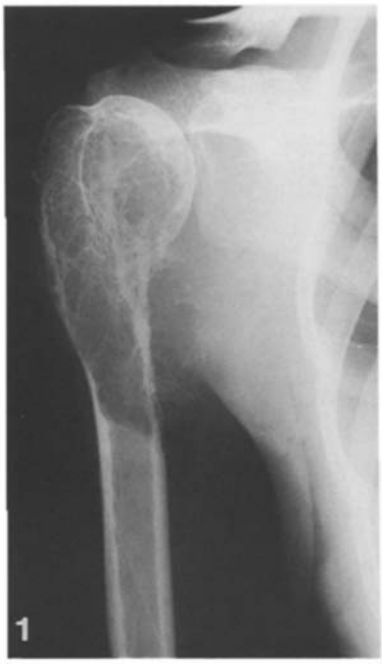
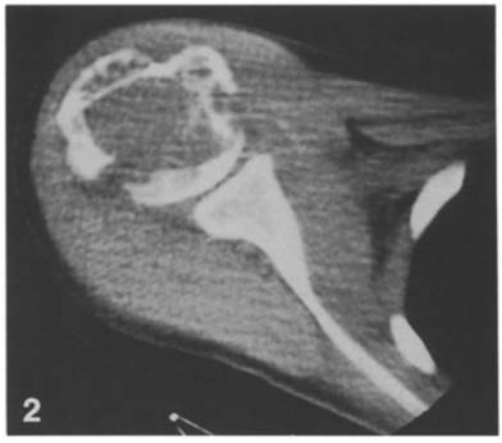
Pathological findings

Grossly, the tumour involved the entire proximal humerus and was largely white and firm with gritty areas; it infiltrated the cortex and extended into surrounding soft tissue on both medial and lateral aspects (Fig. 4).

The tumour was mainly composed of interlacing bundles of spindle-shaped fibroblast-like cells with vesicular and blunt or sharp-ended nuclei. Focally, a storiform pattern of the spindle-shaped tumour cells was seen (Fig. 5). The cell cytoplasm was generally abundant and amphophilic or eosinophilic. Cytoplasmic margins were indistinct and there was little cellular or nuclear pleomorphism. Throughout much of the tumour, this spindle cell component showed only occasional mitotic figures (approximately 1 per 10 high-powered field). In the region where tumour infiltrated the cortex and extended into soft tissue on the medial side, numerous mitotic figures (often more than 5 per 10 high-powered field) were present (Fig. 6). There were no atypical mitotic figures seen. Scattered amongst the fibroblast-like cells there were collections of osteoclast-like giant cells largely related to small areas of haemorrhage. There were also both small and large collections of foamy histiocytes and scattered chronic inflammatory cells.

Occasional cells showed a polygonal or rounded outline; these were notable in areas of fibro-osseous metaplasia (Fig. 7). A prominent component within the tumour was the presence of small trabeculae of woven bone. These were largely surrounded by osteoblasts, some of which were flattened, although many were plump and polygonal (Fig. 8). Some woven-bone trabeculae appeared irregular and showed no osteoblastic rimming (Fig. 9). There were also some larger bone trabeculae, surrounded by osteoblasts. Osteoblasts in relation to this new bone formation showed no mitotic activity or atypical cytological features. Osteoclastic resorption of this woven bone was also noted.





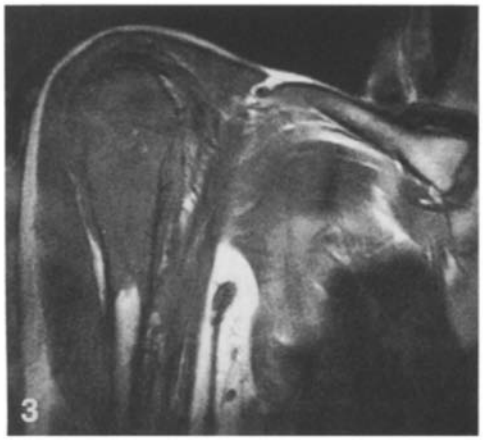


Fig. 1. Radiograph of the proximal right humerus

Fig. 2. Computed tomogram of lesion showing cortical erosion

Fig. 3. Parasagittal magnetic resonance imaging scan showing extracortical extension of tumour (spin echo TR 3.2 sec, TE 17/90)

