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Case Report

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Giant-Cell Tumor of Bone with Pulmonary Metastases:Treatment by Combination of Chemotherapy and Whole-Lung Radiotherapy. Case Report

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ABSTRACT

Giant cell tumors can exhibit malignant behaviour and metastasize in 1% to 9% of patients. Patients with lung metastases from giant cell tumors are treated by surgical resection with very good survival rates. Chemotherapy and radiotherapy have been reserved primarily for patients with unresectable and symptomatic lung metastases. From the authors' literature search, no patients were treated with whole-lung radiotherapy and combined chemotherapy without surgical resection. In this report, we present 8.5 years follow up of a patient with giant cell tumor of bone with pulmonary metastases treated by combination of chemotherapy with whole-lung radiotherapy without surgical resection for lung metastases. *©2007, Fırat University, Medical Faculty*

Key words: *Giant Cell Tumor, Radiotherapy, Chemotherapy, Neoplasm metastasis*

ÖZET

Akciğer Metastazlı, Kemiğin Dev Hücreli Tümörü: Kemoterapi ve Tüm Akciğer Radyoterapi Tedavi Kombinasyonu. Olgu Sunumu

Dev hücreli tümör %1'den %9'a değişen oranlarda malign davranış ve metastaz sergileyebilir. Dev hücreli tümör akciğer metastazlı hastalar cerrahi reseksiyonla çok yüksek oranda tedavi edilir. Kemoterapi ve ışın tedavisi öncelikle semptomatik akciğer metastazlı ve cerrahi olarak rezeke edilemeyen hastalara saklanmalıdır. Cerrahi rezeksiyon yapılmaksızın tüm akciğer ışın tedavisiyle birlikte kemoterapiyle tedavi edilen hastaya literatürde rastlamadık. Bu olgu sunumunda, akciğer metastazı için cerrahi eksizyon yapılmaksızın kemoterapiyle birlikte tüm akciğere ışın tedavisi uygulanan dev hücreli tümör akciğer metastazlı hastanın 8.5 yıllık takibini sunduk. *©2007, Fırat Üniversitesi, Tıp Fakültesi*

Anahtar kelimeler: *Dev hücreli tümör, Işın tedavisi, Kemoterapi, Tümör metastazı*

Giant cell tumors consist approximately 4% to 5% of all primary bone tumors (1-3). This can exhibit malignant behaviour and metastasize in 1% to 9% of patients (2.6% in the largest series) (2,4-10). Histologically benign giant cell tumor of bone with pulmonary metastasis generally does not have a bad prognosis (4,6,11,12). Primary malignant giant cell tumor is quite rare (about 1% of lesion) (3,12). Primary malignant giant cell tumor exists when a frankly sarcomatous lesion is contiguous with a typical histologically benign tumor (12). Secondary malignant tumor results when a sarcoma develops at the site of a previously treated tumor. Most of these have occurred after irradiation of the primary tumor (12). The majority of metastases are to the lung. Metastasis has occurred mainly within 3 years after primary resection (13).

Currently, patients with lung metastases from giant cell tumors are treated by surgical resection with very good survival rates (80%) (1,8). Chemotherapy and radiotherapy have been reserved primarily for patients with unresectable and symptomatic lung metastases (1,4,5,8,13,14). Feigenberg et al. (1) reported three patients treated with whole-lung radiotherapy, surgical excision and chemotherapy. From the authors' literature search, no patients were treated with whole-lung radiotherapy and combined chemotherapy without surgical resection. In this report, we present 8.5 years follow up of a patient with giant cell tumor of bone with pulmonary metastases treated by combination of chemotherapy with whole-lung radiotherapy without surgical resection for lung metastases.

CASE

A 16-year-old man had undergone curettage and bone grafting for a destructive lesion in the left proximal femur at another centre. Previous plain radiographs and CT scans demonstrated a large lytic lesion of the superior femoral neck (Figure 1). Histopathological examination of the biopsy material revealed giant cell tumor. He did well until December 1995 (6 months after surgery) when he had a local recurrence of giant cell tumor. Angiography of this recurrent tumor revealed extreme hypervascularity. There was no evidence of metastasis on chest x-ray. He had Enneking (15) grade 3 lesion. Enbloc resection of the proximal part of the femur was carried out with reconstruction by total hip arthroplasty (Müller cemented acetabular component, Cramascoli modular femoral stem) (Figure 2).

