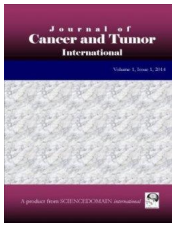

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Aggressive Recurrent Giant Cell Tumour of Distal Ulna with Pulmonary Metastasis: A Case Report

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Authors' contributions

This work was carried out in collaboration between all authors. Authors AFK and WW designed the study, perform surgical procedure, and wrote the first draft of the manuscript. Authors WS and YP managed the literature searches, analysed of the study and performed follow up care. Author NCS performed the histopathology and immunohistochemistry analysis and author MP analysed the radiograph, CT scan, and MRI. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Pulmonary metastasis rarely originates from a benign tumour, but may occur from giant-cell tumours of bone (GCT). It occurs most frequently in recurrent cases and may result in poor outcomes. We report a case with pulmonary metastases from huge ulcerated recurrent GCT at distal ulna, from diagnostic to limb salvage surgery procedure. Five months after surgery, unfortunately he passed away due to pulmonary metastases.

Keywords: Recurrent GCT; distal ulna; metastasis.

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1. INTRODUCTION

Pulmonary metastasis rarely originates from a benign tumour, but may occur in giant-cell tumours of bone (GCT) [1] and chondroblastoma [2]. The incidence rate of pulmonary metastases of GCT ranges from 1% to 9% [2-4]. It occurs most frequently in recurrent cases [2,5] and may result in poor outcomes.

2. CASE PRESENTATION

A 29 year-old man presented to our hospital with a recurrent mass on his right wrist. Three years before admission, he had had a mass on his right wrist. He went to bonesetter several times and got massages. Since the mass became bigger and painful, he came to an orthopaedic surgeon in another hospital. He had two times surgery at the same sites, eleven and seven months prior to admission. The second surgery was performed (by the same surgeon) due to local recurrence. Three months after the second surgery, unfortunately, the mass recurred. The patient was then suggested to have amputation but he refused. Therefore, the surgeon referred him to our hospital with recurrent GCT of distal ulna. No family history of malignancy or similar tumour was noted.

On physical examination, there was a big mass (12 x 10 x 8 cm) accompanied by necrotic tissue and a large ulcer on the ulnar side of the wrist. No swelling or oedema on distal part of the tumour (Fig. 1). The wrist movement was limited. The laboratory findings showed haemoglobin level 10.8 g/dL, white blood cells 9,840 cells/μL, increase in erythrocyte sedimentation rate 62 mm/h (<20) and increase of lactic dehydrogenase 828 u/L (100-190).

Radiograph showed an expansile lytic lesion on the right distal ulna with soft tissue extension, deformity of the radial styloid was noted (Fig. 2). This finding suggests a benign aggressive bone tumour of right distal ulna. Magnetic resonance imaging (MRI) showed a multilobulated enhancing solid mass, expanding to the ulnar-side soft tissue (Fig. 3). There was a small area of cystic component, most probably a secondary aneurysmal bone cyst. Chest radiography and computerized tomography (CT) scanning showed multiple nodules on both lungs, consistent with lung metastases (Fig. 4). We did not performed biopsy from lung nodules.

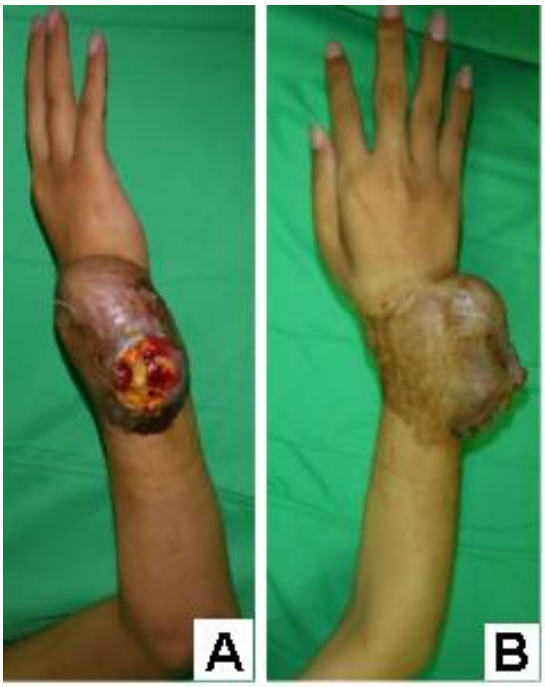

Fig. 1. Mass at ulnar side (12 x 10 x 8 cm) accompanied by necrotic tissue and a large ulcer at ulnar side of the wrist. No swelling or oedema on distal part of the tumour

Despite there were ulcerated mass and pulmonary metastases, we decided to perform limb salvage surgery. The patient underwent wide resection of both (ulna and radius) bones and reconstruction of the defect with free vascularized fibular graft (Fig. 5).

