

Case Report

What role for radiobiphosphonates bone scintigraphy in the monitoring of an unusual bone giant cell tumor: a case report and literature review

Salah Nabih Oueriagli, Imad Ghfir, Hassna El Guerrouj, Nouzha Ben Raïs

Department of Nuclear Medicine, IBN-SINA Hospital Center, University Med V-Rabat, Morocco

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Abstract: We report the case of 24 years old female patient, followed since ten years ago for bone giant cell tumor (GCT) of the right knee, which was complicated by pulmonary metastases. Surgical treatment and pulmonary metastasectomies have not allowed definitive cure of this disease with the appearance of metachronous bone lesions after eight years of evolution. The literature review confirms the originality of this observation: the age of the patient, the initial and metastasis locations and the occurrence of lung metastases with unfavorable prognosis. Through this clinical case, the authors highlight the role of radiobiphosphonates bone scintigraphy in detecting synchronous or metachronous bone lesions, and in monitoring of these locations under medical treatment.

Keywords: Bone giant cell tumor (GCT), radiobiphosphonates bone scintigraphy, metachronous bone lesions, lung metastases, denosumab

Introduction

Giant cell tumors (GCT) are typically rare benign tumors, and usually, they appear as an osteolytic epiphyseal long bone tumor. GCT affects primarily young adults [1, 2], have aggressive character and possibility of malignant transformation. They have mostly histological diagnosis and they specially affect epiphyso-metaphyseal regions of long bones of members. The evolution can be marked by the occurrence of unique or multiple benign lung metastases, bilateral in the majority of cases, resectable or not, testifying to initial tumor aggressiveness. We report a case of 24 years old female patient with giant cell tumor, complicated by lung metastases with the appearance of unusual other locations especially in bone tissue. For this purpose, radiobiphosphonates bone scan can be described as an effective nuclear imaging: in detecting synchronous or metachronous bone lesions before medical treatment and for monitoring metachronous bone lesions when the surgical treatment is difficult.

Clinical observation

We report the case of 24 years old girl patient, followed since ten years ago for bone giant cell

tumor of right patellar and the lower end of right femur (**Figure 1A, 1B**). The positive diagnosis was established on standard radiological and computed tomography (CT) aspects of the initial lesion and also on the anatomic-pathological results obtained after biopsy. A surgical curettage of lesions with filling by acrylic cement was achieved without disarticulation.

The outcome was favorable for 2 years before that the patient present dyspnea with pleural effusion syndrome. A chest CT, made in emergency, objectified bilateral nodular parenchyma lesions, and especially a large mass of the left lower lobe with intratumoral necrosis (**Figure 2A, 2B**). The scanno-guided biopsy of the most voluminous nodule showed metastases of bone giant cell tumor and the patient was immediately operated for its pulmonary parenchymal lesions. Two months later, the patient presented intense pain of the right leg whose radiographic exploration showed upper tibial tumor location. The patient was also treated by the same surgical gesture (acrylic cement).

Eight years later, our patient presented bone pains of shoulders, hands and right ankle. Bone scintigraphy with radiobiphosphonates was immediately requested looking for other loca-