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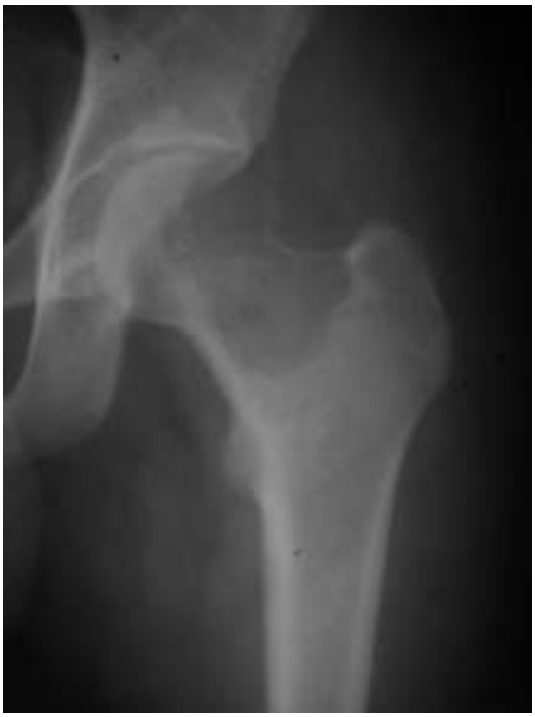

Figure 1. Preoperative antero-posterior radiograph shows severe lytic lesion involving the posterosuperior aspect of the left femur neck.

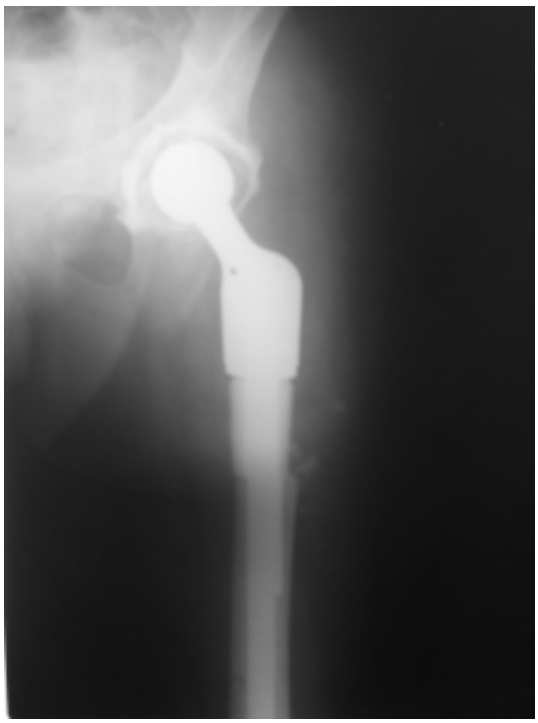

Figure 2. Postoperative antero-posterior radiograph shows of this recurrent tumor after total hip arthroplasty.

One month after the recurrent surgery, metastases were observed in the lung. Pulmonary symptoms, shortness of breath prompted discovery of the pulmonary metastases. Chest X-Rays showed bilateral multiple pulmonary nodules and a mass at the right hilar paracardiac region and some areas of pleural thickening, which was confirmed by computed tomography scans (Figure 3,4).

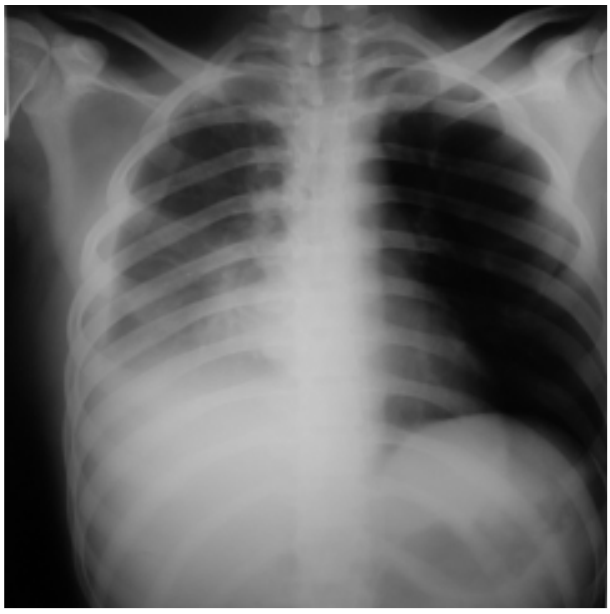

Figure 3. Chest radiograph obtained one month after enbloc resection and total hip arthroplasty. Showing multiple pulmonary nodules and mass at the right hillar paracardiac region.

