International Orthopaedics (SICOT) (1998) 22:200–204

International Orthopaedics

Giant cell tumour of bone with pulmonary metastases

A report of three cases

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Accepted: 8 September 1997

Summary. *Three cases of giant-cell tumour of bone with pulmonary metastases are reported. New metastases appeared and the existing nodules continued to progress after treatment in two patients who were kept under observation and no further treatment was given. When patients with giant cell tumours of bone present with lung metastases, it should be presumed that they are probably from the known tumour. However, tissue should be taken to establish the diagnosis and to exclude other concurrent lesions. Pulmonary metastases have a good long term prognosis, and so should be kept under observation, avoiding radical treatment such as lobectomy, chemotherapy and radiotherapy.*

Resumé: *Les auteurs rapportent 3 cas de tumeur osseuse à cellules géantes avec métastases pulmonaires. Les nodules métastatiques existants ont continué à progresser et de nouveaux nodules sont apparus chez 2 patients malgré le traitement. Une surveillance à long terme montre pour 2 malades la disparition des nodules métastatiques. Le troisième qui n'a eu qu'une biopsie diagnostique sans traitement particulier est toujours sous surveillance. Quand un patient présentant une tumeur à cellules géantes osseuses a des métastases pulmonaires, elles sont présumées être en rapport avec la tumeur connue. Les auteurs préconisent cependant la biopsie pour établir avec certitude le diagnostic ce qui permet de ne pas faire de traitement ni chirurgical ni chimiothérapique ni radiothérapique mais simplement d'établir une surveillance régulière.*

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Introduction

The incidence of pulmonary metastases from giant cell tumour (GCT) of bone varies in different series from 2% to 9% [2, 4, 10, 15, 25]. The incidence of metastases is low in India, China and Saudi Arabia, although GCT of bone is the commonest primary bone tumour in these countries [14, 22].

Between 1975 and 1995, 1567 patients with primary bone tumours were treated in our department; GCT occurred in 69 (23%) and only 3 patients (4%) developed lung metastases. These three are presented in this study.

Case reports

Case 1

A man, 25 years of age, was referred in October 1987 with a recurrent giant cell tumour of his right proximal humerus. He had been operated on 18 months previously, and a second procedure was carried out for a local recurrence elsewhere 4 months before he was seen by us. All laboratory investigations were normal, except for the alkaline phosphatase which was 143 IU/l (normal range 39–117 IU/l). Radiographs of the right humerus showed recurrence of the tumour. Chest radiographs did not show lung metastases. A radical resection of the tumour and prosthetic replacement of right proximal humerus was done in December 1987. The pathology showed a GCT of bone (Fig. 1).

A chest radiograph taken in May 1989 showed pulmonary metastases which remained unchanged over the next 2 years. A chest CT scan and radiographs (Fig. 2a, b) taken in June 1991, two years after diagnosis of metastases, showed that the number and size of the nodules had increased. Fine needle aspiration from the lung nodules confirmed metastatic GCT. In August 1991, 8 nodules were excised from both lungs, and microscopy confirmed the diagnosis of GCT (Fig. 3). Chest radiographs and CT scans in May 1993 (Fig. 4a, b) after this operation showed that new nodules had appeared, and a previous one had increased in size. The follow-up radiographs showed

