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Original Article

Metachronous multicentric giant cell tumor in the spine: a case report and review of published reports

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Abstract: Giant cell tumors (GCTs) of bone commonly affect a single bone. Most of vertebral lesions occur in the sacrum rather than in the spine above the sacrum. Multicentric GCTs are rare. They may occur synchronously or metachronously and therefore may be identified at the same time in different anatomic locations or at different times in different anatomic locations. Synchronous tumors reportedly occur more frequently than metachronous tumors. Multicentric GCTs affected vertebrae are extremely rare. The present report details the case of multicentric GCTs restricted to the spine with surgically proved. To our knowledge, this is the 3 case of reported multicentric GCTs restricted the spine so far.

Keywords: Multicentric giant cell tumor, metachronous and synchronous, spine, radiographic

Introduction

Giant cell tumors (GCTs) of bone account for approximately 5% of primary bone neoplasms [1]. GCTs of bone are known for their local aggressiveness and high recurrence rate. These neoplasms commonly affect a single bone. The term multicentric denotes simultaneous presentation of more than one lesion in multiple sites, suggesting their synchronous development, whereas the term metachronous denotes development of another lesion subsequent to a first lesion; 68% of metachronous GCTs occur within less than 4 years after treatment of the initial lesion [2]. Synchronous tumors reportedly occur more frequently than metachronous tumors [2]. Herein, the authors report a rare case of metachronous multicentric GCTs in the spine and review published reports concerning multicentric GCTs.

Case illustration

Presentation and examination

A 17-year-old female patient was admitted with a 15 day history of back pain. The pain had intensified and paraparesis of both lower limbs had developed 1 week previously. Physical examination revealed painful dysesthesia of both lower extremities and sensory deficits in the perineal region. Neurological examination revealed hyperreflexia of both triceps muscles.

She had noted neither weight loss nor fever during the previous month. Her medical history was uneventful. Laboratory studies revealed normal calcium and phosphorus concentrations. There was no inguinal lymphadenopathy. A chest radiograph and CT scan of the chest were negative.

Neuroimaging

An anteroposterior radiograph showed an expansile osteolytic lesion in the L1 vertebral body with decrease in height of that vertebra (**Figure 1A**).

Computed tomography (CT) of the lumbar spine showed an expanding osteolytic lesion involving the vertebral body, right transverse process, pedicle, lamina, and spinous process and vertebral body collapse with spinal canal extension in L1. The mass was typically isodense with respect to the paraspinal muscle (**Figure 1B**, **1C**).

