Skeletal Radiol (1998) 27:341–345

CASE REPORT

Giant cell tumor of bone with selective metastases to mediastinal lymph nodes

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Presented at the Closed Meeting of the International Skeletal Society in Santa Fé, New Mexico, September 1997

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Abstract We report an unusual case of a recurrent giant cell tumor of the patella which presented with metastatic disease to the posterior mediastinal lymph nodes with no evidence of pulmonary metastases. The patient underwent chemotherapy with subsequent successful removal of the mediastinal mass. A review of the reported cases of mediastinal giant cell tumor metastases is provided.

Key words Giant cell tumor · Metastases · Mediastinum · CT

Introduction

Giant cell tumors of bone account for approximately 5% of primary skeletal neoplasms [1, 2]. Local recurrence after treatment is not uncommon and is usually amenable to re-excision. Most of these tumors are histologically benign, but giant cell tumors of bone metastasize in up to 2–3% of cases [3–11]. Metastases from giant cell tumors occur most frequently in the lungs, though exceptionally spread to other sites including lymph nodes can occur [3, 5, 12–15]. We report the case of a 44-year-old patient who initially presented with a giant cell tumor of his right patella and later developed metastases to the posterior mediastinal lymph nodes without evidence of pulmonary metastases.

Case report

A 44-year-old man presented with pain and a pathologic fracture of the right patella. A giant cell tumor of the patella was diagnosed and a patellectomy was performed. Ten months after an unremarkable post-operative recovery he noticed local nodularity at the resection site with progressive swelling in the region. MR imaging demonstrated a large fungating mass with its epicenter within the soft tissues at the anterior aspect of the knee (Fig. 1). The tumor invaded the medial quadriceps muscles, medial knee ligaments, and femoral cortex. Helical CT (5-mm slices) at the time of confirmed tumor recurrence showed no evidence of any intrathoracic disease. Complete surgical excision was achieved and a myocutaneous flap was placed in the operative bed. Five months after the second operation, the patient complained of shortness of breath. Chest radiographs revealed a lobulated mass situated in the left para-aortic region in continuity with the posterior aspect of the cardiac silhouette, accompanied by a large