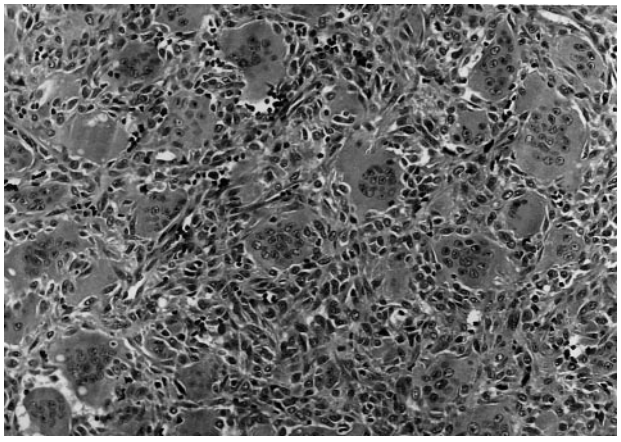

Fig. 1. *Case 1.* Photomicrograph of the primary tumour

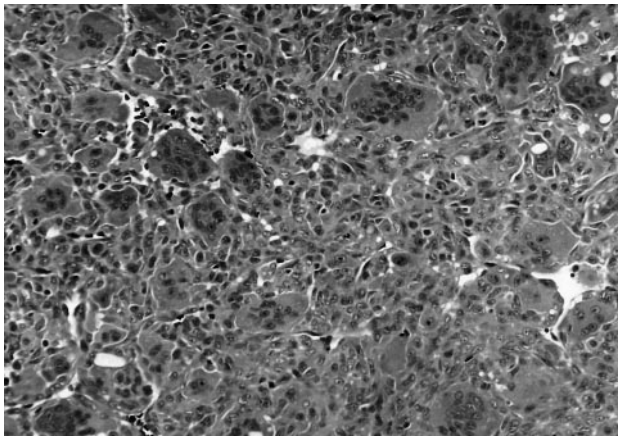

Fig. 3. *Case 1.* Photomicrograph of a lung metastatic nodule

that the nodules had begun to decrease in size in both lungs, and they had all disappeared by May 1995 (Fig. 5). At the last follow-up 6 years after the diagnosis of lung metastases, the patient had no symptoms and had reasonable function in his shoulder.

Case 2

A woman, 17 years of age, was referred in August 1980 with a recurrent GCT of the left fifth metacarpal and lung metastases [19].

She had already been treated by amputation of the fifth ray. Radiographs showed no evidence of lung metastases. Microscopy showed that the tumour was destroying cancellous bone and invading the surrounding tissues. Three months later she had developed a soft tissue recurrence and multiple nodules in both lungs. Her only symptom was an occasional cough.

She was then seen by us and the nodule in her left hand was excised; microscopy showed a GCT. Needle biopsy of the right lung was suggestive of a metastatic GCT and she was treated with chemotherapy. Radiographs during this period showed no change in the lung nodules. Six months later, the nodule in her right upper lobe had increased in size. By 1983 more nodules had appeared, some were larger, but others were smaller, and a bone scan showed no bony metastases. In 1984, a skeletal survey and a further bone scan showed metastases in the skull and cervical spine, but she had no symptoms, although the lung lesions were progressing. A year later, a repeat bone scan showed increased uptake in the hamate in the left wrist. In 1987, there were new hot spots in the left and right upper ribs, and until then the lung metastases had increased or were static.

The nodules began to regress 8 years after diagnosis, and a year later in 1989 all the large lesions had disappeared, except for one in the right lung. In 1994, a radiograph showed that the large nodules were no longer present; she had no symp-

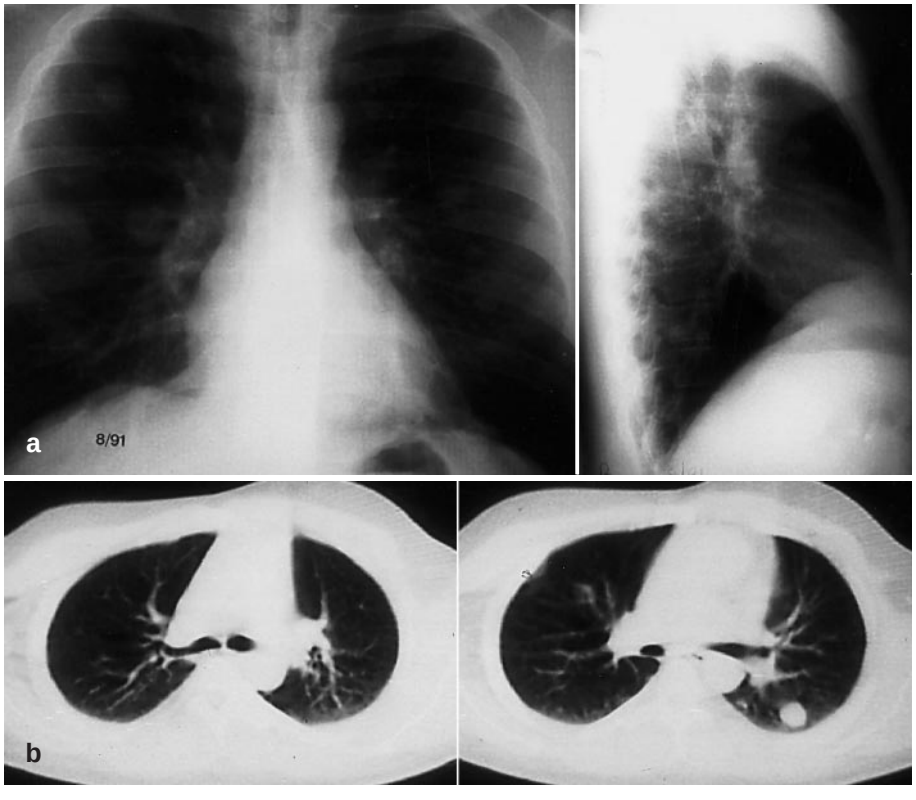

Fig. 2a, b. *Case 1.* **a** Chest radiographs and **b** CT scan 2 years after the first diagnosis of the lung metastases; their number and size have increased