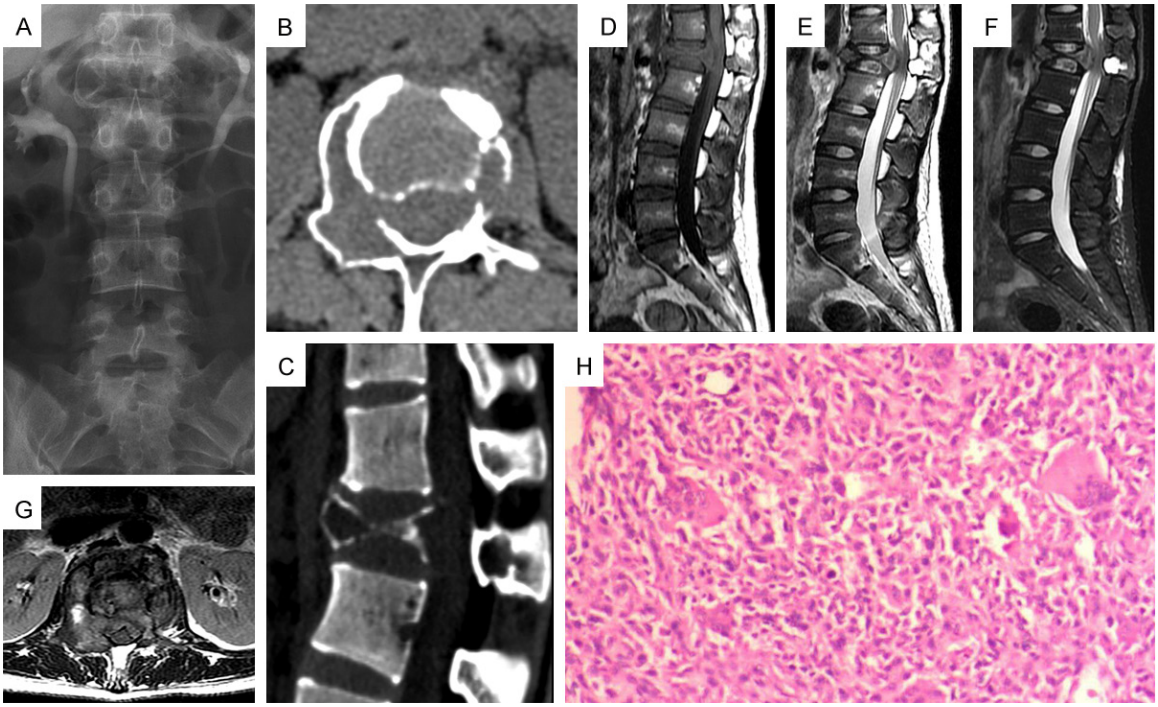

Figure 1. (A-H) A 17-year-old girl was admitted with a 15 days history of back pain. (A) AP radiograph of the lumbar spine reveal expansile osteolytic destruction of L1. (B) Axial CT image shows that the lesion arises from the vertebral body and extends to the right pedicle. (C) Sagittal reconstructed CT image reveals an L1 tumor with collapse of the vertebral body. (D) Sagittal T1-weighted MR images shows the lesion displaying similar signal intensity to the normal spinal cord. (E) Sagittal T2-weighted MR image shows the lesion bulged into the canal and compressed the dural sac and spinal cord. (F) Cystic area in the spinous process was high signal on T2-weighted image (arrow). (G) Cystic area in the right of vertebral body (arrow) was high signal on T2-weighted images. Photomicrograph shows that tumor is composed of round-to-oval mononuclear cells and multinucleated giant cells. Giant cells with varying numbers of nuclei are arranged more or less uniformly (H *arrows*). (H&E, ×200).

On MR imaging, the component of the lesion in the right vertebral body and spinous process was hypointense on T1-weighted and hyperintense on T2-weighted images indicating cystic areas, whereas the rest of the lesion was homogeneous and had similar signal intensity to the normal spinal cord on T1- and T2-weighted images (**Figure 1D-F**). The lesion extended into the spinal canal, resulting in marked thecal sac and spinal cord compression (**Figure 1D-G**).

Surgical procedure and histopathological examination

The tumor was resected via a T12-L2 laminectomy. The skin and thoracolumbar fascia were incised in the midline. The paraspinal muscles were then stripped from the spinous processes and retracted laterally to visualize the T12-L2 facet joints and associated transverse processes. After opening the dura, an epidural yellowish, soft mass became visible. The tumor was not adherent to the dura. The pedicle, lamina and spinous process of L1 were removed, the intraspinal canal mass resected completely by curettage and the cavity filled with bone cement.

Histological examination of the resected lesion showed findings typical of a giant cell tumor of bone; namely, large osteoclasts, uniform mononuclear cells with ovoid nuclei, and numerous oval to polygonal multinucleated giant cells. Hyperchromatic nuclei were distributed throughout the lesion. No evidence of malignancy was noted.

The patient's postoperative period was uneventful. Her neurological condition improved progressively and follow-up examinations showed that the paraparesis had almost completely resolved.

