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Short communication

An unusual cause of calcified pulmonary opacity: A metastasis of a benign giant cell tumour of bone

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1. Introduction

Calcification of pulmonary nodules or masses is frequent. According to appearance and distribution of the calcifications, clinicians usually discuss calcified infectious granuloma including tuberculosis and histoplasmosis, pneumoconiosis lung fibrosis, amyloidosis, hyperparathyroidism, and primary or secondary lung tumors including hamartoma, osteosarcoma, chondrosarcoma, lung metastasis, and primary bronchogenic carcinoma. We report herein a case of lung metastases of benign giant cell tumour of bone (GCTB), an unusual cause of calcified opacities that might be unrecognised by pulmonologists.

2. Case presentation

A 27-year-old woman was referred to our medical centre on December 2016 with a left lung opacity. She was a law student and had never smoked. She did not report any respiratory or general symptoms. Examination identified reduced breath sounds on the left side, and painless swelling and flexion-extension limitation of the right wrist (Fig. 1A). Chest X-ray performed as part of routine screening showed a well-defined opacity of the left lower lobe (Fig. 1B). Chest CT scan confirmed a large partially calcified mass in the left lower lobe and smaller bilateral opacities with no lymph nodes (Fig. 1C–D). Pulmonary function tests demonstrated a mild restrictive pattern (FEV1 = 69%, FVC = 68%, TLC = 83%, FEV1/FVC = 0.88).

Her medical past history was marked by a right patella surgical curettage in 2003. Histological examination showed a benign GCTB. In 2004, several bone relapses (Fig. 2A) and a pulmonary mass with bone scan activity on both sites were found. Chest CT-scan demonstrated a well-circumscribed 10-cm diameter mass in the left lower lobe with no calcification and a heterogeneous pattern with necrotic area (Fig. 2B). No rib lysis was noted. The patient underwent a pulmonary left surgery without complete resection because of no cleavage plane between the mass and the diaphragm. Macroscopic examination identified a buff yellow appearance with a crumbly texture (data not shown). Histological examination showed a proliferation with numerous multinucleated osteoclasts ("giant cells") characterised by the absence of atypical nuclei and a high mitotic index, within mononuclear stromal cells forming a syncytium (Fig. 2 C). Haemorrhagic and congestive foci were also present. The final histological diagnosis was a lung metastasis of GCTB.

Abbreviations: GCTB, giant cell tumour of bone.

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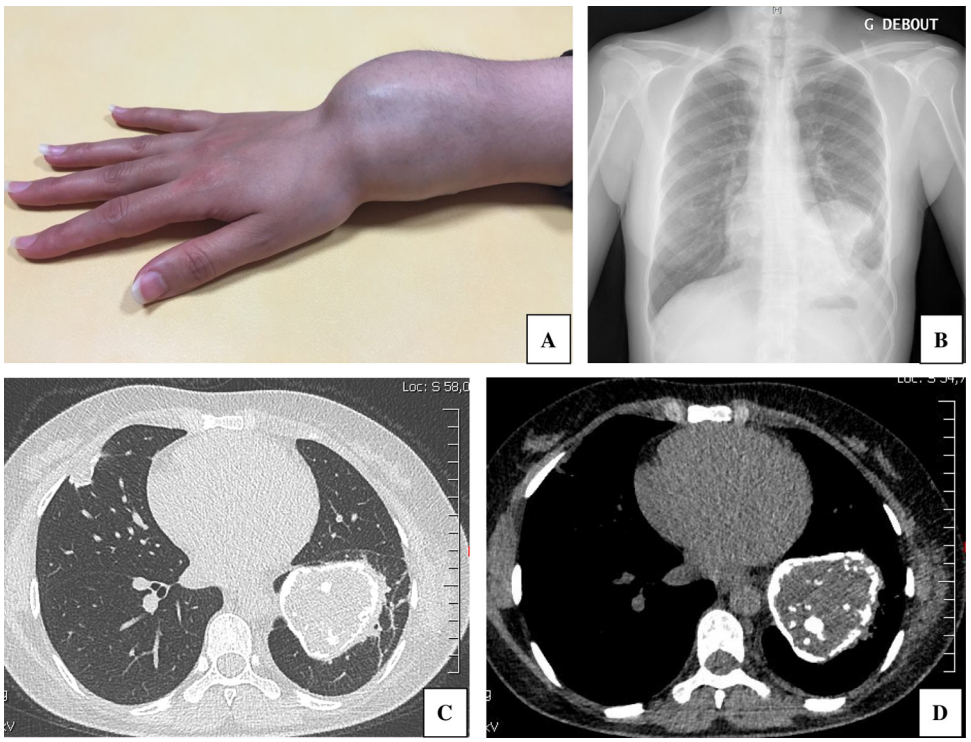