Histopathological examination showed the characteristics of typical benign GCT, consist of mononuclear stromal cells and the presence of multinucleated giant cells, which contain more than 20 nuclei (Fig. 6). The nuclei of the giant cells were similar to those of the stroma. Expression of Ki-67 and p53 protein was evaluated by immunohistochemical staining. Ki-67 was positive in 30% of the nuclei of mononuclear stromal cells (Fig. 7). P 53 staining was focally positive in the stromal cells as well (Fig. 8).

We gave biphosphonate for the lung metastases. Chemotherapy and whole lung radiotherapy were not performed. After surgery, he routinely came to our clinic. We found superficial infection, but healed well. He could grip and write well. Unfortunately, 5 months after surgery, he passed away due to massive haemoptisis due to pulmonary metastases.

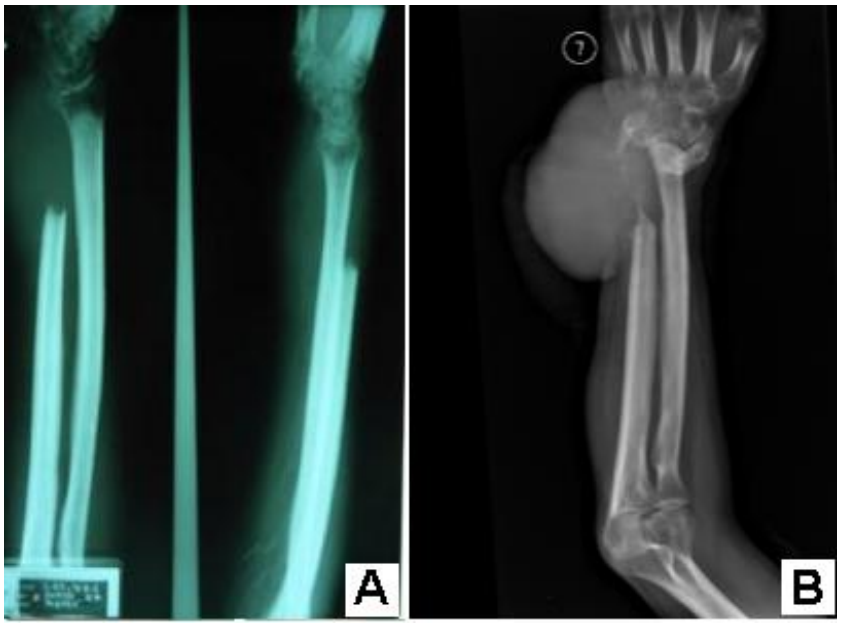

Fig. 2. Radiographic pictures. A. Anteroposterior and lateral projections showed nonsclerotic lytic lesion at right distal ulna before surgery; B. Anteroposterior projection showed lytic lesion at right distal ulna with a bigger soft tissue mass than before surgery (recurrent case)

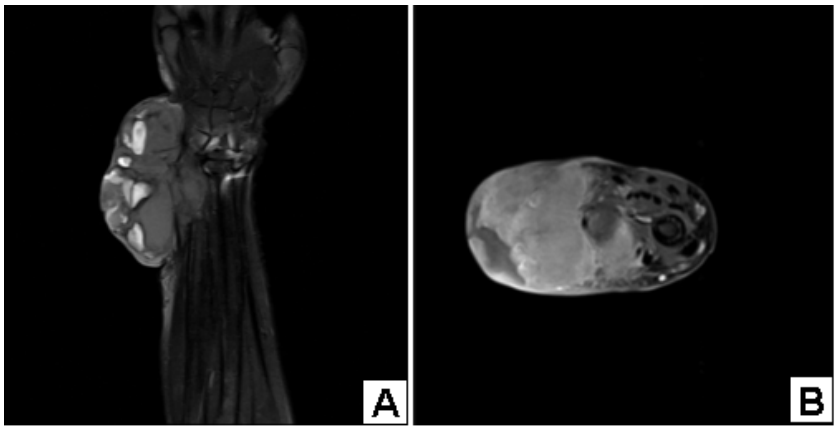

Fig. 3. MRI showed multilobulated enhancing solid mass, expanding to the ulnar-side soft tissue. There was small area of cystic component, most probably secondary aneurysmal bone cyst

3. DISCUSSION

GCT accounts for 5% of all primary bone tumours and 20% of benign skeletal tumours [6,7]. It is common in East and South Asia [8,9]. GCT at the distal ulna is very rare, with a reported incidence from 0.45% to 3.2% [10]. The characteristic appearance of GCT is best demonstrated on conventional plain X rays, that show a lytic lesion with well-defined, but nonsclerotic margin and normally the tumour extends near the articular surface (epiphysis) [7,11]. Despite being categorized as a benign lesion, GCT may be locally aggressive and have a higher incidence of local recurrence after surgical resection. The rate of local recurrence of GCT ranges from 20% to 50% [12,13].

