



CASE REPORT
OLGU SUNUMU

Pulmonary Metastasis of Benign Giant Cell Tumour of Bone Diagnosed By Fine-Needle Aspiration Cytology

Kemiğin Dev Hücreli Tümörünün Akciğer Metastazı: İnce İğne Aspirasyon Tanısı

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ABSTRACT
ÖZET

Giant cell tumour of the bone is a locally destructive tumour that usually occurs in young adults. It frequently recurs and can produce metastatic lesions, most commonly in the lungs. We report a case of a metastatic pulmonary giant cell tumour, diagnosed by fine-needle aspiration cytology, in a young woman. Diagnosis can be challenging, because of its rarity and differential diagnosis. The correlation of the clinical and radiological findings is essential for the correct diagnosis.

Key words: Lung, giant cell tumour of bone, fine-needle aspiration

Kemiğin dev hücreli tümörü çoğunlukla genç erişkinlerde görülen lokal destrüktif bir tümördür. Sıklıkla tekrarlar ve akciğer başta olmak üzere metastaz yapar. Burada, genç bir kadın hastada akciğer ince iğne aspirasyon sitolojisi ile tanı konan metastatik dev hücreli tümör olgusu sunulmuştur. Nadir görülmesi ve ayırıcı tanısı nedeniyle tanıda zorluklar oluşturabilmektedir. Doğru tanı için klinik ve radyolojik bulguların korelasyonu esastır.

Anahtar kelimeler: Akciğer, kemiğin dev hücreli tümörü, ince iğne aspirasyon

Introduction

Giant cell tumour of the bone (GCTB) is a benign, locally aggressive neoplasm that is composed of sheets of neoplastic ovoid mononuclear cells interspersed with uniformly distributed large, osteoclast-like giant cells (1). Giant cell tumour (GCT) represents around 4-5% of all primary bone tumours. It is most common in the second and third decades of life and the majority of cases occur in females. The epiphyses of long bones are common sites (1, 2). The majority of GCTs are treated by aggressive curettage or resection. However, it frequently recurs, most commonly producing metastatic lesions in the lungs of approximately 2-3% of patients (3-5). Fine-needle aspiration cytology (FNAC) is a reliable, relatively non-invasive and cost-effective diagnostic tool in the diagnosis of visceral metastases in GCTs.

Although the cytologic features of GCTB have been described, very few cases of pulmonary metastases diagnosed by FNAC have been documented in the cytological literature (Table 1) (4-10). Here we report a case of pulmonary metastasis of GCTB diagnosed by FNAC.

Case Report

A 22-year-old woman was diagnosed with a GTC of the right tibia at another institution in September 2008. She underwent extensive surgical resection, followed by radiotherapy. One year later, in December 2009, the patient had a local recurrence of the tumour, which was treated with curettage. Histological sections of the patient's bone curettage specimen showed classical GCTB with multinucleated giant cells admixed with round and spindle mononuclear cells (Figure 1).

The patient was admitted to our institution in December 2011 with back pain. A routine chest X-ray and computerised tomography (CT) scan showed multiple bilateral lung masses; the largest one, which was 12 cm, was situated in the right superior lobe and was compressing the superior vena cava (Figure 2). A CT-guided FNAC of this lesion was performed using a 22-gauge needle. Fine-needle aspiration slides were stained with Giemsa and haematoxylin and eosin stains. A portion of the aspirate was processed for a cell block and stained with haematoxylin and eosin. The smears were cellular, with a dual population of cells, comprising mononuclear round to oval cells and many osteoclastic giant cells (Figure 3A). The mononuclear cells had a moderate amount of well-defined cytoplasm with ovoid or round uniform nuclei and one or two small nucleoli (Figure 3B). The other cell type resembled osteoclasts with abundant cytoplasm and numerous uniform rounded nuclei. The nuclei of both cell populations appeared bland, without cytological evidence of malignancy. There were no inflammatory cells, and no necrosis was seen in the background. The cell block sections showed multinucleated giant cells admixed with round and spindle