Fig. 1. A. Swelling of the right wrist. B. Chest X-ray showing the opacity of the left lower lobe. C. Chest soft tissue CT scan showing bilateral nodules and mass. D. Chest mediastinal CT scan showing the partially calcified pulmonary mass.

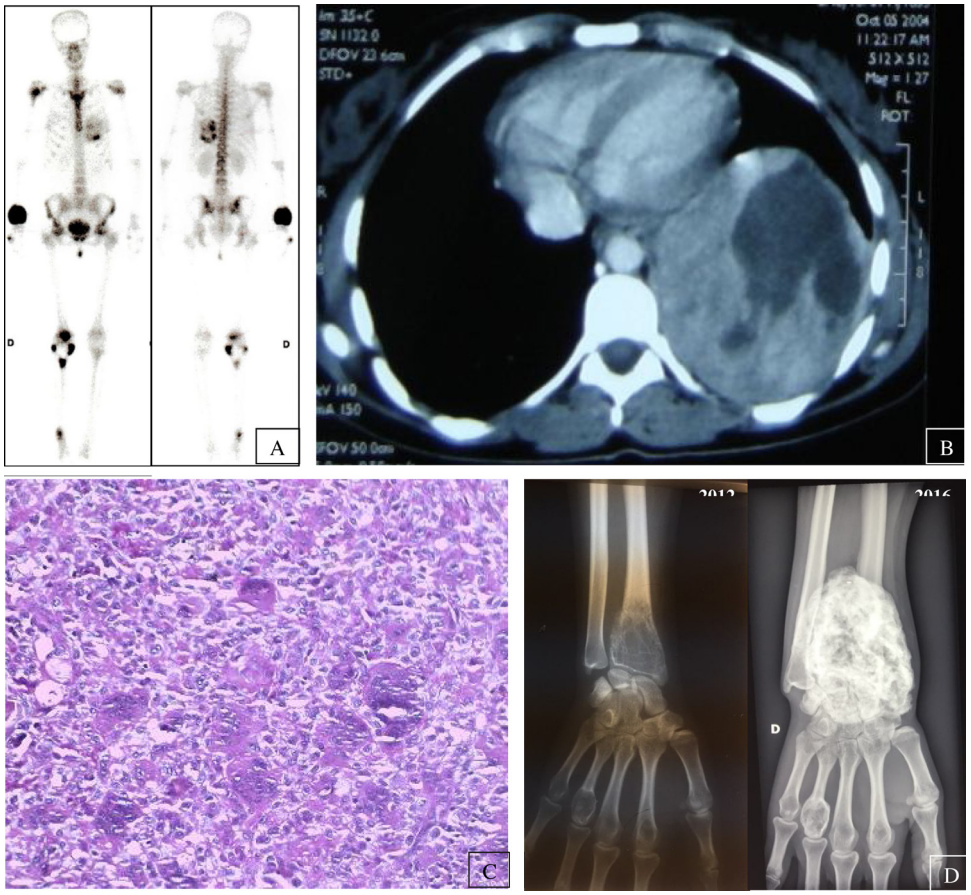

Fig. 2. A. Bone scan in 2013: abnormal uptake in right ankle, tibia, patella and wrist. B. Chest CT scan showing a very large mass in the left lower lung without calcification in 2004. (C) Haematoxylin-eosin staining (× 20) of lung biopsy showing numerous giant multinucleated cells in a stroma of spindle cells without mitotic figures or increased nucleocytoplasmic index. No tumour necrosis was observed. D. X-ray of right wrist showing an eccentric osteolytic lesion with cortical extension of the right distal radius and fourth metacarpal head in 2012 progressing to almost complete destruction and calcifications in 2016.

