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A Very Rare Case of Metachronous Multicentric Giant Cell Tumor of Bone with Benign Lung Metastasis in form of a Very Large Mass Lesion

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ABSTRACT

Giant cell tumour (GCT) is a benign, locally aggressive tumour of the bone that accounts for 5% of primary bone tumors and 21% of benign bone tumours. This tumour more commonly presents as a single (solitary) lesion; however, it may appear with multiple (multicentric) lesions in less than 1% of the cases. According to the literature, 1-9% of solitary GCTs metastasizes to the lung, more commonly in cases with local recurrence. There are limited case reports on multicentric GCT (MCGCT) in the literature. The MCGCT can be synchronous or metachronous depending upon the time interval between the two lesions. Herein, we presented a very rare case of metachronous MCGCT with benign lung metastasis in form of a huge lung mass.

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Introduction

Giant cell tumour (GCT) is a benign locally aggressive intramedullary tumor of the bone with a high tendency for local recurrence. This tumor rarely (1-9% cases) produces unique benign metastatic lesions in the lung (1-4). Less than 1% of the GCTs has multifocal lesions, called as multicentric GCT (MCGCT) (5, 6). They can be synchronous (i.e., lesions that are remote from one another but discovered within a short period of time and at similar stages of development) or metachronous (i.e., lesions that occur at different times and in different locations) (5). Benign lung metastasis is also reported in MCGCT; however, it is very rare (5, 6). Herein, we reported a very rare case of metachronous MCGCT with benign metastasis to the lung in form of a huge mass lesion, detected 14 years after the first GCT lesion.

Case Presentation

A 34-year-old female teacher, who was single and non-addict, had complaints of dizziness and grade I dyspnea initiated for seven days, in September 2015. There was no history of fall or other symptoms. On examination, the patient's hemodynamics were stable with normal oxygen saturation. The trachea was shifted to the right side, and breath sounds were decreased in the left hemithorax. Chest X-ray showed homogenous opacity in the left hemithorax with the

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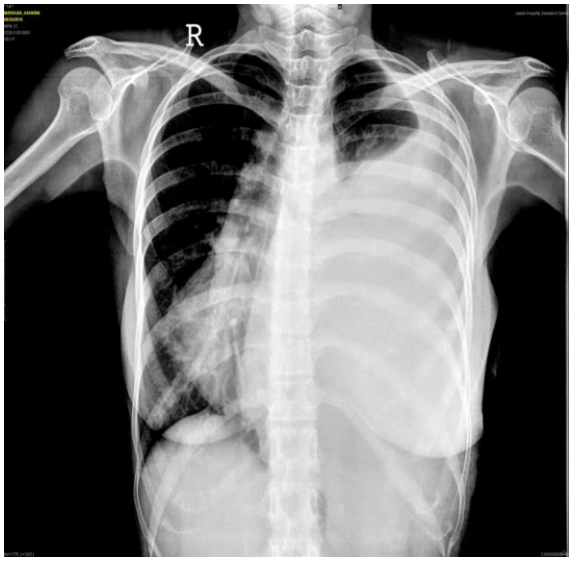

Figure 1. Chest x ray PA view on admission showing homogenous opacity in left hemithorax with shift of medistinum to right

obliteration of left costophrenic angle with the shift of mediastinum to the right (Figure 1).

The computed tomography of the thorax showed a heterogeneously enhancing lobulated mass in the left pleural place. The mass had solid cystic areas of 14×13 cm protruding into the posterior mediastinum causing the caudal displacement of the spleen and kidney, anterior displacement of the stomach, and inferior displacement and distortion of the left hemidiaphragm. There was a mild pleural effusion in the left hemithorax. The mass and pleural effusion had the Hounsfield unit of 87 and 37, respectively.

The patient had a history of bony overgrowth on the metacarpal bone of the left little finger in 2001, followed by second bony overgrowth on the metacarpal bone of the left thumb in 2006. In 2007, there was a recurrence of overgrowth on the metacarpal bone of the left thumb. The patient underwent the curettage of the bone lesion each time. In 2006, she had undergone bone grafting in addition to the curettage surgery. The bone lesion was diagnosed as a benign giant cell tumor every time by the histopathologists.

Ultrasound guided true cut biopsy of the mass lesion was done from left posterior axillary line in 9 th intercostals space, which showed benign giant cell rich lesion involving lung. So the lung mass was diagnosed as benign metastasis of giant cell tumor of bone. Since, patient had giant cell tumors at 2 separate locations (metacarpal bone of left little finger, metacarpal bone of left thumb) and at different times (2001 and 2006); giant cell tumor was diagnosed as metachronous multicentric giant cell tumor, with the third lesion at metacarpal bone of left thumb in 2007 being the local recurrence of the lesion in 2006.

