

Case Report

Benign giant cell tumor of bone with pulmonary metastasis- report of two cases and review of literature

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ABSTRACT

Tumors that are metastasizing generally considered as malignant. But there are exceptions. Giant cell tumor of bone is well known for its potential to metastasize without sarcomatous transformation. Potential of benign GCT to metastasize was first reported by Jaffe et al in 1940. Prevalence of pulmonary metastasis in benign GCT is between 1-9%. Factors favoring metastasis include recurrence of tumor, surgical manipulation of initial bone tumor, location of femur etc. Peripheral or basilar portion of pulmonary parenchyma is involved commonly. Eventhough death reported in 16-25% of cases, overall it has a favorable prognosis. Surgical resection is preferred treatment for pulmonary metastasis. In the present study 2 case studies were done. In 1st study 18 year old female, known case of GCT Lt tibia, with history of curetting and cementing presented with pain and swelling at same site and pulmonary metastasis 1 year later. Biopsy from initial as well as recurrent tumor confirmed benign GCT without any features of atypia, mitosis or necrosis. Aspirate from pulmonary lesion showed osteoclastic giant cells. No treatment given to metastatic deposits and is asymptomatic even though size of pulmonary lesions is increasing. And in second study a 22 year old female, with past history of GCT referred to our institution for evaluation of lung lesion detected in X-ray. Patient underwent metastatectomy here and histopathology was similar to that of bone lesion. There was no evidence of sarcomatous transformation both in initial and recurrent lesion. Patient is asymptomatic other wise and doing well.

Keywords: Benign, GCT, Pulmonary metastasis

INTRODUCTION

Giant cell tumour is a benign, locally aggressive neoplasm which is composed of sheets of neoplastic ovoid mononuclear cells interspersed with uniformly distributed large, osteoclast- like giant cells.¹ Giant cell tumor accounts for around 4-5% of bone tumors. The peak incidence is between the ages of 20 and 45. i.e. after attaining skeletal maturity. It presents as a lytic lesion at the epiphyseal end of long bones like distal femur, proximal tibia and distal radius.² Though considered as a benign tumor, it has an unusual ability to metastasize. We report 2 cases of benign GCT having pulmonary

metastasis from the same institution and review the characteristics of such distant metastasis.

CASE REPORT

Case 1

An 18 year old female, presented with pain and swelling of proximal part of Left tibia of few days' duration. She gives history of GCT at same site and had undergone curetting and cementing 1 year back from the same institution. Patient was evaluated radiologically and found to have recurrence of lesion at tibial tuberosity

(Figure 1). Computed Tomography thorax showed multiple enhancing nodular lesions of varying sizes in both lung fields, largest measuring 14x13mm in posterior segment of left upper lobe.



Figure 1: Anteroposterior radiograph of left knee joint of 18 year old female, showing recurrent lytic lesion on tibial tuberosity.

Other investigations were within normal limits. She gave no history of respiratory symptoms. Open biopsy from the recurrent tumor performed and gross pathology showed multiple tiny bits of grey white tissue aggregate measuring 2x1x1 cm. Microscopic examination revealed benign GCT without any features of atypia, mitosis or necrosis (Figure 2B). Biopsy from initial tumor reviewed which also had a similar histopathological picture (Figure 2A). Radiologically guided aspirate from pulmonary lesion showed osteoclastic giant cells followed which patient was treated with Enneking arthrodesis. No treatment was given to metastatic deposits. She is asymptomatic after follow up of 1 year even though size of pulmonary lesions is increasing.

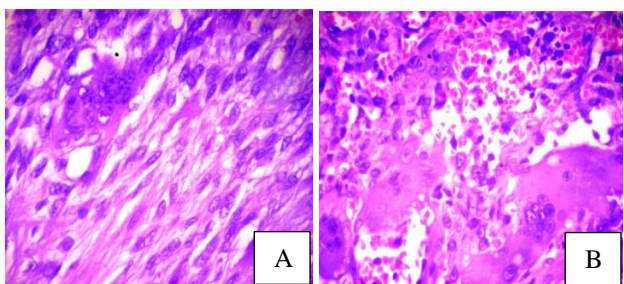


Figure 2: Microscopic findings of the primary (A) and of the recurrent (B) lesion. The tumor consisted of osteoclast-like giant cells and mononuclear stromal cells. No nuclear atypia or increased mitosis noted (H&E stain, 400X).

