Metastatic behaviour of giant cell tumour of the spine

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Abstract Lung metastases from giant cell tumours (GCT) of the spine have not been specifically addressed in the literature. We reviewed our cases and compared the incidence, treatment, and outcomes with those from the extremities. Between 1970 and 2006, we identified seven cases (three females and four males) of lung metastases from a total of 51 cases of GCT of the spine (13.7%). Four of the seven patients had presented to our institution with a spine recurrence after previous treatments and the rest developed recurrences later. The treatments for the lung nodules consisted of metastectomy in two and chemotherapy in six patients. At the latest follow-up (ranging from 18 to 126 months), two had died of the disease, two had no evidence of the disease, and three were alive with disease. Our series shows a higher metastatic rate from spine GCT as compared to those from the extremities, but the overall behaviour and treatment outcomes of the lung metastases are similar. When there is a recurrence of GCT, with or without metastases, the local and possibly the metastases should be biopsied to confirm the original diagnosis. Progression of benign GCT into an

aggressive sarcoma has been documented, and the method of management should be altered.

Résumé Les métastases pulmonaires des tumeurs à cellules géantes (GCT) du rachis n'ont jamais été bien étudiées de façon spécifique dans la littérature. Nous avons revu nos observations et comparé l'incidence de ces complications et de leurs traitements avec celles observées au niveau des extrémités. Matériel et méthode: entre 1970 et 2006, nous avons identifié 7 cas (3 femmes et 4 hommes) de métastases pulmonaires sur 51 tumeurs à cellules géantes du rachis (13,7%). 4 de ces 7 patients ont présenté une récurrence au niveau de la colonne après traitement et les autres présentaient une récurrence beaucoup plus tardive. Résultats: le traitement de ces nodules pulmonaires a consisté en une métastatectomie dans deux cas, une chimiothérapie dans 6 cas. Au plus long suivi (18 à 26 mois), deux patients sont décédés de cette pathologie, 2 semblent indemnes de toute récurrence et 3 sont toujours vivant avec la tumeur. En conclusion, notre série montre qu'il existe un taux élevé de métastases dans les tumeurs à cellules géantes du rachis comparée à celle des extrémités mais, le devenir clinique et le traitement des métastases pulmonaires est identique.

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Introduction

Giant cell tumour (GCT) of bone has been extensively studied and published. The incidence in the extremities is about 5% of the primary tumours [20], and of those, 1.4–9.4% affect the spine [7, 9, 16]. In the literature, reports of metastases from GCT of the spine are few in number and do not discuss the potential risks for the metastases.

We retrospectively reviewed cases of giant cell tumour of the mobile spine and identified seven cases of lung

Table 1 Patient history on admission to our institution

Case	Age (yrs)	Sex	Primary location	Stage	Presentation group	Local recurrence	Lung metastasis
1	16	F	L3	3	A	–	–
2	17	M	C3	3	B	+	–
3	22	M	T1	3	A	–	–
4	28	F	T10	3	A	–	–
5	36	M	C5	3	B	+	+
6	39	M	C3	3	B	+	–
7	51	F	L1	3	B	+	+

metastases. This paper reviews the clinical details of the cases and compares the incidence and outcomes with those from the extremities.

Patients and methods

On a retrospective review of the spine tumour cases from 1970 to 2006, we identified seven cases of lung metastases from a total of 51 cases of GCT of the spine (13.7%). The detailed imaging studies showed that these patients only had lung metastases and no other foci.

There were three females and four males, with ages ranging from 16 to 51 years (mean age of 30 years). The locations of the primary tumours were: three in the cervical spine, two in the thoracic and two in the lumbar spine. The primary tumours had been assessed using Enneking's staging [5], and all of them were stage 3 tumours (Table 1).

Treatment

Five of the seven patients underwent an intralesional excision, with one undergoing a wide en bloc resection (spondylectomy). Another patient (case 7) had previous

treatments elsewhere, and presented to our institution with an L1 local recurrence and lung metastases. Since tumour load in the lung was a major concern, we initiated chemotherapy without any surgical intervention for the local tumour.