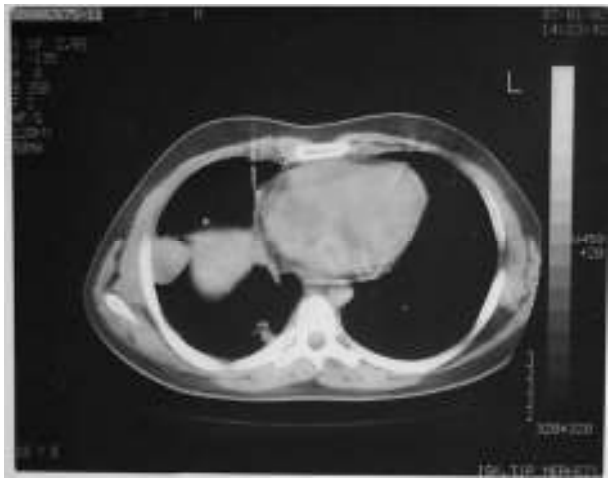

Figure 4. Chest computed tomography shows multiple pulmonary nodules in the right and left lung, mass at the right hillar paracardiac region and some areas pleural thickening.

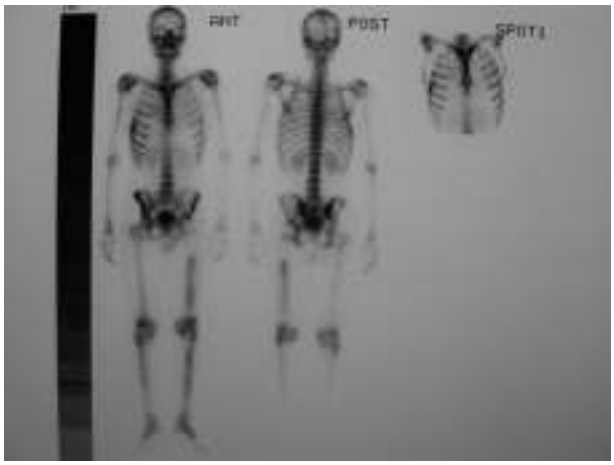

Figure 5. A triple-phase bone scan of the patient's entire body showed the known solitary lesion which revealed focal uptake in the right lung.

A triple-phase bone scan of the entire body showed the known solitary lesion which revealed focal uptake in the right lung (Figure 5). The patient underwent thoracotomy for biopsy with removal of the nodules in possible. Histopathologic examination was consistent with giant cell tumor (Figure 6). He was then treated with whole lung radiotherapy by a total dose of 42 Gy (3 Gy x 14 day). This patient had also a regimen of chemotherapy of Cisplatin (120mg/m^2 x 4) and Adriamycin (65mg/m^2 x 4).

The patient was followed up for 8.5 years from the operation without any recurrence of the primary lesion (Figure 7). The patient was 25 years old at the time of analysis and has remained very active, with no symptoms of pulmonary dysfunction and chest radiographs showed no progression in the metastases compared with the previous films (Figure 8). He remains under observation.

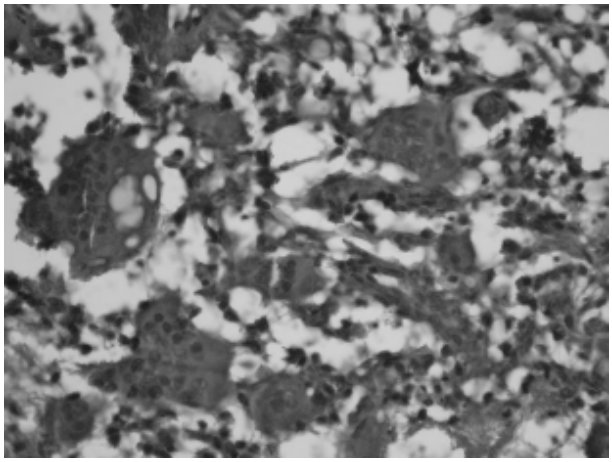

Figure 6. Biopsy of metastatic lung lesion demonstrates a conventional giant cell tumor (Stain, haematoxylin and eosin; original magnification, x250).