Whole body PET-CT scan was done to know the extent of the disease spread. It showed mass lesion in left hemithorax measuring 15 x 15 x 18 cm with caudal displacement of spleen and left kidney by mass (Image 2,3). There was FDG

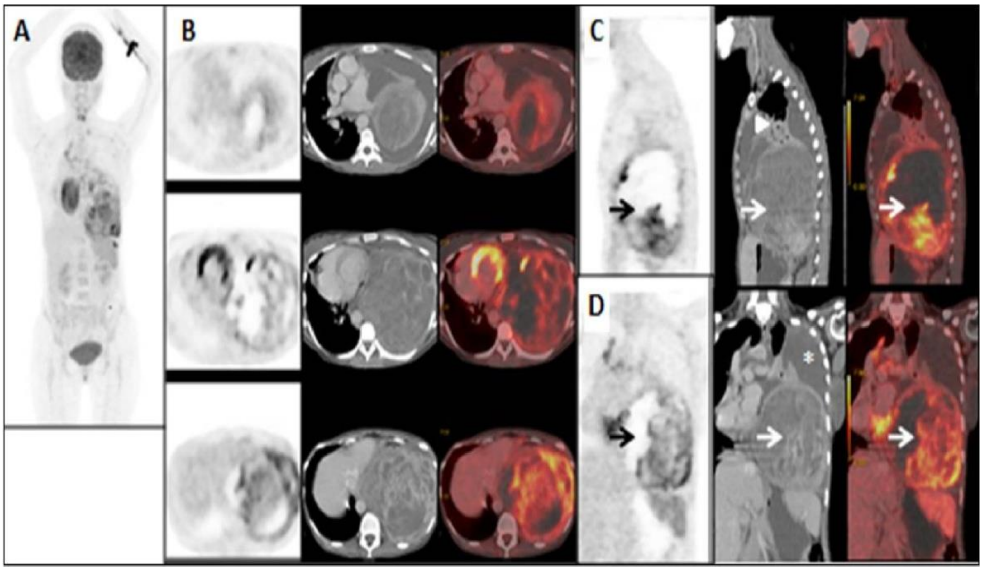

Figure 2. (A)Maximum intensity projection (MIP) PET image (B)Three rows of axial images (PET, CT and fused PET/CT)at different level showing the lesion. The lesion is large in left hemithorax, shifting the mediastinum. It has hypodense and necrotic areas within and shows inhomogeneous FDG uptake (C) Sagittal images (PET, CT and fused PET/CT) showing the lesion. The lesion (marked by arrow) pushes the left lung superiorly with resultant collapse in left lung (arrowhead) (D) Coronal images (PET, CT and fused PET/CT) showing the lesion (marked by arrow). There is reactive pleural effusion seen superior to this lesion (marked by asterisk) and the spleen is seen to be pushed inferiorly by this lesion.

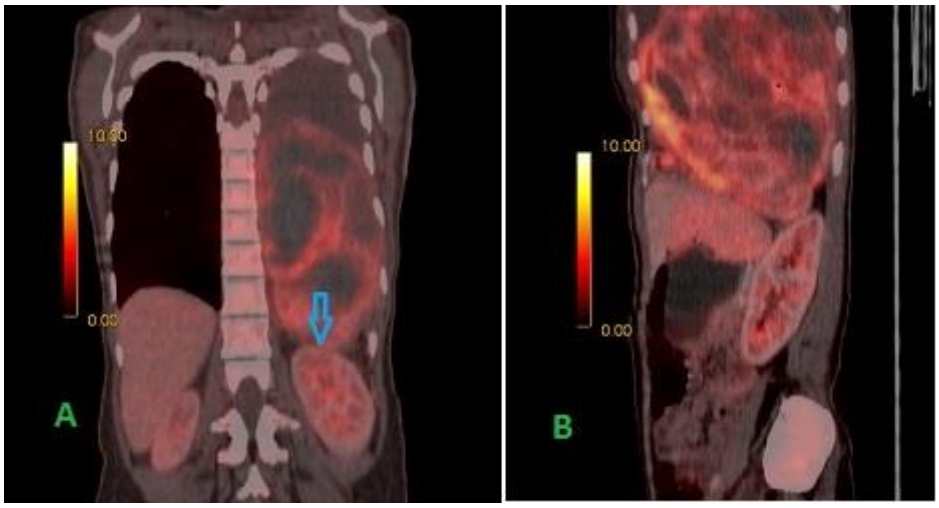

Figure 3. (A): Coronal PET/CT image showing mass in left hemithorax breaching left diaphragm (shown with arrow) causing caudal displacement of left kidney. (B): Sagital PET/CT image showing mass in left hemithorax with loss of fat plane.