Subsequent presentation and examination findings

The patient returned 30 months later because of pain in the lower back and hip extending into

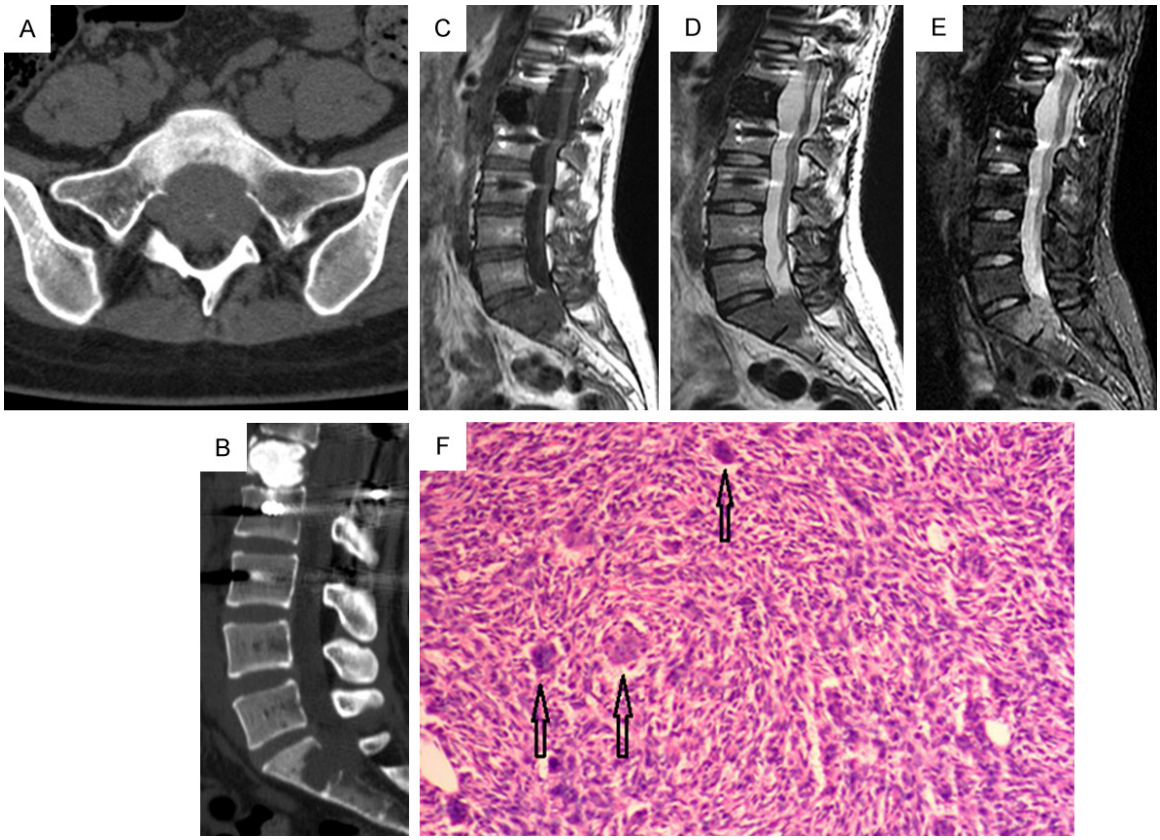

Figure 2. A-F: On repeated radiographics. A: A well-defined osteolytic lesion involves S2-S3 vertebra with surrounding osteosclerosis. No calcification is seen within mass on CT image. B: The cavity of L1 vertebral body was filled with methylmethacrylate. C: The lesion showed homogeneous signal intensity on T1-weighted image. D: The mass extends to spinal canal causing the dural sac compression. E: On STIR image, the mass showed high signal intensity. F: Classic microscopic pattern of GCT showing numerous multinucleated giant cells are scattered throughout a background of round-oval mononucleated stromal cells with indistinct cellular outlines. (H&E, ×200).

the left lower extremity for 7 days. Neurological examination showed hyperreflexia of both patellar tendons and the left Achilles tendon. Parathyroid hormone levels were normal.