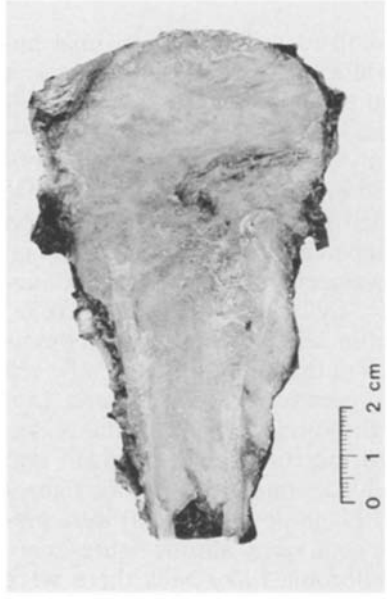


Fig. 4. Gross appearance of tumour

The tumour had largely replaced medullary cancellous bone, but a few surviving viable host bone trabeculae remained. Tumour extended into and thinned the bony cortex, which showed some reactive and endosteal bone formation and bone resorption. At several points, however, tumour infiltrated through the bone cortex into surrounding soft tissue (muscle and fat) on both the lateral and medial aspects (Fig. 10). Although much of the tumour lay beneath the elevated periosteal coat, some also lay outside the periosteum in fat and muscle.

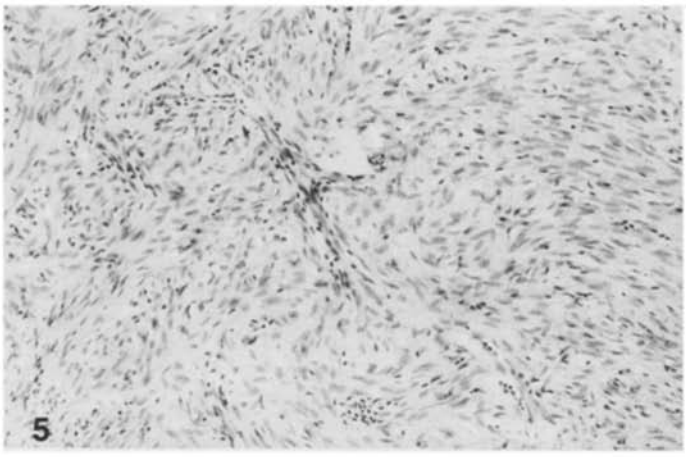
Tumor filled the entire epiphysis and extended up to the subchondral bone plate, which was thinned and focally replaced by expanding tumour. Also present in the superior aspect of the head close to the articular surface were nodules of cartilage (Fig. 11). These nodules merged with surrounding spindle-shaped tumour cells. Endochondral ossification was also noted focally in some of the cartilage nodules. The cartilage component was both hyaline cartilage and fibrocartilage and a few binucleate cells were present in the cartilage nodules. On the postero-medial aspect of the articular surface, tumour extended through the articular cartilage, carrying with it hyaline articular cartilage derived from the articular surface.

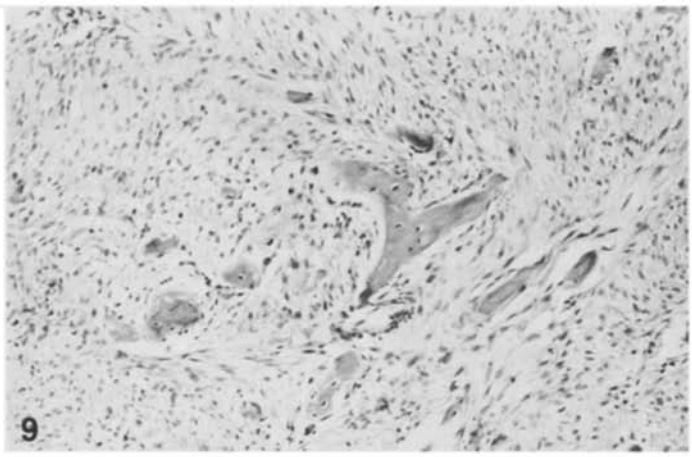
The spindle-shaped tumour cells were alkaline phosphatase-positive, particularly in areas of fibro-osseous metaplasia. Immunohistochemistry showed that these cells contained vimentin but not cytokeratin or desmin intermediate filaments. They were also negative for neurofilament, epithelial membrane antigen and leucocyte common antigen, but focally positive for S100 protein. The chondrocytes in the metaplastic cartilage nodules were also S100-positive.