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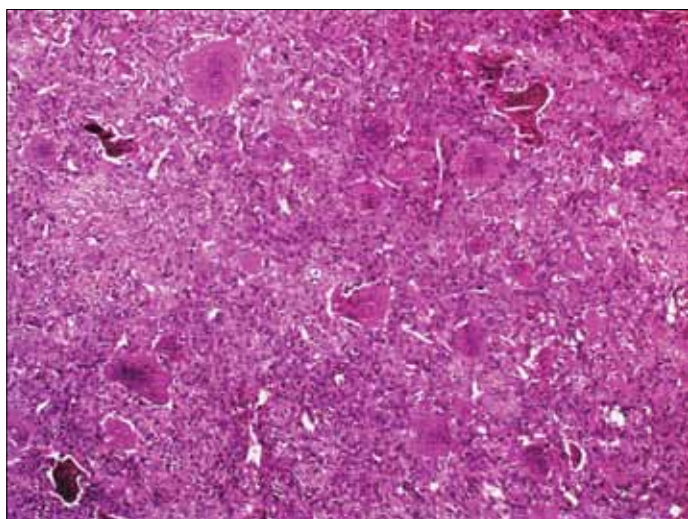
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Table 1. Clinical findings of pulmonary metastasis of GCTB diagnosed by FNAC

Case	Year	Age	Sex	Primary site	Time interval (mo)	Radiography	Treatment
Szyfelbein et al.4	1979	NA	NA	NA	NA	NA	NA
Powers et al.5	1991	NA	NA	Femur	NA	NA	Chemotherapy
Van Hoeven et al.6	1994	36	Female	Left humerus	24	Two left lung nodules	Wedge resection
Lawsan et al.7	1996	27	Male	Right middle finger	24	Multiple bilateral nodules	No treatment
Nagesh et al.8	2002	24	Male	Right fibula	18	Multiple bilateral nodules	Unknown
Çiftçi et al.9	2002	41	Male	Right forearm	36	One right lung nodule	Chemotherapy
Cai et al.10	2007	22	Female	Left femur	18	Multiple bilateral nodules	No treatment
Our case	2012	22	Female	Right tibia	36	Multiple bilateral nodules	Chemotherapy

NA: not available (This was due to the fact that these reports were published quite some time ago and it was not possible for us to access the entire article. We therefore based our analysis on the abstracts that were available to us.)

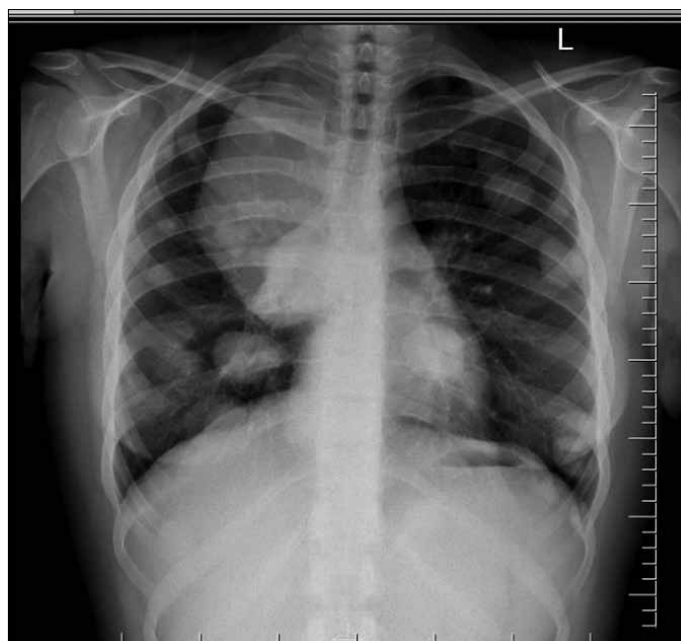
**Figure 1. Histologic section of the GCT showing an intimate admixture of giant and mononuclear cells (H&E, x100)**

mononuclear cells (Figure 4). In the immunohistochemical studies of the cell blocks, all of the multinucleated cells and a subset of the mononuclear cells showed immunoreactivity to CD68, a histiocytic marker (Figure 5).

Discussion

GCTB is an uncommon neoplasm, representing <5% of all primary bone tumours. They usually arise in the epiphysis of long bones (1, 2). When first described by Jaffe et al. in 1940, GCTB was supposed to be a neoplasm of the osteoclast lineage and was called an 'osteoclastoma' (3). The histology of the tumour is characterised by three cell types: mononuclear ovoid, mononuclear spindle-shaped, and osteoclast-like multinucleated giant cells.

It is thought that the mononuclear stromal cells are the neoplastic component of the GCTB and that they produce substances, including osteoprotegerin ligand, that promote multinucleated osteoclast-like cell formation (3, 4). The number of multinucleated giant cells varies between the different cases (3-6).