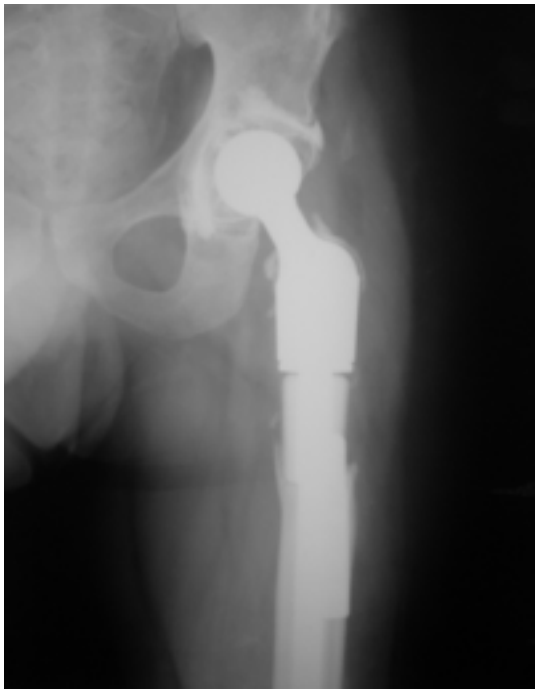

Figure 7. Antero-posterior hip radiograph obtained 8.5 year after enbloc resection and total hip arthroplasty.

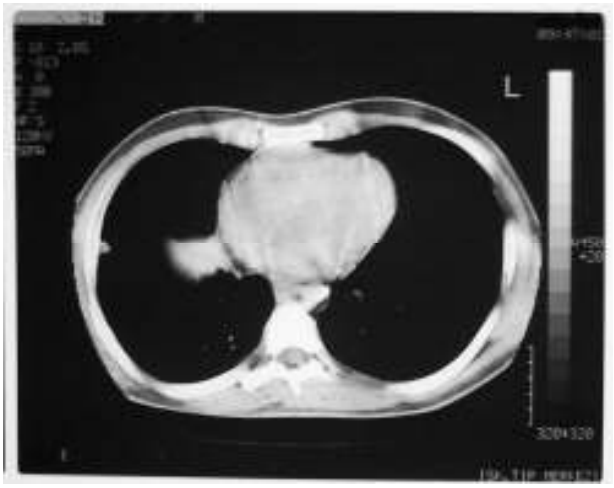

Figure 8. 8.5 year later, chest computed tomography showed no progression in the metastases compared with the previous films.

DISCUSSION

Giant cell tumor of bone is a challenging clinicopathologic entity. Giant cell tumor of bone is a benign but potentially aggressive lesion with local recurrence and metastasis (11,15,16).

Risk factors suggested for the development of lung metastases are local recurrence (4,5,8,11,16), location of the primary giant cell tumors (distal radius, proximal femur and sacrum) (5,8,11,15), Musculoskeletal Tumor Society Stage 2 or 3 lesion (4,6,8,11,12,15,16) and immunocompromised state (11). Aggressive, destructive primary lesions require wide excision, because such tumors tend to metastasize readily.