Bisphosphonates treatment by pamidronate disodium was then started and subsequently switched by zoledronic acid in 2006 due to the absence of response. In 2008, the patient presented bone relapse in particular on the right ankle and progression of the pulmonary left lower metastasis up to 14 cm diameter. Bisphosphonates were then stopped and monthly injection of denosumab–a monoclonal antibody that inhibits RANKL–was started in June 2013. After 3.5 years of denosumab treatment, the size of the lower left pulmonary mass decreased from 14-cm to 8-cm diameter. Because of pain and joint dysfunction, an orthopedic surgery of the right wrist was planned in 2017 (Fig. 2D).

3. Discussion

GCTB is a primary intramedullary tumour accounting for 21% of all benign bone tumours. Its histogenesis remains unclear. GCTB is characterised by a proliferation of three types of cells including mononuclear histiocytic cells, neoplastic stromal cells and many multi-nucleated giant cells mimicking osteoclasts [1,2]. Mononuclear cells express a high level of receptor activator of nuclear factor-kappa ligand (RANKL) that potentiates the osteoclast differentiation leading to bone resorption.

GCTB preferentially occurs between 20 and 40 years with a slight female predominance. The most common sites are the metaepiphyseal region of long bones [3]. Multifocal GCTB are very rare (1%) [1]. Clinical presentation typically includes pain, swelling, and in some cases pathological fracture and/or joint dysfunction. Despite typical imaging features, a bone biopsy is required to confirm the diagnosis [2]. Recommendations for wide resection can be limited by the risk of impairment of adjacent joint function. Because of the risk of recurrence after incomplete resection [3], radiotherapy may be proposed [1]. Alternatively, bisphosphonates through anti-osteoclastic effects, and denosumab, a monoclonal antibody that inhibits RANKL, may be used [3–6]. Malignant transformation to sarcoma is unusual. Spontaneous malignant transformation of GCTB is described and the potential relationships with prior exposure to radiotherapy or denosumab are debated [7].

Metastases to other sites are very rare. Lung is the most common site (3%). The time to lung metastases appearance ranges from a few months to 10 years after GTCB diagnosis. The risk of lung metastases probably depends on tumour grade, site of primary lesion, local recurrence and cytokine expression [3]. On chest CT scan, lung metastases appear as homogeneous, nodular opacities, ranging from 0.5 to 8 cm in diameter predominantly in the peripheral/basal regions. Calcification of metastatic nodules is frequent [8]. Segmental resection of solitary lung metastases is recommended to prevent potential complications associated with local growth [3,9]. Radiotherapy, bisphosphonates and denosumab may be considered in unresectable cases [3]. A case report described a long-term effect of denosumab in reducing pulmonary metastases [10]. Long-term outcome of GCTB lung metastases remains unpredictable [9] ranging from rare spontaneous regression to respiratory failure with progression of lung metastases in up to 25% of patients [8,9].

4. Conclusion

GCTB is a rare benign bone tumour. Some forms may be multifocal with calcified lung metastasis, representing an unusual cause of calcified lung opacities. The course of the disease is variable. Segmental resection of solitary lung metastases is recommended to prevent potential complications. Radiotherapy, bisphosphonates and denosumab should be considered in other cases.

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Patient agreement

The patient has given his agreement for this publication.

Contributors

Established the diagnosis, prepared the manuscript: SD, AM, MM, CL, JP, GD, FL.
Performed the literature review: SD, FL.
Provided histopathology slides and descriptions: AM.
Performed the intervention procedure: MM.
Obtained informed consent: SD.
Critical review of the article: GD, FL, CL, JP, SD.

Disclosure of interest

The authors declare that they have no competing interest.

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