Multiple skeletal metastases from a giant cell tumour of the distal fibula with fatal outcome

A giant cell tumour is a primary lesion of bone of intermediate severity. Its histogenesis is unclear. In a few cases pulmonary metastases have been described. Multiple skeletal metastases in the absence of sarcomatous change have been observed.

We present a case report of a 25-year-old woman with a recurrent giant cell tumour of the distal fibula. After a second recurrence and six years after the initial diagnosis, she rapidly developed multiple bony metastases. The outcome was fatal.

Giant cell tumours account for 15% of benign tumours of bone and between 3% and 8% of all primary tumours of bone. Almost half the cases occur adjacent to the knee joint. Other more commonly affected sites are the distal radius, proximal humerus, fibula and pelvis. Typically, the tumour first appears close to a joint and then grows eccentrically to infiltrate the metaphysis. Usually, they are benign lesions, but in 25% of cases locally aggressive behaviour is observed. Previously described as semi-malignant, they are now known as intermediate tumours, indicating that the prognosis cannot be determined with certainty by means of any histological or radiological classification.

Curettage is common treatment with filling of the cavity with bone cement which, providing recurrence does not occur, can later be replaced by spongiosa grafts. In about a third of cases, local recurrence has been observed within a few years. Recurrent tumours require resection rather than curettage and the patients are at greater risk of developing pulmonary metastases.1

The histological appearance of giant cell tumours is very variable. It mainly consists of giant cells containing multiple nuclei as well as single nucleus stroma cells. The histogenetic origin of the tumour is unknown.

Malignancy occurs in 10% of cases and has mainly been found following previous treatment by radiotherapy. Also, spontaneous sarcomatous change has developed in some cases, several years after the primary diagnosis.2

We describe a 25-year-old woman with a giant cell tumour of the distal fibula which recurred twice. Resection of the second recurrence was followed after eight months by the appearance of multiple bony metastases. The outcome was fatal. To our knowledge, such a case has not been described before. The histological and radiological evidence has been re-examined to see if it might have been possible to predict the malignant change. A possible treatment regime and indications for possible malignancy in the histomorphology and on radiographs will be discussed.

Case report

A 25-year-old woman with no significant past medical history underwent curettage and grafting with spongiosa for a lesion at the lateral malleolus in 1997. Histological examination confirmed the presence of a giant cell tumour. Malignancy was not suspected and recovery was uneventful. In April 2002, the tumour recurred locally and was treated again with curettage and grafting. Biopsies were sent to a bone tumour reference centre as well as to the local pathology laboratory. In both cases a recurrent giant cell tumour was diagnosed.

In February 2003, the patient presented in our department for the first time, complaining of recurrent pain in the lateral aspect of her right ankle. Progressive destruction of the distal fibula was seen on the radiographs, indicating a recurrence of the giant cell tumour (Fig. 1). Further investigation included MRI with contrast medium as well as a whole body technetium bone scan. Radiographs of the chest were taken in two planes. The MRI report confirmed a lesion in the distal fibula, 4 cm long and 3 cm wide. Extensive destruction of bone was localised to the area of the lateral malleolus. Following radiographs of the pelvic region, a complete body bone scan in three phases and
a whole body CT scan were carried out. None of these investigations showed evidence of bony metastasis or pulmonary involvement.

We treated this second recurrence with en bloc resection of the lateral malleolus, including part of the tendon sheath of the peroneal tendons. A sliding fibula graft was used to reconstruct the outer side of the ankle joint (Fig. 2). Histological assessment at the local laboratory and at the bone tumour reference centre confirmed the preliminary diagnosis of a giant cell tumour. The tumour tissue was composed of mononuclear cells, spindle cells with mild to moderate nuclear atypia and some mitosis. Polynuclear giant cells were present. In larger areas the mononuclear spindle cells were predominant, sometimes in a storiform pattern. Focally up to four mitoses per high power field were identifiable (Fig. 3). The portion of the peroneal tendon sheath attached to the specimen revealed normal synovial tissue.

She mobilised non-weight-bearing wearing an ankle splint for six weeks followed by a gradual increase in weight-bearing.

At three months radiographs of the ankle and chest were taken and it was considered that all was well; a view that was re-affirmed at the six-month check.