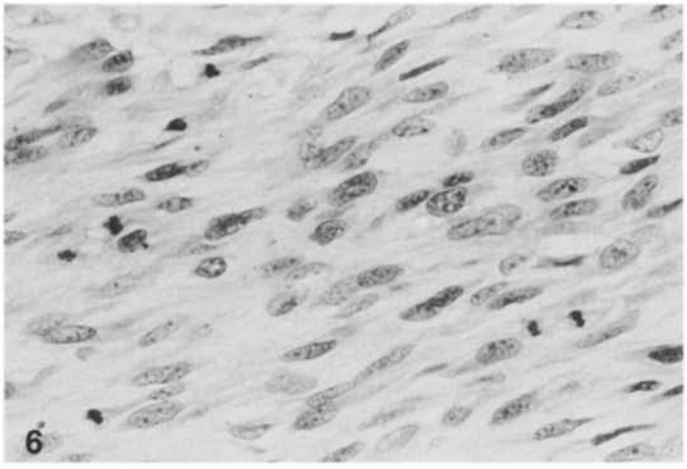
The tumour was diagnosed as a case of locally aggressive fibrous dysplasia. The differential diagnosis included low-grade, well-differentiated osteosarcoma, fibrocartilaginous mesenchymoma and malignant fibrous histiocytoma.

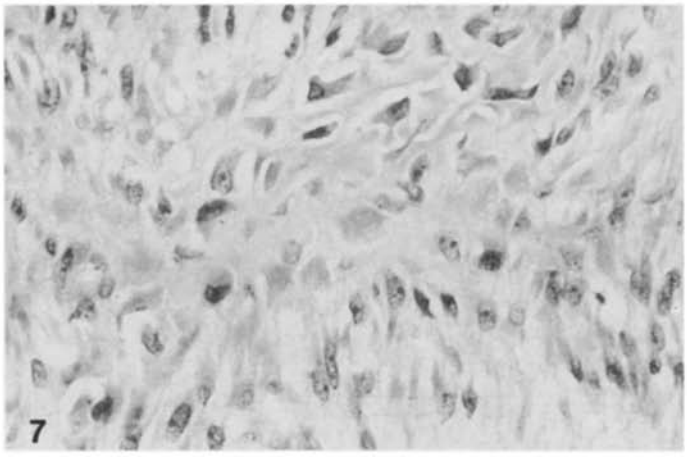
Discussion

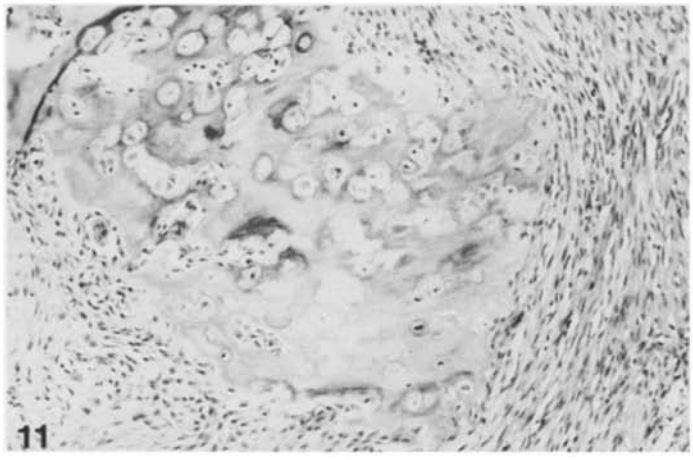
Transformation of fibrous dysplasia to a high-grade sarcoma, most commonly osteosarcoma, less commonly fibrosarcoma or chondrosarcoma, is a well-recognised entity, occurring in 0.4% of all cases [9, 10, 11]. The clinical, radiological and pathological features of this case would indicate that locally aggressive behaviour, as well as high-grade malignant change, can occur in fibrous dysplasia. Clinical evolution of the humeral lesion was slow, taking place over a number of years. Radiological and gross pathological features indicated that this was a











