Clinical practice

Metachronous multicentric giant cell tumor of bone with retroperitoneal metastasis

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Giant cell tumor (GCT) of bone is a benign but locally aggressive tumor that usually involves the epiphysis of long bones.[1] Rarely, these tumors metastasize to the lung, and these metastases generally have the same benign histological appearance as the primary tumor. Multicentric giant cell tumor (M-GCT) is rarer. We herein report a case of M-GCT involving the left distal radius, with retroperitoneal metastasis, and subsequent lesions in the left proximal and distal femur. The patient and family members were informed that data concerning the case would be submitted for publication, and they consented.

In 2001, a 37-year-old male presented to doctors in Guangzhou (China) having experienced 1 month of left distal forearm pain and limited range of motion of the wrist. The pain worsened at night and was not relieved by non-steroidal anti-inflammatory medication. A radiograph showed a lytic lesion involving the epiphysis and metaphysis of the left distal radius. A biopsy was performed and a GCT was diagnosed. Curettage and cementation was performed. The diagnosis after surgery was a benign GCT (Figure 1A).

In 2005, the patient presented to our clinic with a painful enlarging mass on the distal part of his left forearm. Radiographs and computed tomography (CT) scanning showed a lytic lesion around the cement. Emission computed tomography (ECT) showed no other lesion except the one present in the left distal radius. A biopsy was performed and the diagnosis was the recurrence of benign GCT (Figure 1B–1E). The patient underwent a wide local excision of the tumor, and received an autologous fibular transfer with plate fixation. The histological findings were consistent with a benign GCT, consisting of mononuclear cells and multinucleated giant cells. Atypical mitoses or cytological atypia were not present. The findings for microbiological examination were also negative.

In November, 2010, the patient presented to the hospital with an abdominal mass on his right side. CT scanning of the abdomen showed a 15 cm×12 cm×10 cm soft, smooth mass in the retroperitoneal region that was in close proximity to the kidney (Figure 1F). Serum calcium, phosphate, and alkaline phosphatase levels were normal. The retroperitoneal mass was completely removed. The histopathological finding was a GCT with strong aggressiveness and invasion of the right kidney cortex (Figure 1G). A CT scan showed no metastasis to the lungs. No adjuvant treatment was given. An immunohistochemical analysis was performed to rule out mesothelioma. The results of the analysis showed that the tumor was CD68 (+), vimentin (+), Ki67 <5%, EMA (−), calretinin (−), MC (−), CK5/6 (−), P53 (−), P63 (−), S-100 (−), TTF-1 (−), CD34 (−), CEA (−). This indicated that the tumor was a histiocytoma and not a retroperitoneal mesothelioma.

In October, 2011, the patient presented to the emergency room with left hip pain and limitation of movement. Plain film radiographs and CT scans showed a circumscribed, radiolucent lesion involving the proximal femoral neck with fracture (Figure 1H and 1I). The positron emission tomography (PET)/CT scans showed no local recurrence of the radial and retroperitoneal tumors or lung metastasis, but found another lesion located in the left distal epiphysis of the femur (Figure 1J–1L). The proximal femoral lesion was resected and reconstructed with prosthesis replacement. The distal femoral lesion was treated with curettage and cementation. Both the hip and femoral lesions were diagnosed as benign GCTs without malignant transformation (Figure 1M and 1N).

GCTs of bone are regarded as aggressive and the most unpredictable neoplasms of the skeletal system. Despite their innocent appearance, GCTs of the bone recur locally, metastasize to distal sites, and undergo malignant transformation,[1] with the incidence of metastasis varying from 1% to 9%.[2,3] Curettage is the preferred treatment for most cases of GCT. Historically, local recurrence rates were reported in 25%−50% of the cases. The most recent series, which have included modern imaging techniques and extended curettage through the use of power burrs, report improved local recurrence rates (8.6%–20%).[2] The patient in this case report was treated with curettage for the distal radial lesion in another hospital in 2001, yet had tumor recurrence four years after surgery. After our resection of the radius in 2005, the patient has yet to show local