Case 2

22 year old female, with past history of bone tumor referred to our institution for evaluation of lung lesion detected in X-ray. She was a known case of giant cell tumor of right femur, for which she had undergone

intralesional curetting and cementing 3 years back and was on regular follow up thereafter. She married later and diagnosed to have recurrent growth after 2 years, when she was 4 months pregnant. Patient underwent wide excision and custom total knee replacement from elsewhere. Histopathology report showed Benign GCT with foci of prominent mitosis of 3-6/10 high power field. No nuclear atypia/ atypical mitosis or necrosis noted. During preoperative work up, multiple nodular lesions of 5mm to 28mm size noted in both lung fields, more towards periphery of lung fields without lobar predominance (Figure 3).

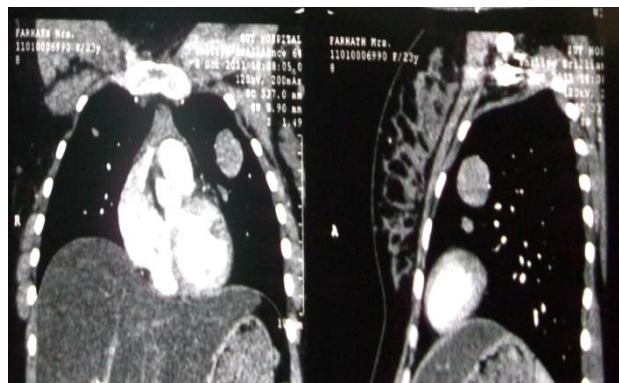


Figure 3: CT scan showing multiple pulmonary metastasis.

But metastatectomy deferred as she was pregnant. After giving birth to a healthy baby through Caesarian section after 6 months, patient underwent metastatectomy in our institution. She had no respiratory symptoms and was normal during general & respiratory system examination. Largest lesion which was located in periphery of upper lobe of left lung excised. Wedge resection specimen of lung showed a well circumscribed lesion of 4x4x3 cm involving the resected margin and a satellite lesion measuring 2x1x1 cm (Figure 4).



Figure 4: Pulmonary wedge resection specimen showing a well circumscribed lesion of 4x4x3 cm which involves the resected margin and a satellite lesion measuring 2x1x1 cm.

Cut surface of lesion was grey brown with grey white areas in between. The histological appearance of the

resected metastatic lung tumor was remarkably similar to that of the bone lesion (Figure 5 A&B). There was no evidence of sarcomatous transformation either in recurrent lesion or in metastasis. Patient was asymptomatic other wise and doing well.

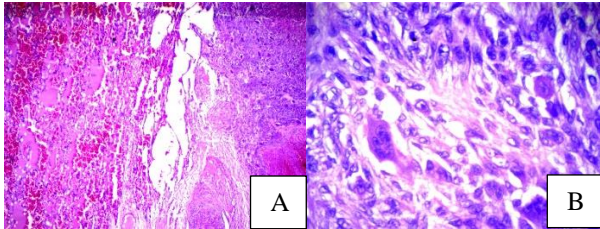


Figure 5: Microscopic findings of metastatic lesion showing (A) Congested lung parenchyma with a metastatic deposit (H&E stain, 100X) (B) The tumor consisted of many osteoclast-like giant cells and mononuclear stromal cells, which are compatible with a typical GCT. The histological features of the metastatic lesion closely resembled those of the primary lesion. No nuclear atypia or increased mitosis noted. (H&E stain, 400X).

DISCUSSION

It is clear that any neoplastic condition that exhibits spread and subsequent growth at distant sites is by definition malignant. One of the exceptions to this rule is GCT. Although distant metastasis from GCT is known to be rare, cases were reported in locations like bone, muscle, lymph node, breast, penis, skin, brain, adrenal, GIT, kidney with lung being the common site having an incidence between 1-9%.^{2-12,15}

Clinical data from literature shows that age of the patients ranges between 15-61 with mean age being 31.8 with a male predominance.¹⁶ Risk factors for pulmonary metastasis include primary site, locally aggressive tumors, multiple recurrences and modality of treatment of primary tumor.^{4,7,10,11} Most of the cases reported show distal femur as the common primary site followed by proximal tibia and distal radius.^{5,7,16} According to Enneking system, there are 3 stages for benign GCT: stage 1, latent; stage 2, active; and stage 3, aggressive.¹⁸ Study conducted by Chun-Chieh Chen shows that pulmonary metastasis developed more commonly in stage 3 lesions with cortical erosions.¹¹ Benign GCT of bone with pulmonary metastasis occurs most frequently in recurrent cases; these recurrent tumours have the potential to develop malignant biological behavior.⁸⁻¹⁰