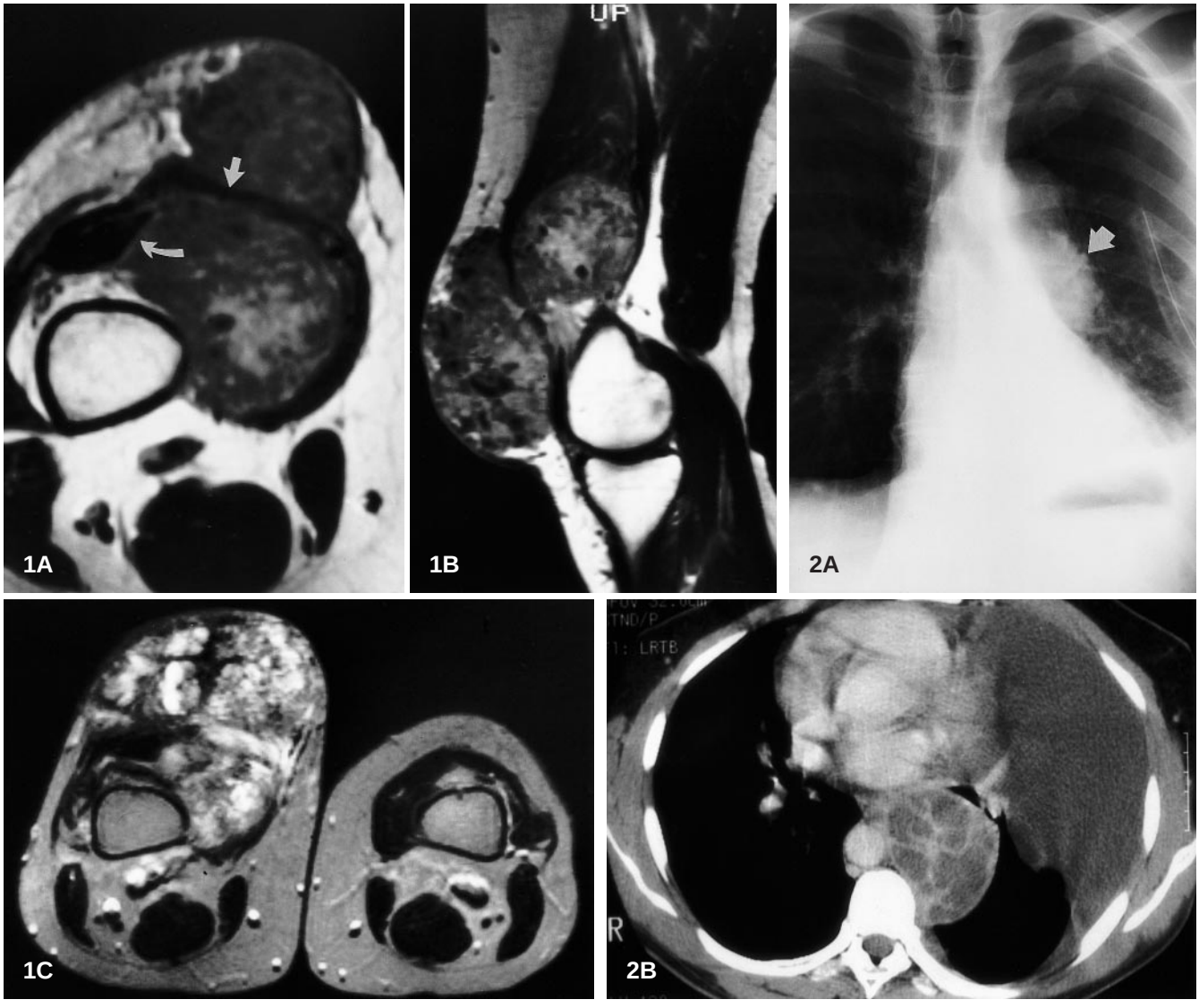

Fig. 1A–C Recurrent peripatellar mass. **A** Axial and **B** sagittal T1-weighted image (TR 600 ms, TE 15 ms) demonstrates a lobulated mass at the medial aspect of the distal femur enveloping the medial retinaculum (*arrow*), thinning and displacing the vastus medialis, and enveloping the medial aspect of the quadriceps tendon (*curved arrow*). Note the numerous foci of high signal intensity throughout the otherwise low-signal tumor, representing areas of hemorrhage. **C** Axial T2-weighted image (TR 2800 ms, TE 90 ms), slightly more cranial, through the thickest portion of the mass shows extension to the skin surface over a broad expanse. The femoral cortex is abutted by tumor. The lesion is of inhomogeneous high signal intensity

Fig. 2A, B Metastatic mediastinal mass. **A** Posteroanterior chest radiograph obtained after fine-needle aspiration of posterior mediastinal mass and placement of chest tube for evacuation of a large pleural effusion. A lobulated mass in seen superimposed over the left hilum (*arrow*). **B** Contrast-enhanced axial CT image obtained with patient prone. A lobulated mass with enhancing septations is seen in the posterior mediastinum abutting the spinal column, descending aorta and posterior cardiac silhouette. A large pleural effusion has shifted anteriorly

pleural effusion (Fig. 2A). Contrast-enhanced CT examination confirmed a low-attenuation mixed-density mass measuring 12×7×6 cm, extending from the left hilum, posteriorly and inferiorly along the descending aorta (Fig. 2B). No pulmonary nodules were present. The appearance was consistent with a mass of necrotic matted lymph nodes. Fine-needle aspiration biopsy of the mass showed numerous multinucleated giant cells of osteoclastic type and large groups of small spindle-shaped cells, consistent with metastatic giant cell tumor. Pleural fluid aspirated at the time of the mediastinal biopsy yielded only reactive mesothelial cells with no evidence of tumor. Histology of the metastasis was identical to the primary tumor.

The patient was treated with a chemotherapy protocol containing Cis-platinum and Adriamycin with