**Figure 2. Chest radiograph showing multiple bilateral pulmonary parenchymal nodules**

GCTB has a variable and unpredictable course, ranging from indolent, static tumours to locally aggressive lesions associated with significant bone destruction and soft tissue extension. GCTB frequently recurs following curettage and can produce metastatic lesions, most commonly in the lungs, in approximately 2–3% of patients (6-10). In benign metastasising GCTBs, the histology of the nodules found in the lungs is identical to that of the benign tumours of the primary site. Some authors explain this as secondary to the tumour emboli often seen in the peripheral vessels of GCTBs and regard the nodules found in the lungs as implants and not true metastases (8-10).

Cytological diagnosis of GCTB metastasising to the lung has rarely been reported in the literature (Table 1) (4-10). Our findings are similar to the other cases that have been described, in that a dual population of mononuclear round to oval cells in large clusters with adherent giant cells in close approximation was seen in all of the cytologic smears. The nuclei of mononuclear and multi-

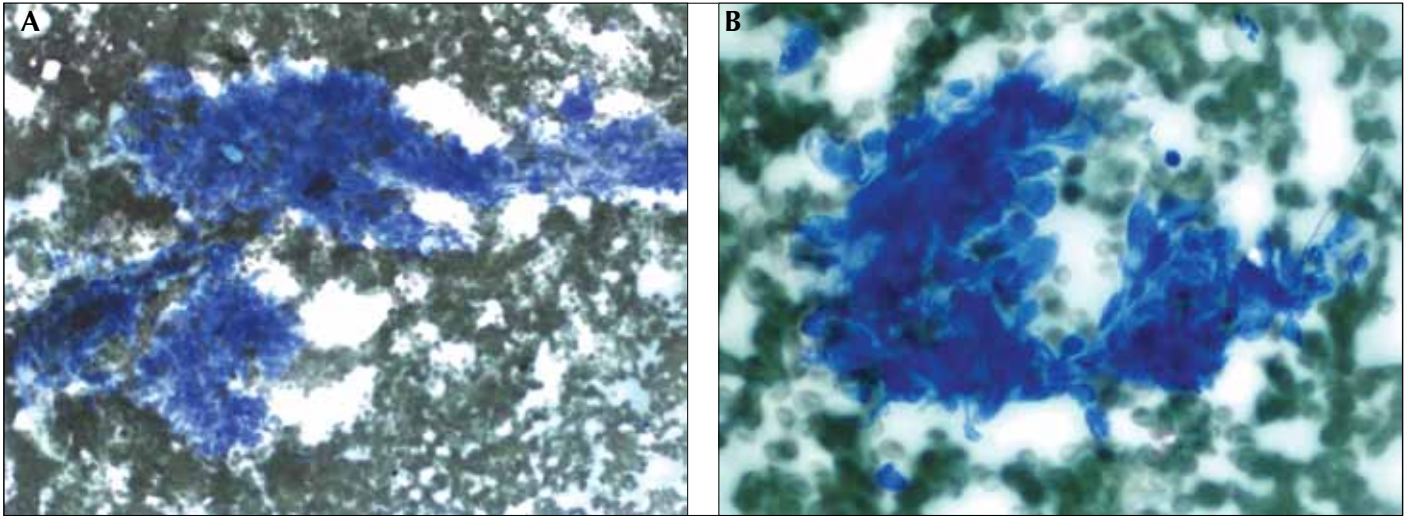


Figure 3. A) FNAC smear of a case of GCT showing a dual population of mononuclear round to oval cells in large clusters with adherent giant cells in close approximation (Giemsa, x100) B) A high-magnification image showing a cluster of round and spindled mononuclear cells (Giemsa, x400)

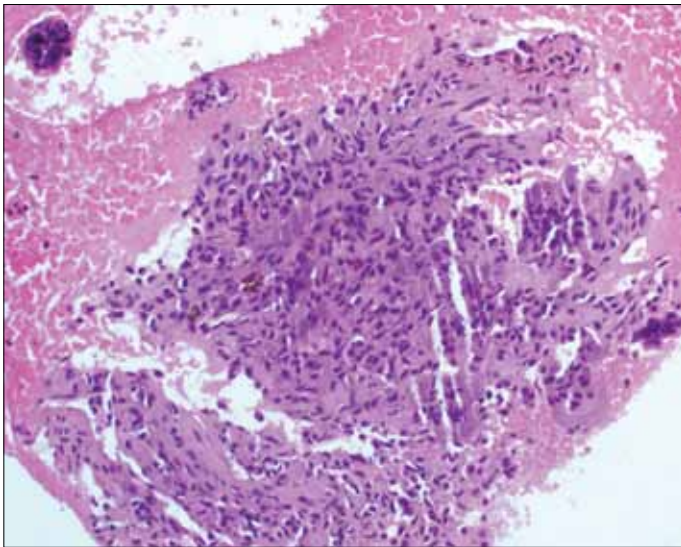


Figure 4. The cell block section of the FNAC sample showing mononuclear cells intermixed with osteoclast-like giant cells (H&E, x200) nuclear giant cells were bland and uniform, without any cytological atypia.