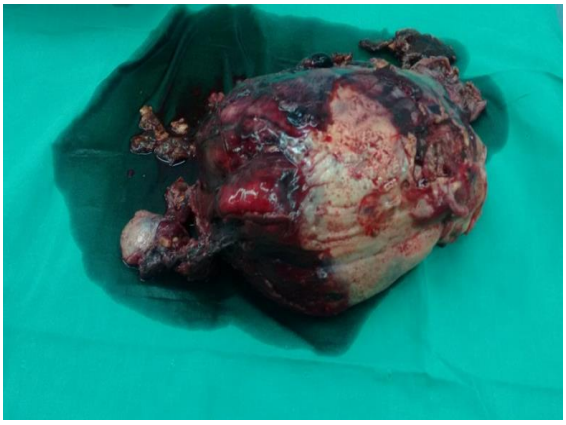

Figure 4. Gross excised specimen of benign lung metastasis obtained after left hemithoracotomy

uptake in solid component of the mass lesion (SUV max 9.1) and mild reactive pleural effusion. FDG uptake was also seen in mediastinal (pre vascular, pre-carinal, aortopulmonary, sub-carinal), left supraclavicular lymph nodes and low grade uptake in left internal mammary lymph node. There were no other distant metastatic foci in body. Fine needle aspiration of left supraclavicular lymph node was done which was negative for giant cell involvement.

So, patient was subjected to excision surgery for mass in view of overall favorable prognosis with excision surgeries in patient of GCT with lung metastasis. Intra operatively mass was not originating from pleural cavity as suspected on PET-CT but was covered by visceral pleura and was adherent to lingula, left lower lobe, left phrenic nerve and was traversing across left hemi-diaphragm. Entire mass was removed along with lingula and part of left lower lobe of lung(Image 4). Histopathology of the excised lung mass reconfirmed the diagnosis of benign metastatic giant cell tumor involving left lower lobe (Image 5). Since there was no active bone GCT or lung lesions post excision of the mass, denosumab was not used. Repeat PET- CT, 3 months after the surgery did not show any new lesion except a residual small pleural fluid collection. Patient is in good health for last 2.5 years post-surgery.

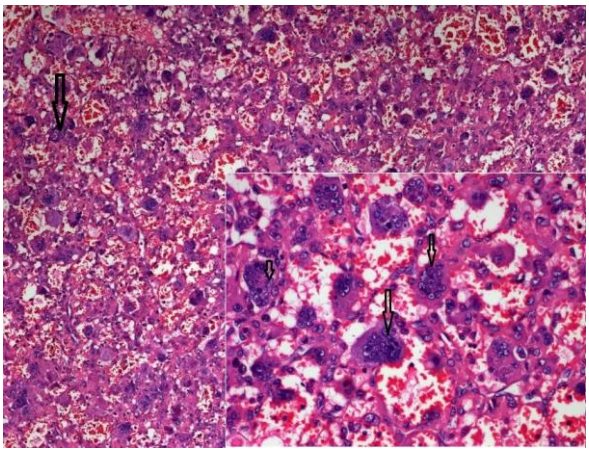

Figure 5. Histopathological image showing prominent vascular channels in which intervening stroma is loose edematous and shows scattered multinucleated giant cells (Arrow marked).

Discussion

Giant cell tumor (GCT) is primarily an intra medullary tumour of bone. It more commonly affects the epiphysis of distal femur, distal radius or proximal tibia and is commonly found in age group 20 to 40 years, with slight female preponderance (M:F : 0.9:1)(1,3). It is a locally aggressive tumor with high tendency for local recurrence and can metastasize to lung in 1 to 9% cases(3).