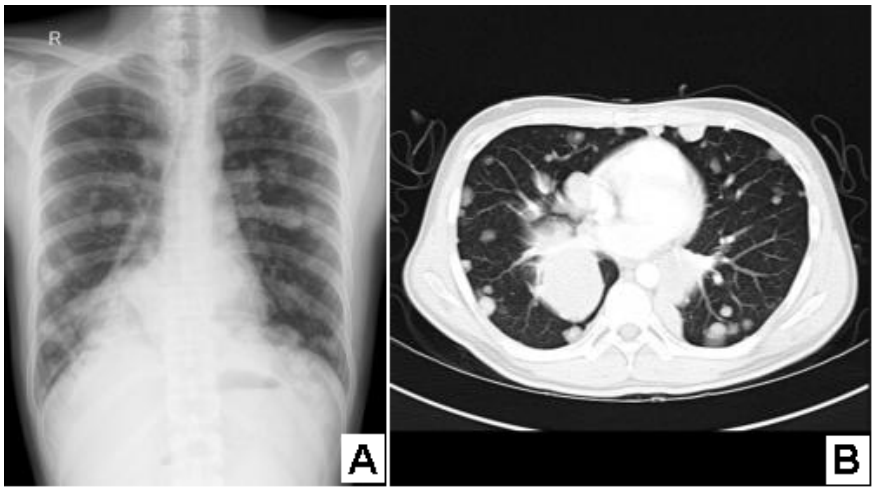

Fig. 4. Chest Radiography (A) and CT scan (B). Chest radiography dan CT scan showed multiple nodules on both lungs, consistent with lung metastases

Fig. 5. Intraoperative pictures of limb salvage surgery. A. this picture showed wide resection including both (ulnar and radius) bones; B. it showed bone defect reconstruction with free vascularized fibular graft

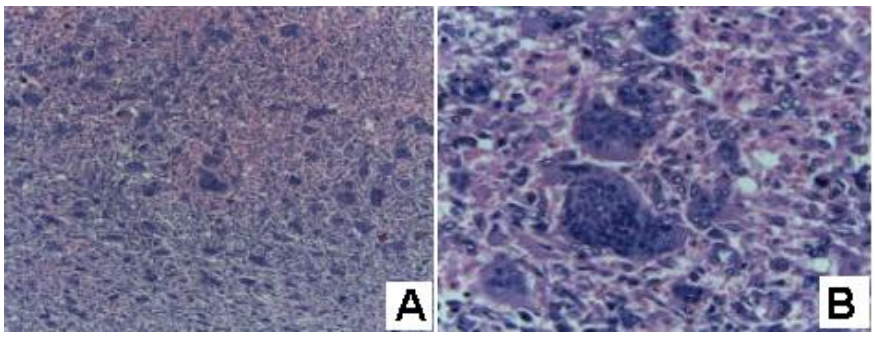

Fig. 6. Microscopic of GCT. A. It showed multiple giant cells and mononuclear stromal cells (HE. 100x). B. The tumour consists of mononuclear stromal cells and multinucleated giant cells which contain more than 20 nuclei (HE, 400x)

Our patient had had a recurred mass at the same site since 3 years before. Slow tumour growth for 3 years, local recurrence, and classic appearance of plain X ray in this case showed that the tumour had the benign aggressive characteristics. Large ulcerated tumour with wide necrotic tissue also depicted clinically aggressiveness of the tumour or probable

character shift from benign to malignant lesion [14].

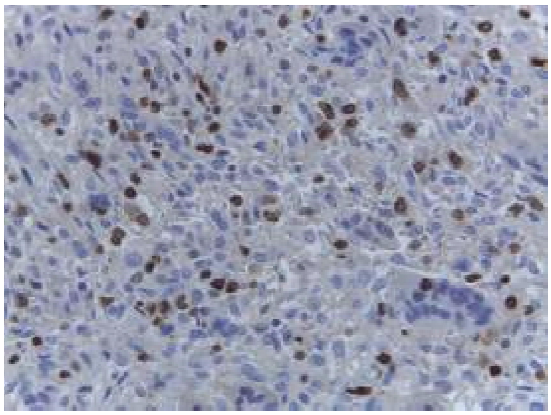

Fig. 7. Immunohistochemical stainning of Ki-67 showed positivity in 30% of the nuclei of mononuclear stromal cells (400x)

Regarding the literature, benign GCT with pulmonary metastases occurs more often (two until six folds) in recurrent cases [15]. The other risk factors suggested for the development of pulmonary metastases are the location of the tumour (distal radius), stage/grade 2 or 3, and immuno-compromised condition [1-3,15]. In our case, there are three risk factors of pulmonary metastases that were found: local recurrence, location of the primary GCT at distal radius-ulna, and grade 3 Campanacci. In addition, we also consider that pulmonary metastases in this patient were due to physical manipulations (massage) and previous operations. However, we do not know exactly when pulmonary metastasis occurred. He had had metastasis when he was presented to our hospital.