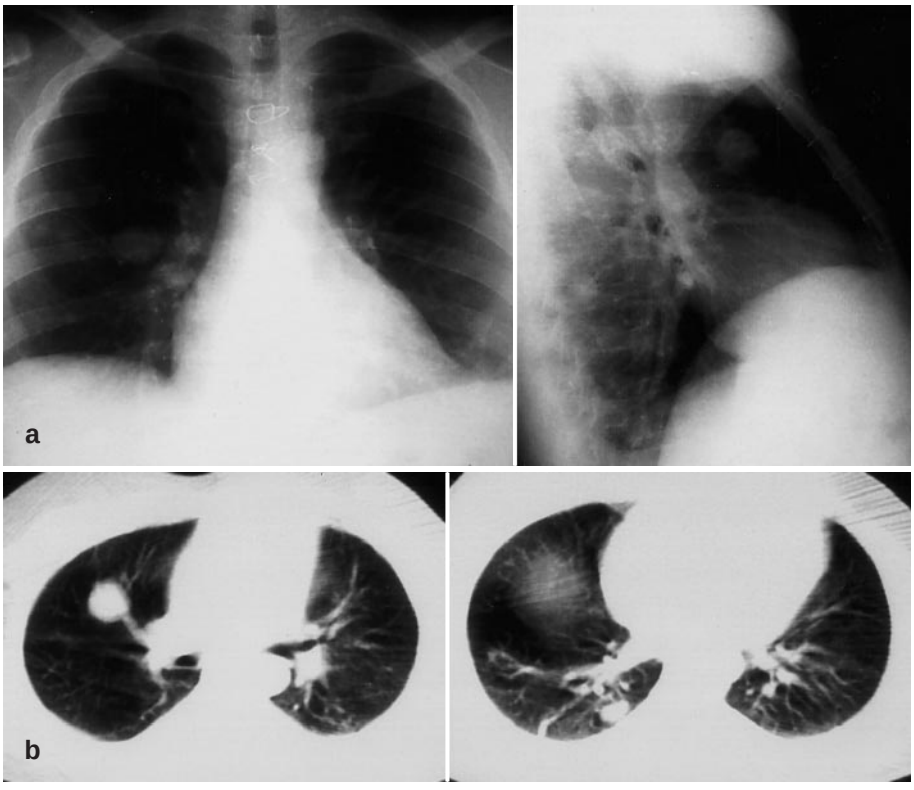

Fig. 4a, b. *Case 1.* **a** Chest radiographs and **b** CT scan in May 1993, 2 years after removal of the metastases, show that new nodules have appeared and the previous one has increased in size

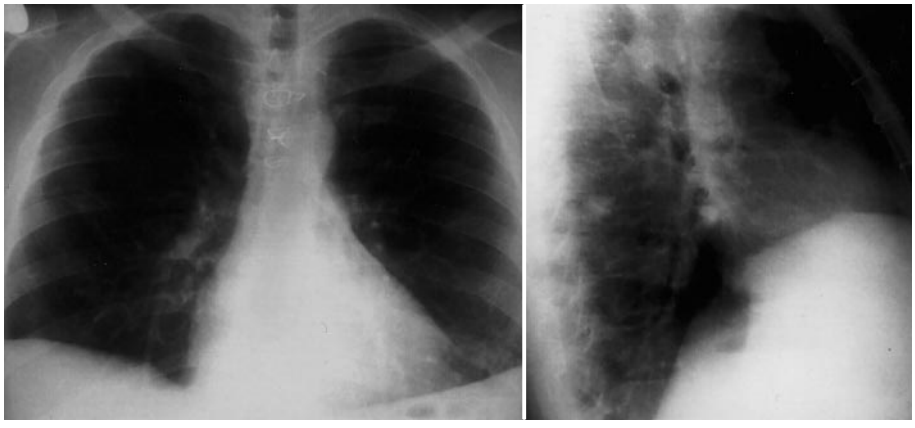

Fig. 5. *Case 1.* Chest radiograph in May 1995, 4 years after operation showing that all the nodules have disappeared

toms. There were still hot spots in the skull, cervical spine, ribs and the hamate, but they had not changed since the previous scans.