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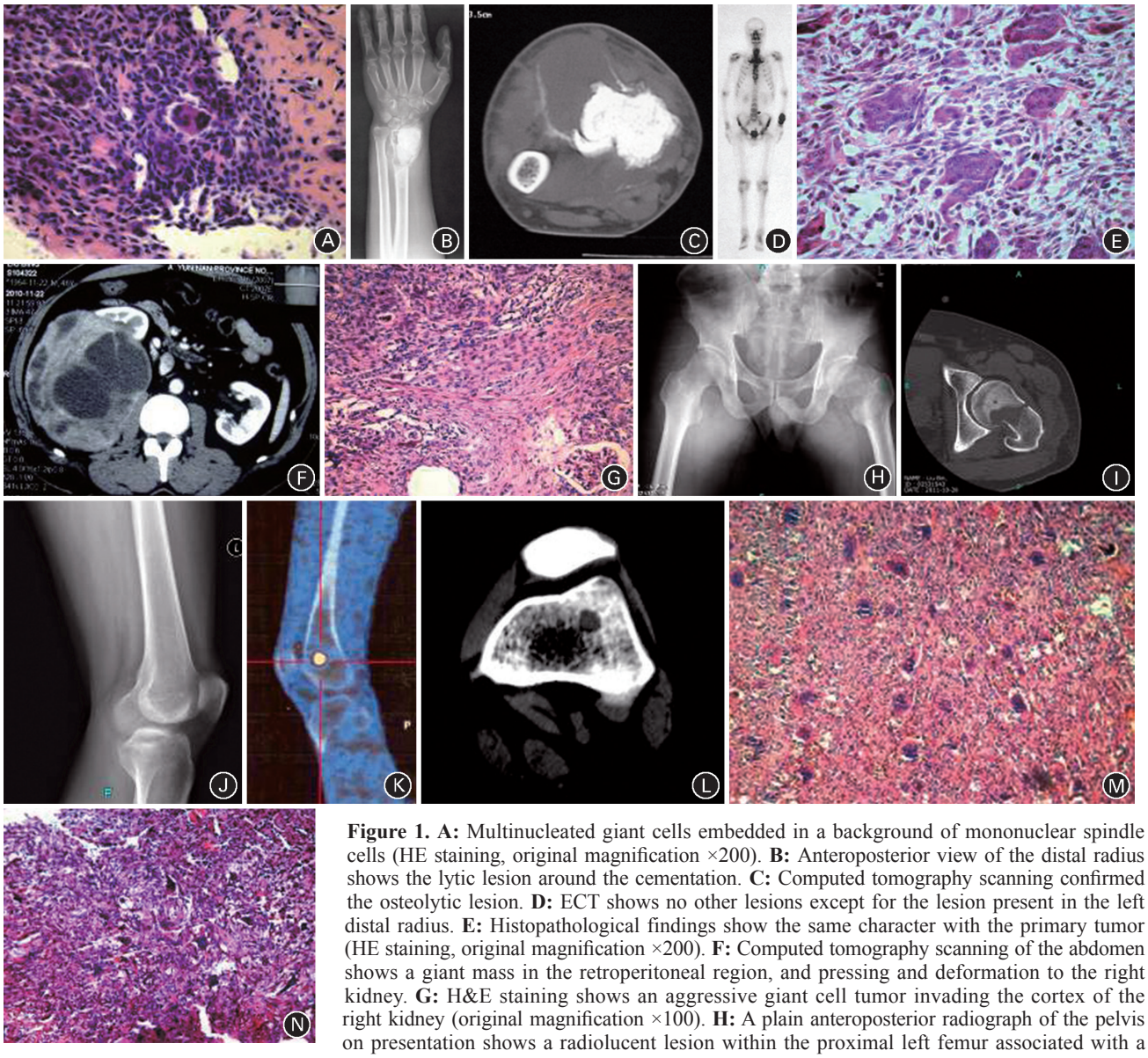