The cause of the metastasis is unclear. There have been many hypotheses regarding why bening giant cell tumors metastasize. Mechanisms that have been implicated include vascular invasion and iatrogenic seeding at the time of surgery (9,11,13,14). It has been shown that giant cell tumors exhibit thrombi in vascular and lymphatic channels beyond the confines of the original tumor (9,11,14-17). However, vascular invasion does not correlate convincingly with pulmonary metastases (6,9). Vascular metastasis is not the only pathway for giant cell; lymph node metastases have also been reported (4,9). Vascular invasion is a common feature of stage-3 giant-cell lesions (11). Iatrogenic seeding at the time of surgery has been postulated as another mechanism for metastasis, pulmonary lesions often occured before or simultaneously with surgical intervention (11,14). It does not seem likely that operations play a major role in metastasis. Some authors have suggested that metastasis can be predicted by aggressive histologic grades (17) or radiographic appearance (12). Several large series have found histologic grading and radiographic appearance (roentgenographically aggressive, especially those with soft-tissue extension) to be an unreliable predictor for giant cell tumor metastasis (2,9,13-14). Deoxyribonucleic acid flow cytometric analysis has also been found to have limited value in predicting the behaviour of this tumor (14). Almost all cases with lung metastasis studied by DNA flow cytometry have been reported to be diploid1. Chromosomal analysis has shown abnormalities in most giant cell tumors (14). Bertoni et al (11) and Enneking (15) developed a modified staging system for giant cell tumors that is based on a combination of pathologic, radiographic and clinical findings. Aggressive lesions as defined by Enneking's staging and recurrence were

found to be risk factors for pulmonary metastasis (14). Enneking stage III tumors, despite their reported rarity, account for the majority of pulmonary metastasis (4,11,16). For this reason, wide excision is the initial treatment of choice for local control of stage-3 giant cell lesions (11).

Computed tomography scanning is helpful in diagnosing metastases. Plain radiograph and computed tomography of the chest should be obtained in patients with giant cell tumor at follow-up with six months intervals. Computed tomography scans of the chest can help to delineate the number of lesions, mediastinal involvement and are valuable in preoperative planning for surgical removal of the metastases (5). With appropriate window cuts, additional lesions not seen in plain radiographs can often be detected. Serial chest radiographs are recommended in patients with recurrence of giant cell tumors.

The outcome and degree of pulmonary disease progression in patients with metastatic giant cell tumors in the lungs are variable. The pulmonary metastatic lesions were divided into 3 types: [1] spontaneous regression or growing cessation, [2] continuously slow growing and [3] rapid growing (7,16).

The results after surgery, chemotherapy and radiotherapy have varied in different series. Metastases have been asymptomatic for long periods without any treatment (9,17) and in some cases metastases have regressed without treatment (9,10). The authors' findings concur with other case reports that extensive surgical excision of metastases result in excellent long term survival (very good survival rates 80%) (4-6,8,9,12,14,17). If complete resection of all lung metastases can not be done, the survival rates are still high, because the incompletely resected tumors may stabilize and/or regress spontaneously or because the patients receive adjuvant chemotherapy or/and radiotherapy (4,6,8,9,11,16,17). Some literature strongly favours surgical extirpation of all pulmonary nodules (4,13).

There is little information regarding chemotherapy alone for metastatic giant cell tumor of bone (1,5,8). The role for chemotherapy after pulmonary surgery is still unclear (11). Most patients die from the side effects of chemotherapy treatment, rather than the metastases (4,5,8,13,14,16).

Radiotherapy has been used selectively as primary treatment with acceptable control rates for unresectable, recurrent and difficult primary spinal tumors (1,14). The current authors found results of only eleven patients treated with radiotherapy for lung metastasis before current series (1,6,8,10,12,13,14,16). Only three patients were treated with whole-lung radiotherapy (1). Of the eleven patients, two had progressive disease (1,14), one died of chemotherapy-related complications (6), one had radiotherapy-induced malignancy (14), and other seven had a good response to treatment. Radiotherapy has been reported in the literature for treatment of unresectable pulmonary metastases with variable results (1,6,8,10,12,13,14,16). It is recommended that radiation therapy alone should be reserved only for symptomatic, inoperable lesions in the lung (13).

Several patients were treated by chemotherapy and radiotherapy for unresectable giant cell tumor metastases in the literature (6,8,16). Feigenberg et al. (1) reported three patients treated with whole-lung radiotherapy, surgical excision and chemotherapy. From the authors' literature search, no patients were treated with whole-lung radiotherapy and chemotherapy. We used whole-lung radiotherapy and chemotherapy for the inoperable patient.

We recommend whole-lung radiotherapy and chemotherapy for patients who have lung metastasis arising from giant cell tumors of bone in case they refuse surgery or if they are not candidates for surgery with unresectable or progressive pulmonary lesions.

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