Case 3

A woman, 26 years of age, was treated elsewhere for a GCT of the right ilium with external radiation with a total dose of 6000 rads. Radiographs showed no evidence of lung metastases.

She was referred to us in September 1995 with a painful mass in the right sacroiliac region. CT scan showed an expanding osteolytic lesion destroying almost one third of right ilium with only a thin rim of cortex remaining. MRI confirmed the presence of a lesion 10×10 cm in size involving the posteromedial part of the ilium and extending into right half of the sacrum. The diagnosis was an aggressive GCT and the recurrence was treated by curretage. Microscopy showed a GCT.

Chest radiographs and CT scans at this time showed multiple small peripheral nodules in both lungs, but she had no symptoms and was kept under observation. After 3 months, a CT scan of the chest showed that the metastatic nodules had increased slightly in size and number, but she still had no symptoms and pulmonary function tests were normal. Biopsies from both lungs confirmed metastatic GCT.

At the last follow-up, she was doing well and chest radiographs showed no changes in the metastases compared with the previous films. She remains under observation.

Discussion

The natural history of GCT of bone is unpredictable. It may metastasise to lung and bone at a varying time from 16 months to 5 years [2, 7, 10, 15, 18, 23]. Metastases have been reported at the time of the first

presentation [2, 7, 18, 23]. The most common site is the lung, and bony metastases are rare [11, 15, 19, 26]. The histological appearance is the same as the primary lesion [3, 4, 5], as shown in our case 1 (Figs. 1, 3).

Recurrence was more frequent in 55% to 90% of cases in tumours that metastasise [2, 10, 15, 25] and it has been suggested that multiple operations on the primary tumour may promote metastases [3, 8, 24]. Cases have been reported with radiological evidence of metastases before any operation [3, 7, 18, 23].

Approximately 2% of GCTs involve the matacarpal bones [17] and, although metastases have been reported from almost all sites, it is more common from small bones [1, 2, 3, 10, 13, 15]. GCTs of the hand bones are more aggressive, and associated with an earlier and higher incidence of recurrences, but are more likely to metastasise to the lungs.

Like the primary lesion [6], the natural history of the metastases is also unpredictable. The results after treatment by operation, chemotherapy and radiotherapy have varied in different series [2, 3, 7, 8, 11, 15, 19, 23, 25]. In one of our patients (case 2) whose metastases were treated by chemotherapy; they continued to grow, but they began to regress 8 years after the initial diagnosis, and they all had disappeared after 14 years. In case 1, metastatic nodules were treated by surgical removal, new nodules appeared, and the old ones recurred 2 years after their removal. They remained stationary for 4 years after diagnosis and then started to decrease in size in both lungs; all had disappeared by 6 years. Later, spontaneous regression of the nodules occurred and they all disappeared from both lungs. He was free of disease 7 years after the first operation. Case 3 had no specific treatment for her metastases.

Metastases have not caused symptoms after their diagnosis in all 3 cases. At present, these patients are all under observation with regular follow-up, including radiological examination, but no other treatment.

Histological grading [8, 16], radiological grading [4], DNA flow cytometry [12, 20] and cytogenic analysis [21] of this tumour have not shown any correlation which would predict the metastatic potential of benign GCT. A study of growth rate analysis of lung metastases from GCT of bone has shown that these grow more slowly than metastases from other tumours, and this correlates with the long survival time [9].

Considering the low incidence of metastases and the better prognosis regardless of treatment [2, 3, 10, 15, 19, 25, 26], it does not seem to be logical to subject these patients to extensive investigations, such as CT and bone scans, as has been advocated in a recent study [10], in order to make an early diagnosis of lung metastases. Moreover, it is not practical to subject such patients to these investigations in countries like India, China and Saudi Arabia where resources are limited; the incidence of GCT is 20% to 30%, but that of metastases is 0 to 4% [14, 22]. We believe that the only patients with GCT who should be screened are those involving the hand, and aggressive and recurrent tumours. Chest radiography can be an adequate screening test for lung metastases.

It can be presumed that when patients with GCT are found to have lung metastases these have come from the primary tumour. Nevertheless, biopsy is necessary to establish the diagnosis and rule out other pulmonary lesions. Excision of a single accessible localised nodule may be justified as a biopsy. No attempt should be made to remove all the nodules, carry out a lobectomy or use radiotherapy. When the diagnosis is established, no other treatment may be needed.

Acknowledgements. We would like to thank Ms Marilyn Gregorio for her secretarial assistance and Dr M.A. Ali, pathologist, for reviewing the histological slides.

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