There can be single lesion of GCT of bone, or multiple lesions occuring simultaneously or after some duration (multicentric GCT). Majority of GCT of bone are single (solitary) lesions. Only less than 1% GCT of bone are multicentric. Dhilion et al (5) described multicentric GCT (MCGCT) as synchronous, when lesions are remote from one another but discovered within a short period of time and at similar stages of development;or metachronous when lesions occur at different locations and with time gap. Synchronous MCGCT are more common than metachronous MCGCT. Very few cases of MCGCT are reported in literature with the largest case series of 30 patients by Hooch et al (6) and later Dhilion et al (5) described the literature review of total 101 patients of MCGCT with 69 cases having complete data. MCGCT is reported to occur in younger individuals than solitary GCT. Most commonly they arise in lower extremities especially knee joint followed by proximal humerus, distal radius and more commonly involves metaphyseo-diaphyseal region of bone (5). Generally have 2 or 3 lesions but maximum 12 tumors are reported in single patient[7].

In solitary GCT, benign lung metastasis can occur as early as 3 months to as late as 24 years, with average duration being 3 to 4 years after initial diagnosis of primary bone GCT (1-4). There is six fold high risk of lung metastasis in patients who have local recurrence (3, 8). Benign lung metastasis is also reported in MCGCT but is less common than in solitary GCT (3). In review of MCGCT by Dhilion et al (3), out of 69 cases of MCGCT only 4 patients had lung metastasis. Most common radiological presentation of lung metastasis in solitary GCT is in the form of multiple lung nodules of varying size in both lungs (1,3). Less commonly they present as a huge lung mass with or without nodules or pleural effusion (9-11); and very rarely GCT metastasizes to lung in the form of an endobronchial lesion with or without lung nodules (12,13). In cases of synchronous MCGCT reported by Tandra (14) and Naam et al (15) benign lung metastasis was in the form of bilateral lung irregular opacities and lung nodules respectively. We could not find any case of metachronous MCGCT with benign lung metastasis among accessible case reports in literature.

In our patient, though CT and PET-CT was suggestive of pleural origin of the mass, intra operatively it was found to be covered by visceral pleura and was adherent to underlying left lower lobe and lingula suggesting lung parenchymal origin of the mass. Histopathology of lung metastasis is similar to histopathology of primary benign GCT in both solitary and MCGCT (3, 5).Giant cell tumors show fairly high FDG uptake (16). Metastasis from giant cell tumor also show increased glucose metabolic activity and FDG PET/CT may be used to determine the metastatic burden.

Majority lung metastases are asymptomatic and are detected on routine follow up. Patients become symptomatic only with extensive metastatic nodules or huge lung mass with or without pleural effusion causing breathlessness further enforcing the benign nature of the disease. The benign lung metastasis has been found to have unpredictable course with or without treatment. However appropriate lung resection surgery (lobectomy, wedge resection or metastasectomy) is now the most widely accepted standard treatment of lung metastasis since it prevents progressive pulmonary dysfunction and majority of patients have overall good survival post lung resection surgery (3).Mortality due to progressively increasing benign lung metastasis is 14 to 23%,as per the literature (1,17). However with newer chemotherapeutic options available these mortality rates are set to decrease significantly. In 2013, US FDA approved denosumab [a fully human monoclonal antibody against the receptor activator KB (RANK) ligand (RANKL)] for use in patients with recurrent, unresectable metastatic GCT of bone or for patients in whom surgery would be morbid (18). Akaikeet al (19) reported good response to denosumab in patients with GCT of bone with lung metastasis.

Our patient had GCT of metacarpal bone of left little finger in the year 2001. After 5 years, she developed second lesion at different site (metacarpal bone of left thumb), hence diagnosis of metachronous MCGCT was made. Despite curettage with bone grafting in 2006, patient developed recurrence at second lesion after 1 year, but no further recurrence of bone lesions thereafter. Patient developed benign lung metastasis in the form of a huge mass in left hemi thorax of lung parenchymal origin, 14 years after the first lesion was detected. There is no case reported in literature of metachronous MCGCT metastasizing to lung in the form of huge lung mass. So this is a very rare case of huge benign metastasis to lung in a patient of metachronous MCGCT.

Conclusion

Thus, history of giant cell tumor is important while evaluating a patient with lung nodule or lung mass. Patients with solitary or MCGCT of bone, especially those with local recurrence, should frequently undergo screening for lung metastasis at regular interval of 1 to 2 years so that the early detection and treatment of these notorious slow growing benign lung metastasis, prevents further morbidity and mortality. Patients with benign lung metastasis due to solitary or MCGCT, like in our case, have overall good prognosis with excision surgery. New molecule, denosumab, has opened new horizons for treatment of GCT; especially recurrent, unresectable, inoperable GCT or GCT with lung metastases.

Acknowledgments

None.

Conflict of Interest

The authors declare no conflict of interest.

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