Overall, five patients had the primary tumour irradiated during the course of the management, and six of the seven were given chemotherapy for the metastases (Table 2). The chemotherapy regimen was based on the standard osteosarcoma protocol. When radiation was used as part of the treatment regimen to the local site, a total of 35–45 Gy was given in fractionated doses.

Results

Three patients were referred initially to our centre for the full care (group A), and four had already undergone one or more operations at other hospitals and then referred to our centre with a recurrent tumour (group B). The reason for this particular categorisation is that previous publications mention the risk of further recurrences or poorer outcomes if the patient had already begun treatment at a non-specialised centre and also that the subsequent management

Table 2 Treatment and outcomes

Case	LR	LM	Tx	ChT	RT	LR (months)	LM (months)	Tx	Status	Duration (months)	Comment
1	N	N	Wide en bloc	N	N	27	27	LM resection	NED	76	
2	Y	N	IL	N	Y	None	33	ChT	AWD	51	No local tumour; Regression of LM
3	N	N	IL	N	Y	2	4	IL+ LM resection, ChT	DOD	19	4x further LR
4	N	N	IL	N	N	50	59	IL+ ChT+RT	NED	126	Regression of LM
5	Y	Y	IL	Y	Y	32	NC	IL	AWD	132	No local tumour; Regression of LM
6	Y	N	IL	N	Y	18	18	ChT	DOD	77	GCT Sarcoma
7	Y	Y	None	Y	N	Regression	NC	None	AWD	18	No local tumour; Regression of LM

LR local recurrence, LM lung metastases, IL intralesional excision of local tumour, Tx treatment, ChT chemotherapy, RT radiation therapy, NC no change, NED no evidence of disease, AWD alive with disease, DOD died of disease

is more difficult [6]. As such, the group B presented as a local recurrence (LR). Two patients had lung metastases at presentation to our institution, and both of these were in group B (50%).

Local recurrence and lung metastases

Five of the seven patients developed a local recurrence between 2 and 50 months. One patient (case 3) had a total of four recurrences. Apart from the two who had presented with lung metastases, the others developed metastases at 4–59 months after the surgery at our institution. The treatment for the lung nodules consisted of metastectomy in two and chemotherapy in six patients.

At the latest follow-up, there were two patients with no evidence of the disease and three alive with the disease. The lung lesions were noted to have regressed to various degrees in those alive with the disease (decrease in the

number and size of the nodules, becoming dense, and having a sclerotic rim based on the CT imaging in one case). In one patient (case 7), the lung nodules regressed in number and volume after chemotherapy, as well as the local recurrence which resolved completely. Two died from the disease.

Of note, one patient (case 6) had presented with a C3 recurrent tumour and was treated with intralesional excision and radiation. He developed a further recurrence with rapid growth and lung metastasis at 18 months. The biopsy at this time was read as a sarcoma with giant cells. The original presentation slides were reviewed and confirmed to be a benign GCT. As such, this had been a GCT that progressed into a sarcoma. The patient was given chemotherapy based on the osteosarcoma regimen but succumbed to the disease nearly 5 years later.

Two cases are described to further delineate the course of events, one from group A and another from group B.

Fig. 1 28-year-old woman with a T10 lesion (case 4). **a** MRI showing the T10 pathological fracture. Core biopsy was diagnosed as an aneurysmal bone cyst. **b** Recurrence in the primary site. Also note the lung nodule adjacent to the diaphragm in the right posterior lung. **c** Chest CT at presentation. **d** Chest CT at the latest follow-up

Case 4

This patient was a 28-year-old woman who presented to our institution after a car accident and a pain in the mid-back with no prior symptoms. Plain radiographs and a magnetic resonance imaging study (MRI) were suspicious for a pathological fracture (Fig. 1a). A computed tomography (CT) guided biopsy was performed, and the pathology was read as an aneurysmal bone cyst (ABC). As such, the treatment consisted of preoperative selected arterial embolisation, followed by an intralesional excision through an anterior and a posterior approach. An intraoperative biopsy was also diagnosed as an ABC. The patient recovered fully after the surgery and was able to continue her regular daily activities.