Findings on repeated neuroimaging

Repeat CT imaging showed a well-circumscribed osteolytic lesion with surrounding osteosclerosis involving the S2-S3 vertebrae; there was no evidence of mineralized matrix (**Figure 2A**). Bone cement filled in L1 vertebra shows high density in previous surgery (**Figure 2B**). The lesion was homogeneous and had similar signal intensity to the normal spinal cord on T1- and T2-weighted images. On STIR images, the mass showed high signal intensity compared with the normal spinal. It extended posteriorly, causing stenosis of the spinal canal (**Figure 2C-E**).

Second operation and postoperative course

Histological diagnosis of GCT was made on open biopsy. The lesion was approached via a S2-S3 sacral canal laminectomy. It was found to be moderately adherent to the nerve root sheaths. Using a microsurgical technique, the lesion, which was approximately 2 cm ×1 cm ×0.5 cm, was stripped from the nerve roots and totally removed without damaging the dura. The resultant cavity was curetted and filled with methylmethacrylate cement.

Histopathological examination revealed multinucleated giant cells scattered among a background of round to oval mononucleated stromal cell; these findings being compatible with a diagnosis of GCT.

Eighteen months postoperatively, the patient was well with occasional mild back pain. Follow-

up MR scans have shown no evidence of recurrence.

Discussion

GCTs of bone typically arise in the metaphyseal ends of long bones [1, 2]. Almost 50% of these lesions occur adjacent to the knee, followed by the distal radius and proximal humerus [3]. There is a slight female predominance and 70% of patients are in their second to fourth decades at the time of presentation [4]. GCTs frequently recur locally despite aggressive treatment. Wide resection decreases the local recurrence rate but increases patient morbidity. An alternative approach to treatment involves thorough curettage followed by bone-grafting [2].

Vertebral lesions account for 2.7% to 6.4% of all GCTs of bone [5]. Most of occur in the sacrum rather than in the spine craniad to the sacrum [4]. Sacral GCTs are frequently large, with destruction of the sacral foraminal lines and extension across the sacroiliac joint. These lesions appear as well-defined soft-tissue densities with destruction of cortical bone on CT scans. Craniad to the sacrum, these tumors are equally distributed in the cervical, thoracic and lumbar spine [2]. Spinal GCTs are usually located in the vertebral body (55%), less frequently within the body and arch (29%), and rarely in the vertebral arch alone (16%) [2]. They are often expansile osteolytic lesions that result in collapse of the vertebral body. They frequently extend into the paravertebral region and spinal canal, compressing the spinal cord and/or nerve roots. On CT scans, they show soft-tissue attenuation and are typically isodense with respect to the paraspinal muscle with no evidence of mineralized matrix. They often show heterogeneous signal intensity on all MR sequences in and craniad to the sacrum. Focal cystic areas with low signal intensity on T1- and high signal on T2-weighted MR images without internal enhancement are frequently present. In our patient, cystic changes were noted in the right lamina and spinous process. These tumors frequently show marked enhancement on contrast-enhanced CT and MR images because of their hypervascular nature. There are no distinctive radiographic features that differentiate solitary from multicentric GCTs [3].

Multicentric GCTs are rare, accounting for less than 1% of all GCTs of bone. They may occur synchronously or metachronously [6] and therefore may be identified at the same time in different anatomic locations or at different times in different anatomic locations. The distribution of multicentric GCTs is similar to that of solitary GCTs, most occurring adjacent to the knee joint, and less frequently involving the thoracic or lumbar spine vertebrae or sacrum [7]. Synchronous tumors reportedly occur more frequently than metachronous tumors [2]. The number of lesions in patients with multicentric GCTs varies. In the largest single series reported from one institute, Ghostine et al. [8] noted that patients with multicentric GCTs generally have two to three lesions; however, one patient with twelve tumors has been reported [7].