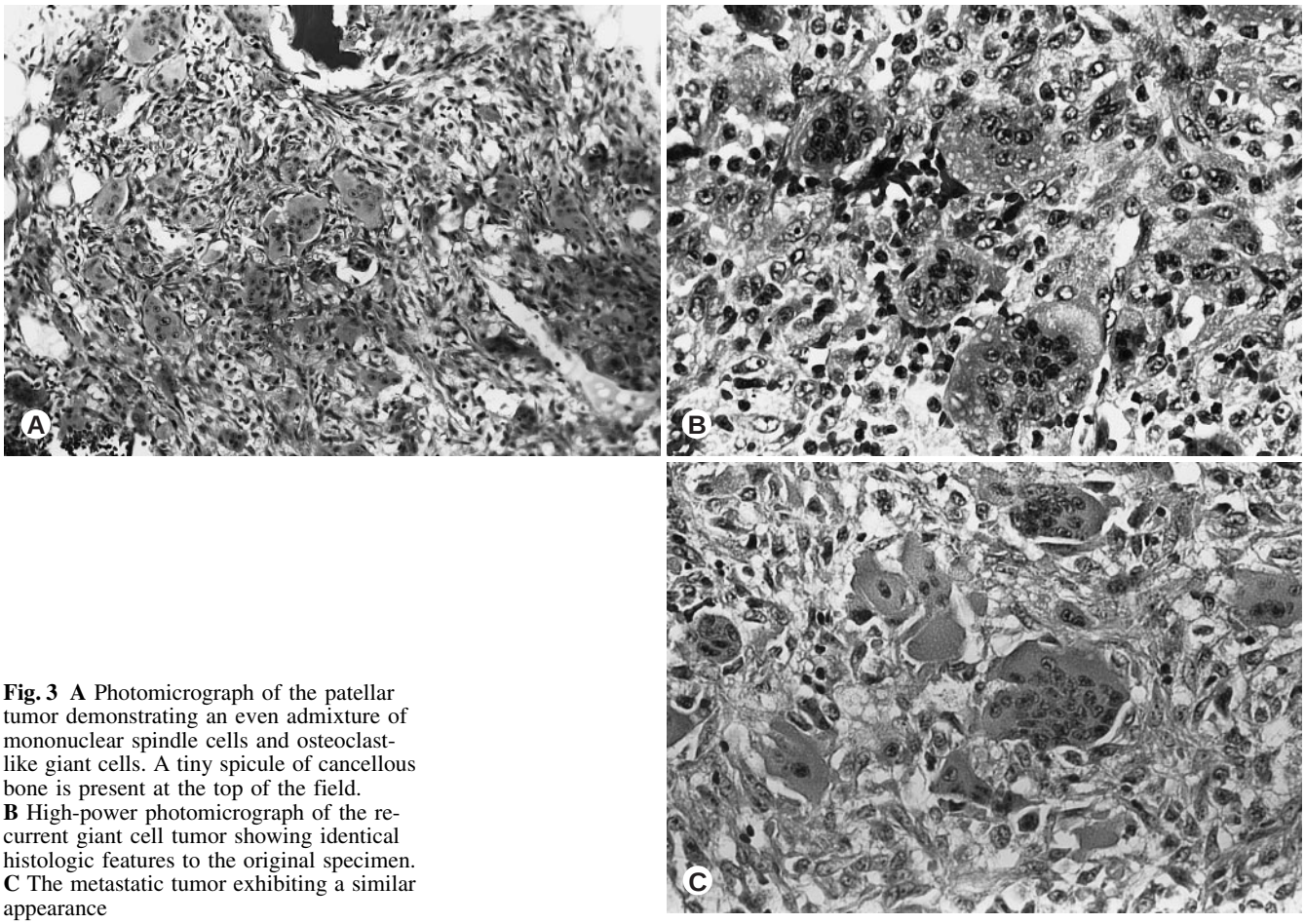

Fig. 3 **A** Photomicrograph of the patellar tumor demonstrating an even admixture of mononuclear spindle cells and osteoclast-like giant cells. A tiny spicule of cancellous bone is present at the top of the field. **B** High-power photomicrograph of the recurrent giant cell tumor showing identical histologic features to the original specimen. **C** The metastatic tumor exhibiting a similar appearance

moderate shrinkage of the tumor (12×5×4 cm). The patient received four cycles of chemotherapy (3-week cycle), interrupted in mid-course due to reluctance to continue treatment because of side effects (nausea, vomiting). The mass was easily removed at the time of surgery 1 month later. Pathology of the surgical specimen was consistent with giant cell tumor. The specimen showed some necrosis, presumably due to the chemotherapy, but was otherwise identical to the original tumor. The patient committed suicide 5 months later, and at that time had no clinical evidence of recurrent tumor.

Pathologic findings

The original patellectomy specimen demonstrated a hemorrhagic soft mass at the pathologic fracture line. This tumor exhibited the characteristic histologic features of giant cell tumor of bone, consisting of a mixture of mononuclear spindle cells with admixed multinucleated osteoclast-like giant cells (Fig. 3A). The nuclei of the mononuclear cells and those within the giant cells were essentially identical, as is typical for giant cell tumor of bone. The soft tissue recurrence specimen consisted of skin, subcutaneous tissue, and skeletal muscle, within which were two adjacent masses of recurrent tumor, measuring 9.0 and 6.0 cm in maximum size respectively. Microscopically these masses appeared histologically identical to the original patellar tumor (Fig. 3B), and of note, there was no evidence of significant nuclear pleomorphism within the spindle cell component of the tumor. Occasional linear strands of reactive woven bone surrounded the soft tissue tumors, but there was no evidence of neoplastic bone formation. The tumor nodules were embedded within scar-like fibrous tissue and, although focal regions suspicious for vascular invasion were identified, there were no unequivocal endothelial-lined spaces that contained tumor emboli. The mediastinal tumor resection specimen measured 12.0 cm in maximum size and was well circumscribed and focally encapsulated. Much of this mass had an appearance identical to the previous two specimens (Fig. 3C), although in other regions it exhibited extensive necrosis, scarring, and interstitial hemorrhage. The latter findings may have been the result of the pre-operatively administered chemotherapy. There was no evidence of sarcoma or neoplastic

bone production in the mediastinal specimen.