Figure 1. A: Multinucleated giant cells embedded in a background of mononuclear spindle cells (HE staining, original magnification ×200). **B:** Anteroposterior view of the distal radius shows the lytic lesion around the cementation. **C:** Computed tomography scanning confirmed the osteolytic lesion. **D:** ECT shows no other lesions except for the lesion present in the left distal radius. **E:** Histopathological findings show the same character with the primary tumor (HE staining, original magnification ×200). **F:** Computed tomography scanning of the abdomen shows a giant mass in the retroperitoneal region, and pressing and deformation to the right kidney. **G:** H&E staining shows an aggressive giant cell tumor invading the cortex of the right kidney (original magnification ×100). **H:** A plain anteroposterior radiograph of the pelvis on presentation shows a radiolucent lesion within the proximal left femur associated with a pathological fracture. **I:** An axial CT scan of the hip confirms the presence of an osteolytic lesion and fracture. **J:** The lesion is not clear in the lateral view of left distal femur. **K:** PET/CT shows a hypermetabolic lesion with increased standard uptake value (SUV). **L:** CT scanning confirms the lesion is located in the distal femur. **M:** A photomicrograph of the proximal femur shows the typical appearance of a giant cell tumor with multinucleated giant cells surrounded by mononuclear cells. **N:** Distal femoral lesion shows the appearance of a benign giant cell tumor. Sections were stained with HE staining (original magnification ×100).

recurrence in the radius.

M-GCT is rare and accounts for <1% of all cases of GCT of the bone.[4] In long bones, M-GCTs generally present as eccentric lesions predominantly involving the metaphysis and epiphysis, with extension into the subchondral region of the bone. In the present case, the proximal and distal femoral lesions were located in the metaphysis of bone, not in the epiphysis, as seen with solitary GCT. Hoch et al[5] classified M-GCT as synchronous when multiple tumors are discovered at the initial presentation or when a second tumor is diagnosed within 6 months after the first. If the second tumor develops more than 6 months after the first lesion, the lesions are considered to be metachronous. In the present case, the second bone lesion developed 10 years after the first lesion.

GCTs can give rise to distant metastases after malignant transformation, most commonly after radiation therapy. However, in 1%−6% of the cases, GCTs can also metastasize without undergoing malignant transformation. Although the lungs have been the most common site of metastases, other organs have also been reported to be involved occasionally. Postulated pathogenic mechanisms of M-GCT include contiguous spread, iatrogenic tumor cell seeding, benign metastasis, malignant transformation, and *de novo* formation. The present case shows metastatic GCT in the retroperitoneal region, but the histological findings were insufficient to diagnose malignancy. Furthermore, the subsequent femoral lesions show benign tumors. We suspect that the mechanism of retroperitoneal and femoral lesion formation could be through benign metastasis.

Tumors located in the retroperitoneal region can be classified into malignant or benign groups. Retroperitoneal sarcomas account for approximately 10% of soft tissue sarcomas and less than 1% of all malignant neoplasms. The common histological types are liposarcoma, leiomyosarcoma, and malignant fibrous histiocytoma. In the present case, the tumor in the retroperitoneal region showed a high level of multinucleated giant cells, and many pathological fields showed the same with the index tumor. Although the kidney cortex was invaded, which shows the strong aggressiveness of the tumor, the percentage of tumor cells in the kidney was insufficient for a malignant diagnosis. The immunohistochemistry study therefore ruled out retroperitoneal mesothelioma. The present case has also showed no evidence of lung metastasis.

Metastatic disease in GCT does not carry the same poor prognosis as malignant tumors. Therapy should be directed toward achieving adequate local control and, if possible, complete excision of the metastatic lesion(s). In the present case, the proximal and distal femoral lesions were treated as primary GCTs with resection and extended curettage, respectively. However, in a patient who has a second focus of GCT, a bone scan or PET/CT should be suggested, as in the current case. Long-term follow-up, therefore, is recommended in these patients.

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