Four years later, while pregnant, she developed progressively worsening back pain. A CT scan was performed a few weeks after she had delivered (Fig. 1b) showing a large soft tissue mass antero-lateral to the spine and arising from the previously operated area. A biopsy was performed and was read as consistent with giant cell tumour. With these findings, the previous pathology tissue was re-examined and interpreted as GCT with areas of secondary ABC. Chest CT revealed multiple nodules, too many for surgical resection. The local recurrence was treated with extensive intralesional excision. Radiation was performed for the local lesion, and the patient also underwent chemotherapy. At the latest follow-up (more than 10 years), the patient is without any evidence of disease and is able to resume her daily activities (Fig. 1c,d).

Case 5

A 36-year-old man with a history of a GCT of the fifth cervical vertebra initially treated at another hospital was referred due to worsening pain and an enlarging mass based on the MRI (Fig. 2). An intralesional excision of the tumour and reconstruction with a cage was carried out, and the area was radiated postoperatively. Although the cervical tumour fully responded and the bone had healed, lung metastases were noted at 33 months after our surgery and the patient was given chemotherapy. At the latest follow-up 132 months after our intervention, he is alive with the lung disease metastases, but reduced in number and size.

Discussion

Giant cell tumour of the bone is a benign primary tumour with an incidence of about 5% of all the primary bone tumours [2]. The incidence in the spine ranges from 1.4% to 9.4% [7, 9, 16]. GCT is a benign tumour which when affecting the spine has the same histological findings as those from the extremities [3]. The risk of metastases from

Fig. 2 36-year-old man (case 5) with a recurrent C5 tumour, presenting with a large anterior mass displacing the trachea

a benign GCT is between 1.8% and 9.1% [1, 8, 13]. The metastatic lesions have the same histological findings as the primary tumour [9, 11]. On review of the literature, metastases from the spine did not constitute a significant portion [4, 7, 16, 17].

Attempts at correlation of the metastases from the primary GCT were at best linked to aggressive stage (Enneking's system) and local recurrence [1, 4, 14]. The presence of local recurrence was associated with a 6% incidence of metastases, and only 1% when absent [14]. A study on the proliferative behaviour based on the Ki-67 staining on a small case series showed that the more aggressive lung metastases had come from primary tumours with higher rates of proliferation [12]. A counter argument for correlation with the stage of GCT was made by Lausten et al. [10] who followed up 31 consecutive patients. Their findings were that the stage of the GCT did not have any effects on the recurrences, but the type of treatment, intralesional versus wide, did. Incidentally, three of their 31 patients had tumours in the vertebrae and were treated with intralesional curettage and radiation. Although intralesional, none of these patients had a local recurrence or lung metastases, with follow-ups ranging from 198 to 278 months. Most of the lung metastases were noted in the periphery or the basilar regions [19]. Our series shows that all of our patients were Enneking stage 3 and had recurrences either at presentation (previously treated group B) or which developed later. This supports the literature in that local recurrence seems to have a higher risk of metastatic disease [13].

Treatment of the lung metastases includes radiation to the lungs, chemotherapy, and surgical resection of the lung nodules [4, 6, 13, 17, 18]. Of these, surgical resection

seems to be the most effective. The behavior of the lung lesions is somewhat unpredictable, with a small percentage regressing with or without any adjuvant treatment. This was noted in our series. There is also a small number which progress regardless of the modality of treatment, and these patients succumb to the disease. Based on the literature, the consensus seems to support surgical resection of the metastatic lesions. Our data shows that two had regression of the lung nodules, and three were alive with the disease and without progression of the lung nodules.

From our study, the metastatic potential of GCT from spine is 13.5% and appears higher than those from extremity GCT lesions. Stage 3 tumours and recurrence were also noted in our cases. Chemotherapy and surgical resection of the nodules should be considered for the treatment. As practised by others in the literature, our oncologists based the chemotherapy regimen on the standard osteosarcoma protocol.

When there is a recurrence of GCT, with or without metastases, the local and possibly the metastases must be biopsied to confirm the original diagnosis. Progression of benign GCT into an aggressive sarcoma has been documented, and the method of management has to be altered [15].