Discussion

Giant cell tumor of bone is a relatively common skeletal neoplasm with a well-known propensity to recur locally following treatment [1, 8, 10, 11, 16]. Local recurrence after excision occurs in a significant minority of cases and infrequently they metastasize. Secondary lesions are typically found in the lungs (2–3% of patients) [10, 17], though rare cases of metastases to other bones – scalp, brain, mediastinum, and regional lymph nodes – have also been reported. Tubbs et al. in their study reported that patients who developed lung metastases manifested them a mean of 3.8 years after diagnosis of the primary giant cell tumor [6]. The mechanism of spread of metastases is uncertain [9, 14, 16, 18]. It has been noted that recurrent giant cell tumors are more likely to metastasize, possibly due to increased iatrogenic trauma increasing opportunity for vascular invasion [17], although not all investigators agree with this assertion [8].

These osteolytic bone tumors are commonly characterized by an irregular trabeculated or multiloculated pattern on plain film [1]. Lung and lymph node metastases appear nonspecific on imaging [6]. Consequently, diagnosis of secondary lesions is usually made on the basis of clinical history and confirmed by biopsy. Attempts have been made to predict the aggressiveness of giant cell tumors based on their radiologic appearance. This has met with limited success, and Huvos advocates not relying on radiographic features for prediction of benign versus aggressive behavior [10]. On the other hand others indicate that a more aggressive course may be associated with the presence of disruption of the typically expanded, thinned cortex and soft-tissue extension [3, 4, 19, 20]. Frank malignant transformation into an overt sarcoma is recognized to occur; however, no reliable way of predicting which tumors will convert is known, although radiation is felt to be a predisposing factor [10]. In addition, no reliable histomorphological or immunohistochemical features have been detected to predict which tumors are liable to follow a more aggressive course [21].

Our search of the literature yielded only six examples of giant cell tumor metastases to mediastinal [3, 5, 14, 15, 22] or hilar lymph nodes [23]. Of these cases, only three reported mediastinal metastases without pulmonary involvement [5, 14, 22]. Lewis et al. presented a case of a 59-year-old man with a giant cell tumor of the distal radius, which metastasized to the anterior mediastinal lymph nodes with no evidence of pulmonary metastases [14]. Metastases appeared 6 years after the initial tumor was treated. The patient was treated for 5 months with 20 mg/day prednisone and then underwent resection of the mediastinal mass. At the time of publication 2 years later, no recurrence was present. A non-contrast CT image of the mediastinum showed a lobulated, inhomogeneous mass of low attenuation. No CT imaging was illustrated for the cases reported by other authors [3, 5, 15, 22]. Vanel et al. provide a radiograph showing a non-specific mass which had originally been suspected to represent an aneurysm [22].

Generally, giant cell tumors do not respond well to chemotherapy or radiotherapy. The favored treatment of primary giant cell tumors of the bone is by curettage or wide excision. A surgical approach has also been favored for secondary lesions. Treatment of metastatic pulmonary nodules is well documented and, given a reasonable number of secondary lesions, surgical excision is recommended either by pulmonary wedge resection or lobectomy [4, 7, 12, 13, 15, 24]. Prognosis for lymph node metastases is poor, treatment options are limited and may be complicated by the concurrent metastatic disease elsewhere in the body. No well-defined, accepted protocol exists for chemotherapy of metastatic giant cell tumors [8]. We chose to use an aggressive chemotherapy protocol in an effort to maximally reduce the size of the mass to facilitate surgery, as well as possibly sterilize any other metastases that may have been present and could not be detected radiologically. We acknowledge that tiny pulmonary lesions may well have been present, but below the resolution capability of CT. As noted above Lewis et al. used steroids successfully to induce regression prior to surgical excision [14]. Limited experience has been reported by others with chemotherapy, the value of which appears questionable. Bertoni et al. used a variety of different protocols (all containing Adriamycin) in seven patients, one of whom was treated pre-operatively and went on to develop pulmonary metastases 3 years after surgery [12]. Rock et al. [3] reported the cases of a few patients in their series treated with doxorubicin-containing regimes. Maloney et al. [8] recommends against the use of chemotherapy in view of the unproven benefit and potentially significant morbidity.

Giant cell tumors have been extensively studied and considerable experience with their diagnosis and treatment has been accrued. In spite of this, as illustrated by this case and others reported in the literature, giant cell tumors can on occasion present with unusual and unpredictable biological behavior.

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