Because many other lung lesions (neoplastic and non-neoplastic) show osteoclast-like giant cells, the diagnosis of GCTB requires a careful clinicoradiological correlation. Non-neoplastic lesions that contain giant cells may be fungal infections, mycobacterial infections, or drug- and ionising radiation-induced lesions (8-10). The giant cells in these conditions have fewer nuclei and are almost always associated with granulomas. Inflammatory background and special histochemical stains are also helpful in the diagnosis of fungal infections.

Although it is usually difficult to see on haematoxylin-eosin stained sections, the detection of the fungal organism is an accurate diagnosis. When clinical and radiographic findings are supported by histologic evidence of epithelioid granulomas with or without necrosis, the diagnosis of mycobacterial infections is easier. However,

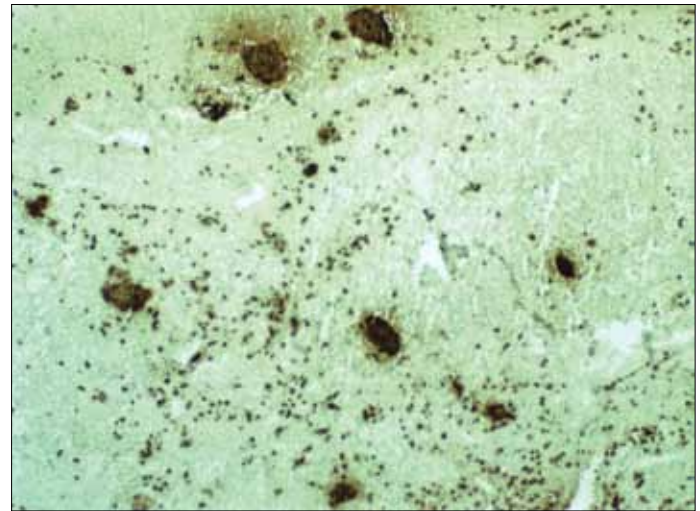


Figure 5. Some mononuclear and all giant cells were immunoreactive for histiocytic marker CD68 (immunoperoxidase, x40)

the detection of acid-fast bacilli by histochemical stains is still necessary for an accurate diagnosis (8-10).

The main concern for pathologists is to rule out neoplastic conditions that contain giant cells, such as giant cell-rich osteosarcoma, giant-cell variant large-cell undifferentiated carcinoma, chondrosarcoma, and malignant fibrous histiocytoma (6-8). The benign appearance of the mononuclear and giant cells, the lack of cellular pleomorphism, atypia, nuclear hyperchromasia, irregularity, or necrosis are helpful in differentiating GCTs from other malign neoplastic conditions. Radiological findings, clinical history of the patient, and immunohistochemistry can also be helpful in the diagnosis.

Segmental resection of the lesions is considered the most effective treatment of lung metastases. In unresectable cases, radiation therapy and/or chemotherapy may be alternative treatments. In our case, because of the localisation of the tumour nodules, a surgical procedure could not be performed and the patient was started on a cisplatin-adriamycin chemotherapy regimen.

Conclusion

In summary, pulmonary metastasis of GCTB is rare. Clinical data, radiological findings, and cytological features are important to reach the correct diagnosis. A radiographically-guided FNAC is the best method for establishing a diagnosis.

Conflict of Interest

No conflict of interest was declared by the authors.

Peer-review: Externally peer-reviewed.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Authors' contributions: Conceived and designed the experiments or case: MT. Performed the experiments or case: MT. Analysed the data: MT and BHO. Wrote the paper: MT and BHO. All authors have read and approved the final manuscript.

Çıkar Çatışması

Yazarlar herhangi bir çıkar çatışması bildirmemişlerdir.

Hakem deęerlendirmesi: Baęımsız hakemlerce deęerlendirilmiştir.

Hasta Onamı: Yazılı hasta onamı bu çalıřmaya katılan hastalardan alınmıştır.

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