The pathogenesis of multicentric GCTs is unclear. Various mechanisms have been suggested, including contiguous spread, iatrogenic seeding of tumor cells, malignant transformation, and benign tumors extending into bone [1-3]. Multicentric GCTs are indistinguishable from solitary GCTs on pathologic examination. Hoch et al. [6] stated that the clinical and radiographic similarities between solitary and multicentric GCTs suggest that multicentric lesions arise independently, rather being multiple sites of metastases from a single tumor.

Patients with multicentric GCTs tend to be considerably younger than those with solitary lesions [9]. Hoch et al. [6] reported a series of 30 cases in which the average patient age at the time of presentation was 21 years. One of these 30 cases presented with multicentric GCTs at the ages of 11 and 12 years; she is the youngest patient with multicentric GCTs reported thus far [6]. The average interval between the first and last lesion varies from 3 months to 21 years, the disease-free interval being shorter than 4 years in 68% of patients with metachronous multicentric GCTs [1, 10]. Haskell et al. [2] have reported the longest disease-free interval between multicentric GCTs; namely, 24 years between the initial tumor presentation and the subsequent one. In our case, there were 30 months between the first diagnosis and the second lesion.

Metachronous multicentric GCTs confined to the spine were first reported in 1977 by Kos et al. [11]. To our knowledge, the present case is the third one of multicentric GCTs restricted to the spine so far reported. Furthermore, multi-

Table 1. Reported multicentric GCTs involving the spine

Author	Age/Sex at diagnosis	Metachronous /Synchronous	First location	Second location	Time between 1st and 2nd GCT	Other location
Tornberg et al. (1975) [14]	21/F	Metachronous	L lower	L1 vertebra	16 Y	-
			Cuneiform			-
Sim et al. (1977) [9]	62/F	Metachronous	C3 vertebra	Ischium	N/A	R ulna
	24/M	Metachronous	L ulna	C3 vertebra	4 Y	-
Kos et al. (1997) [11]	29/F	Metachronous	T6-T8	S1-S2 vertebrae	2 Y	L femoral head Neck et al.
Park et al. (2003) [7]	19/M	Metachronous	R humerus et al.	L5 vertebra	7 M	-
Stratil et al. (2005) [12]	15/M	Metachronous	L fibula et al.	Sacrum et al.	6 M	-
Hoch et al. (2006) [6]	5 cases in cervical	1 case in lumbar	DATE NOT	AVAILABLE		-
Li et al. (2013) [15]	32/M	N/A	L3 vertebra et al.			-
	22/M	N/A	L vertebra et al.			-
	37/F	N/A	L2 vertebra et al.			-
	25/F	N/A	T9 vertebra et al.			-
Tandra et al. (2015) [16]	29/M	N/A	T5 vertebra			-
			L2 vertebra			
	19/F	N/A	T7 vertebra et al.			-
	45/F	Synchronous	R sacral ala et al.			

centric GCTs involving the sacrum are uncommon and S2-S3 was involved in our case. Reported multicentric GCTs involving the spine are listed in **Table 1.**

The local recurrence rate of multicentric GCTs is 28.5%, which is comparable to the 35% recurrence rate of solitary GCTs [3]. The most predictor of recurrence is incomplete surgical removal: wide excision is associated with a recurrence rate of only 5%. A review of published reports indicated that metastatic disease develops in approximately 4% of patients with multicentric GCTs [6]. Two of a series of 30 reported patients developed malignant transformation without having previously received radiation therapy [6].

Conclusion

In summary, GCTs of multicentric origin occur infrequently. To our knowledge, the present case is the second reported case of metachronous multicentric GCTs confined to the spine and the fourth with sacral involvement. Given the tendency for multifocal GCTs to occur more frequently in younger female patients, radiographs and MRI examinations are recommended in all female and pediatric patients presenting with a GCT [12, 13]. These authors suggest that this protocol should be followed half-yearly for at least 5 years and less frequently thereafter [13].

Disclosure of conflict of interest

None.

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