References

- Bertoni F, Present D, Sudanese A, Baldini N, Bacchini P, Campanacci M (1988) Giant-cell tumor of bone with pulmonary metastases. Six case reports and a review of the literature. *Clin Orthop Relat Res* 237:275–285
- Cheng JC, Johnston JO (1997) Giant cell tumor of bone. Prognosis and treatment of pulmonary metastases. *Clin Orthop Relat Res* 338:205–214
- Cohen DM, Dahlin DC, MacCarty CS (1964) Vertebral giant cell tumor and variants. *Cancer* 17:461–472
- Dominkus M, Ruggieri P, Bertoni F, Briccoli A, Picci P, Rocca M, Mercuri M (2006) Histologically verified lung metastases in benign giant cell tumours-14 cases from a single institution. *Int Orthop* 30(6):499–504
- Enneking WF (1983) Giant cell tumor. Musculoskeletal tumor surgery. Churchill Livingstone, New York
- Feigenberg SJ, Marcus RB Jr (2002) Whole lung radiotherapy for giant cell tumors of bone with pulmonary metastases. *Clin Orthop Relat Res* 401:202–208
- Goldenberg RR, Campbell CJ, Bonfiglio M (1970) Giant-cell tumor of bone: an analysis of two hundred and eighteen cases. *J Bone Joint Surg [Am]* 52-A:619–624
- Kay RM, Eckardt JJ, Seeger LL, Mirra JM, Hak DJ (1994) Pulmonary metastasis of benign giant cell tumor of bone. Six histologically confirmed cases, including one of spontaneous regression. *Clin Orthop Relat Res* 302:219–230
- Larsson S-E, Lorentzon R, Boquist L (1975) Giant-cell tumor of bone: a demographic, clinical and histo-pathological study of all cases recorded in the Swedish Cancer Registry for the years 1958 through 1968. *J Bone Joint Surg [Am]* 57-A:167–173
- Lausten GS, Jensen PK, Schiodt T, Lund B (1996) Local recurrences in giant cell tumour of bone. Long-term follow up of 31 cases. *Int Orthop* 20(3):172–176
- McGough RL, Rutledge J, Lewis VO, Lin PP, Yasko AW (2005) Impact severity of local recurrence in giant cell tumor of bone. *Clin Orthop Relat Res* 438:116–122
- Osaka S, Toriyama M, Taira K, Sano S, Saotome K (1997) Analysis of giant cell tumor of bone with pulmonary metastases. *Clin Orthop Relat Res* 335:253–61
- Rock MG, Pritchard DJ, Unni KK (1984) Metastases from histologically benign giant cell tumor of bone. *J Bone Joint Surg [Am]* 66-A:269–274
- Rock M (1990) Curettage of giant cell tumor on bone. Factors influencing local recurrences and metastases. *Chir Organi Mov* 75 (Suppl 1):204–205
- Sanerkin NG (1980) Malignancy, aggressiveness, and recurrence in giant cell tumor of bone. *Cancer* 46(7):1641–1649
- Sanjay BK, Sim FH, Unni KK, McLeod RA, Klassen RA (1993) Giant-cell tumours of the spine. *J Bone Joint Surg [Br]* 75-B:148–154
- Siebenrock KA, Unni KK, Rock MG (1998) Giant-cell tumor of bone metastasising to the lungs. A long-term follow-up. *J Bone Joint Surg [Br]* 80-B:43–47
- Takanami I, Takeuchi K, Naruke M, Kodaira S (1998) Aggressive surgery for treating a pulmonary metastasis of a benign giant cell tumor of the bone: results in four cases. *J Thorac Cardiovasc Surg* 116(4):649–651
- Tubbs WS, Brown LR, Beabout JW, Rock MG, Unni KK (1992) Benign giant-cell tumor of bone with pulmonary metastases: clinical findings and radiologic appearance of metastases in 13 cases. *AJR Am J Roentgenol* 158(2):331–334
- Unni KK (1996) Dahlin's bone tumors: general aspects and data on 11,087 cases, 5th edn. Lippincott-Raven, Philadelphia, pp 263–283