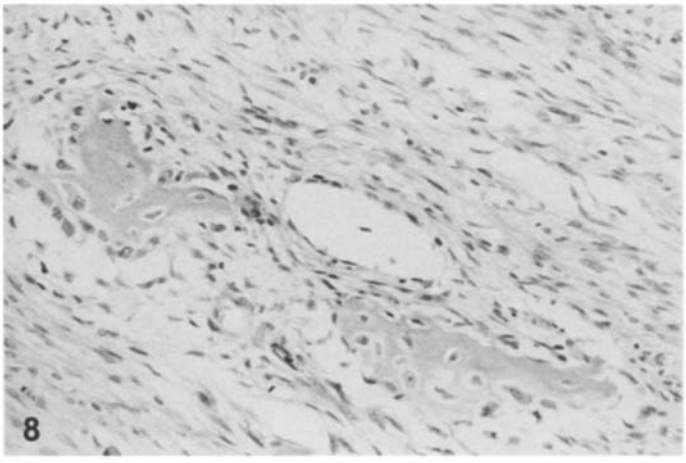


Fig. 5. Fibroblast-like spindle cell component of the tumour arranged in a storiform pattern. There are scattered inflammatory cells amongst the spindle cells. × 100

Fig. 6. High-powered field of tumour in the region of infiltration of the medial cortex, showing numerous mitotic figures, all of typical morphology, amongst spindle cells. × 400

Fig. 7. Area of fibro-osseous metaplasia within the tumour with osteoid in centre and surrounding spindle cells and polygonal osteoblast-type cells × 400

Fig. 8. Woven-bone trabeculae surrounded by plump osteoblasts within tumour × 100

Fig. 9. Irregular woven-bone trabeculae, most of which are lined by flattened osteoblasts. × 100

Fig. 10. Infiltration of tumour beyond cortex *(top right)* into soft tissue *(bottom left)*, which includes muscle and blood vessels × 15

Fig. 11. Nodule of metaplastic cartilage within tumour. × 100

locally aggressive lesion. This was reflected in the histological appearance of the tumour which showed little or no evidence of cellular or nuclear pleomorphism amongst the spindle cells or in the osteoblasts in relation to bone trabeculae. In the region where the lesion had infiltrated the cortex and raised the periosteum, there was a focally high mitotic count. However, no atypical mitoses were present in this location or elsewhere in the tumour. Absence of these features does not favour the diagnosis of a low-grade, well-differentiated or fibrous dysplasia-like variant of osteosarcoma or a high-grade fibroblastic osteosarcoma [5, 7]. The pattern of infiltration through cancellous bone, where viable host bone trabeculae persisted, and the enveloping of muscle fibres, which also remained largely viable, was also suggestive of a low-grade, slowly growing lesion.

The diagnosis and categorisation of the lesion as a variant of fibrous dysplasia was based on the presence of histological components which are typical of this lesion, namely fibroblast-like spindle cells, collagenous connective tissue, foci of osteoid production and irregular trabeculae of woven bone, nodules of metaplastic cartilage and areas containing foamy macrophages, chronic inflammatory cells and giant cells associated with haemorrhage [2]. Although typical irregular woven bone trabeculae surrounded by flattened osteoblasts were present, many bone trabecuale were surrounded by plump active osteoblasts. This feature has previously been noted in young patients with fibrous dysplasia and has been associated with local recurrence within bone [1, 4]. Recurrence and low-grade malignancy is also associated with the presence of growth plate-like cartilage nodules in fibrocartilaginous mesenchymoma [2] although this lesion lacks mitotic activity and evidence of bone formation, features which were prominent in our case.

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