Study by Viswanathan S shows that, out of 24 tumors metastasized, 13 developed recurrence prior.¹⁴ Searching through literature, surgery alone or combined with radiation was the usual treatment modality employed for primary tumor in many of the cases. Most of the primary tumors were treated by curetting and bone grafting. But recurrence treated by excision and arthrodesis. The usual

interval between initial surgery and metastasis ranges from 4 to 132 months.^{9,11,12,16,19} Siebenrock et al reported metastasis even after 24yrs in one patient.¹⁰ In one of the studies, pulmonary metastasis detected even before the primary lesion in sacrum discovered.¹⁷ Even delay for primary treatment can also favor development of pulmonary metastasis.¹¹

Mechanism of metastasis from this histologically benign tumor is considered to be same as that of other malignant tumors. Local vascular permeation and emboli formation is considered by some authors to be the reason for metastasis to lung.^{3,9,20} This can be by the action of tumor itself or by any surgical procedure. ie why some suggested surgical procedure accelerate development of pulmonary metastasis.^{8,10,11,19} Report by Viswanathan et al, shows that there is no association between metastasis and risk factors such as locally aggressive disease and multiple recurrences.

The clinical and roentgenographic stage proposed by Enneking is more predictive of prognosis of giant cell tumor rather than cytological features.¹⁸ The histopathological grade in GCT of bone not indicative of prognosis.⁸ There is currently no definitive method to predict distant metastasis in GCT based on histology.¹⁴ However, radiographic grading using Campanacci's classification system is useful to assess the prognosis.⁸

Pulmonary metastasis can be solitary or multiple. Some metastasis spears to grow very slowly and regress completely spontaneously but some grow very rapidly.^{8,12,16} Pulmonary metastasis are usually seen as round to oval nodular opacities of homogenous density ranging from 0.5cm to 8cm. They are commonly located in peripheral and basilar regions of lung. They are usually parenchymal, although endobronchial metastases rarely have been described.⁵ Eventhough CT is considered to be better than X-ray for their identification, no distinguishing features are described compared to size, edge, shape or distribution.⁴

Gross appearance of the metastatic nodules is yellow-tan variegated with hemorrhage and necrosis.¹⁴ Histologic sections from the primary tumor as well as from the metastases reveals an identical picture of giant cell tumor of bone.^{3,10} Histological findings show sheets of plump oval and spindle shaped cells with many multinucleate giant cells intermingled in between. Distribution of giant cells may be focal or diffuse. The stromal cells usually have regular nuclei. No nuclear atypia seen. Nuclei of giant cells were similar to that of stromal cells. In addition, routine features seen in GCTs such as osteoid, fibrosis, collagenization, ectatic blood channels, and focal storiform pattern also were noted.^{14,16} Spindle cell filled areas were noted near periphery in pulmonary nodule.¹⁶ There was no evidence of any atypical features: no anaplasia observed in the primary, recurrent, or metastatic lesions.

Mitosis upto 7/10 hpf reported in few cases.¹⁶ No atypical mitotic figures were seen in any of the primary or metastatic lesions.¹⁴ DNA analysis by flow cytometry of primary tumor and metastasis shows similar pattern.¹⁵ Treatment for metastatic lesion is still a controversy. According to the various literature surgical excision is the common practice. Wedge resection, lobectomy and thoracotomy were the usual treatment modalities employed.¹⁶ Radiation and or chemotherapy is useful for anatomically inaccessible lesions.¹⁶

As evident from the literature, GCT with pulmonary metastasis usually have an excellent survival rate of 85%.¹⁶ 20% of patients with metastases die of the disease. This excellent prognosis may be due to their self-limited behavior. The pulmonary nodule which usually have giant cell lesion in the centre will gradually convert into a fibrotic bony reactive peripheral rim. Some may regress completely into an ossified tissue, may be mediated by immunological mechanisms.¹⁶

Careful follow up of these lesions is required by serial X rays. Even though they have an indolent nature, few may progress and develop symptoms.

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