In November 2003, eight months after surgery, she was re-admitted as an emergency with severe pain around the right iliac crest. Investigations, including radiographs of the pelvic region, a whole body scan and a whole body CT scan, revealed multiple bony metastases (Figs 4 and 5). No abnormality was detected in the viscera or the lungs. There was extensive involvement of the axial skeleton including osteolytic changes in the cervical, thoracic and lumbar spine as well as the right ilium. Here, there was extensive soft-tissue involvement of gluteus medius and minimus as well as the psoas. There were also metastases in both humeri, both femora and the skull. The precise diagnosis
was unclear and therefore a biopsy was taken from the right ilium. Histological studies confirmed recurrence of the giant cell tumour. The appearances were similar to the previous biopsy in terms of mononuclear and spindle cells but now the multinuclear giant cells were seen more frequently and were more evenly distributed.

The rate of proliferation was always 10% to 20%. A sarcomatous element was not detectable in either biopsy (Fig. 6). In comparison to the first biopsy necrotic areas were more often present. The possibility of the lesions being parathyroid tumours was excluded by normal serum levels of parathormone level and calcium.

Due to the rapid progression of the disease, primary treatment with chemotherapy was planned with radiotherapy for symptomatic tumour and areas at risk of pathological fracture. However, she developed signs and symptoms of raised intracranial pressure. Her condition deteriorated and she died in a state of epileptic shock. In the absence of a post-mortem examination it is not possible to be certain that there was no lung involvement.

Discussion

Lung metastases from a histologically benign giant cell tumour were described by Finch and Gleave in 1926.\(^3\) Hitherto, they had been considered as a type of sarcoma. Today, the concept of benign metastases is well recognised and their occurrence comprises 2% of all metastases.\(^4\) Similar metastases in regional lymph nodes have also been described, and the authors presume a mechanism of lymphatic spread.\(^5,6\) Multifocal lesions following a benign course in the case of giant cell tumours have been mentioned in the literature.

Of 407 cases of giant cell tumour, Dahlin\(^7\) found three patients with ‘multifocal’ growths in whom each of the tumours behaved biologically like an ordinary giant cell tumour. A further case which followed a benign course in spite of tumour at ten locations is described by Feldmann\(^8\) and Singson and Feldmann.\(^9\) Whether multiple giant cell tumours in humans can occur spontaneously or whether...
they are the result of a metastatic process cannot be answered for certain.

In the case presented, the mechanism of tumour spread is unclear, particularly considering the lack of pulmonary metastases. One possible explanation might be retrograde embolisation via superficial veins. Vessel destruction within the tumour does not necessarily indicate a higher risk of metastases. About 40% of all giant cell tumours exhibit vessel destruction but very few of them develop metastases. In 1990, Rock described a patient with metastases in the skull, lung and mediastinum. In this case, as in the case presented, metastasis via the blood stream as seen in other malignant tumours has to be assumed. In our patient, passage through the lung without pulmonary cell colonisation may have occurred.

In retrospect, considering that the radiographs showed a well-defined lesion and that there are difficulties predicting malignancy from histology rapid deterioration could not have been predicted in our patient. Histology of the iliac crest lesion revealed very few areas of recognisable giant cell tumour with malignant cells dominant. Proliferative activity ranged between 10% and 20%, whereas the areas of giant cell tumour with multiple nuclei displayed an even higher rate of proliferation. There was no evidence of sarcomatous change.

Giant cell tumours show a tendency to local recurrence. Curettage and the primary filling of the defect with Palacos cement seems more appropriate than a primary bone graft. This allows more prompt detection of recurrence.

To prevent this, the additional local use of phenol has been described as helpful. There is a distinction between benign and malignant metastasising giant cell tumours. Histologically, benign metastases are indistinguishable from non-metastasising tumours. Mortality from the lesions has not been described to date. Giant cell tumours displaying high mitotic activity and an atypical mitotic appearance without the development of a matrix should be rated as primary malignant. Sarcomatous change is rare. Experience of metastasising giant cell tumours of the bone is limited. A treatment protocol has been developed as part of our interdisciplinary work with oncologists and radiologists. This includes antracylin based palliative chemotherapy. Areas at risk of pathological fracture and symptomatic tumour sites should be treated with radiotherapy.

The initial treatment should include chemotherapy in accordance with the COSS-protocol, when metastases are present.

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References

Fig. 6

Biopsy from the iliac crest (Haematoxylin & eosin x 400).