Generally the cause of the metastasis is unclear. There have been many hypotheses regarding why benign GCTs metastasize. Mechanisms that have been implicated include vascular invasion and iatrogenic manipulation at the time of surgery [1,4,16]. Despite iatrogenic seeding at the time of surgery has been postulated as another mechanism for metastasis, pulmonary lesions often occurred before or simultaneously with surgical intervention [1,4,15-16]. Viswanathan and Jambhekar mentioned several etiologies and mechanisms of metastases in GCT including transformation from a self-limited benign course and true arterial metastases. However, there is also debate regarding whether surgical manipulation promotes pulmonary metastases [17].

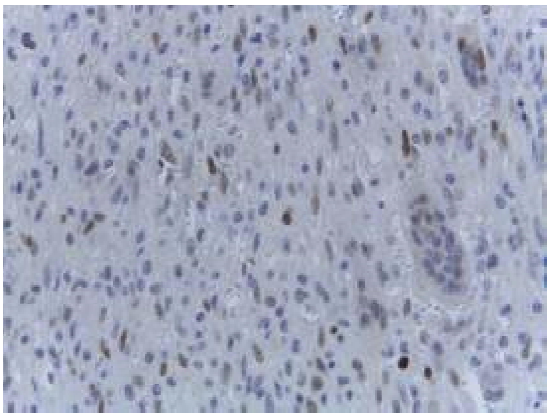

Fig. 8. p53 stainning were focally positive in the nuclei of mononuclear stromal cells (400x)

Numerous studies have attempted to predict the behaviour of GCT. However, there are no definite biological or histological parameters to determine the aggressiveness or prognosis of this lesion. In other words, this kind of tumour is an unpredictable bony lesion [18,19].

Various proliferation markers had been studied to correlate with the aggressive behaviour of GCT and surgical outcome. These included the expression of Ki-67, proliferating cell nuclear antigen, and p53 tumour suppressor gene in the mononuclear histiocytic stromal cell [18,20]. The Ki-67 antigen is a human nuclear protein used as a marker for cellular proliferation [18,21]. Osaka et al. [22] showed that primary and recurrent tumours of the rapid-growing GCT displayed high proportions of positive cells for Ki-67. However, Ismail et al. [18] mentioned that Ki-67 was not a useful marker to predict the risk of recurrence and pulmonary metastases in aggressive GCT. Despite this marker is still controversial about its usefulness to predict the risk of recurrence and pulmonary metastases, we had found that Ki-67 was positive in 30% stromal cell nuclei.

The p53 is a tumour suppressor gene that sense and repair DNA defects in cell cycle. The cells that lack p53 have lost cell cycle control and presumably accumulate damage-induced mutations that result in tumourigenesis. The alterations of p53 had contributed to the progression in bone tumour [23]. In our case, p53 was focally positive in the nuclei of stromal cells. This is similar to those reported by Ismail et al. who said that p53 expression was a good prognostic marker to predict the risk of local recurrence and lung metastases in GCT of the bone [24].

Although this patient had ulcerated recurrent GCT with pulmonary metastases, we still performed limb salvage surgery because of some reasons, such as adequately wide resection of local tumour could be achieved, neurovascular bundle was not involved, and also bone and soft tissue reconstructions could be done. In addition, he refused for amputation. He had superficial infection, which was healed and he could grip well.

Some literatures mentioned chemotherapy and whole lung radiotherapy for unresectable pulmonary metastases and to the patient who refused metastatectomy. Group of patients who had undergone chemotherapy had better outcome [2,4]. We regarded GCT as a benign lesion and the metastases was multiple involving both lungs and also the metastases had been asymptomatic for long periods. Treatment is not always mandatory because in some cases, pulmonary metastases had regressed without treatment [2,4]. We treated him symptomatically and gave biphosphonate (ibandronate). In fact, six months after surgery, he died due to progressive pulmonary metastasis (haemoptysis). We think that he had a rapid-growing type of pulmonary metastasis. Approximately 20% of patients with pulmonary metastases of the rapid-growing type die of the disease [22].

4. CONCLUSION

In conclusion, recurrent GCT of distal ulna, despite its type as a benign bone tumour, has an aggressive manner and has the ability to metastasis to the lung which results in poor outcome. Immunohistochemical staining of Ki-67 and p53 is recommended in aggressive GCT to predict the risk of recurrence and pulmonary metastases. For better outcome, chemotherapy or lung radiotherapy is considered as choice of treatment for GCT of bone with pulmonary metastasis.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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