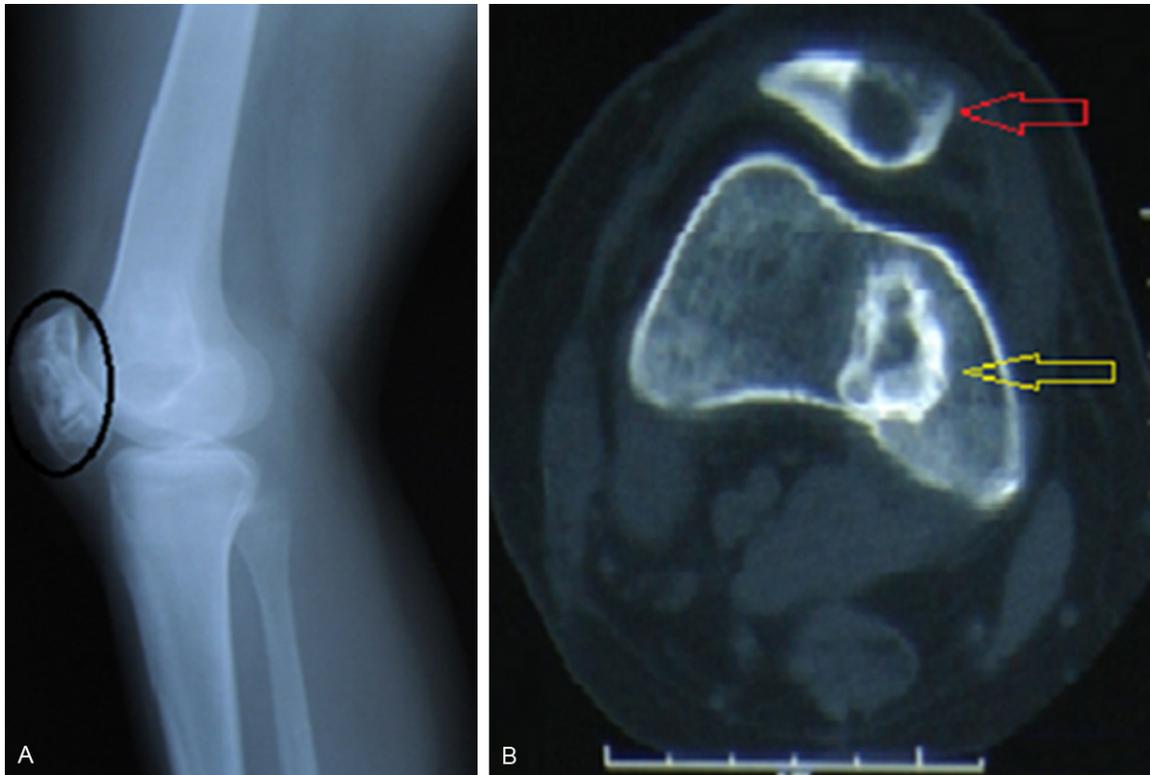


Figure 1. A. Medial radiography of the right knee showing multiple lytic lesions with fuzzy limits on the right patella (black circle). B. CT image in axial section of the right knee showing two lacunar images: of the right knee with cortical break (red arrow) and the lower femoral epiphysis with geographical aspect (yellow arrow).

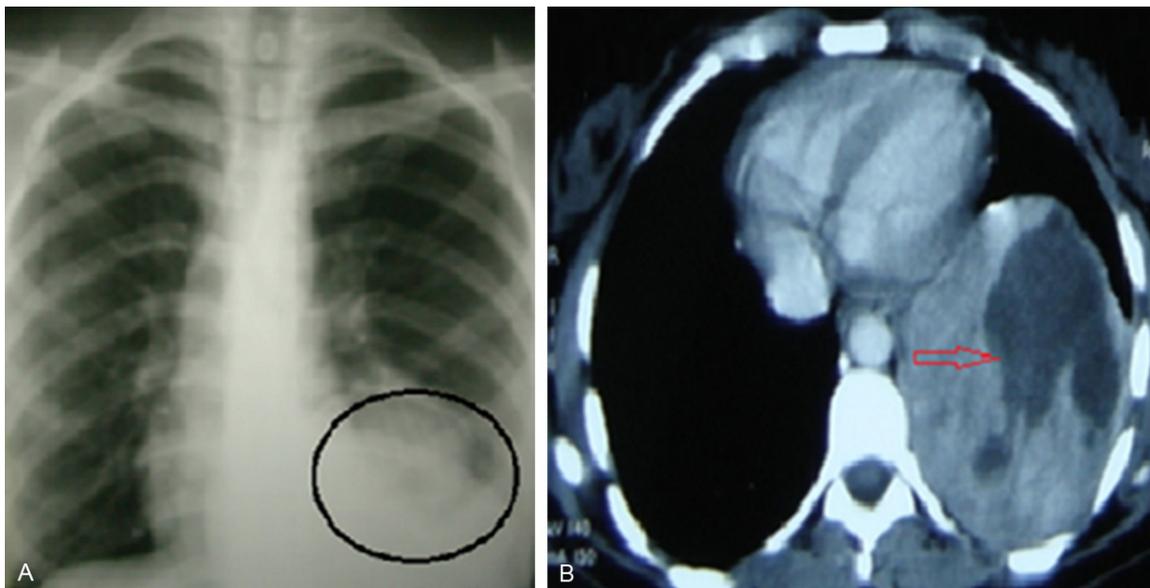


Figure 2. A. Anterior chest radiography showing a huge left inferior pulmonary opacity with ipsilateral pleural effusion (black circle). B. CT image/C + in axial section showing a large lung mass of the left lower lobe with intratumoral necrosis (red arrow).

tions of bone tumor. Our patient has received an intravenous injection of 680 MBq of ^{99m}Tc -

HMDP in the left elbow and whole body scanning was acquired after a delay of 2 h 30 min. It

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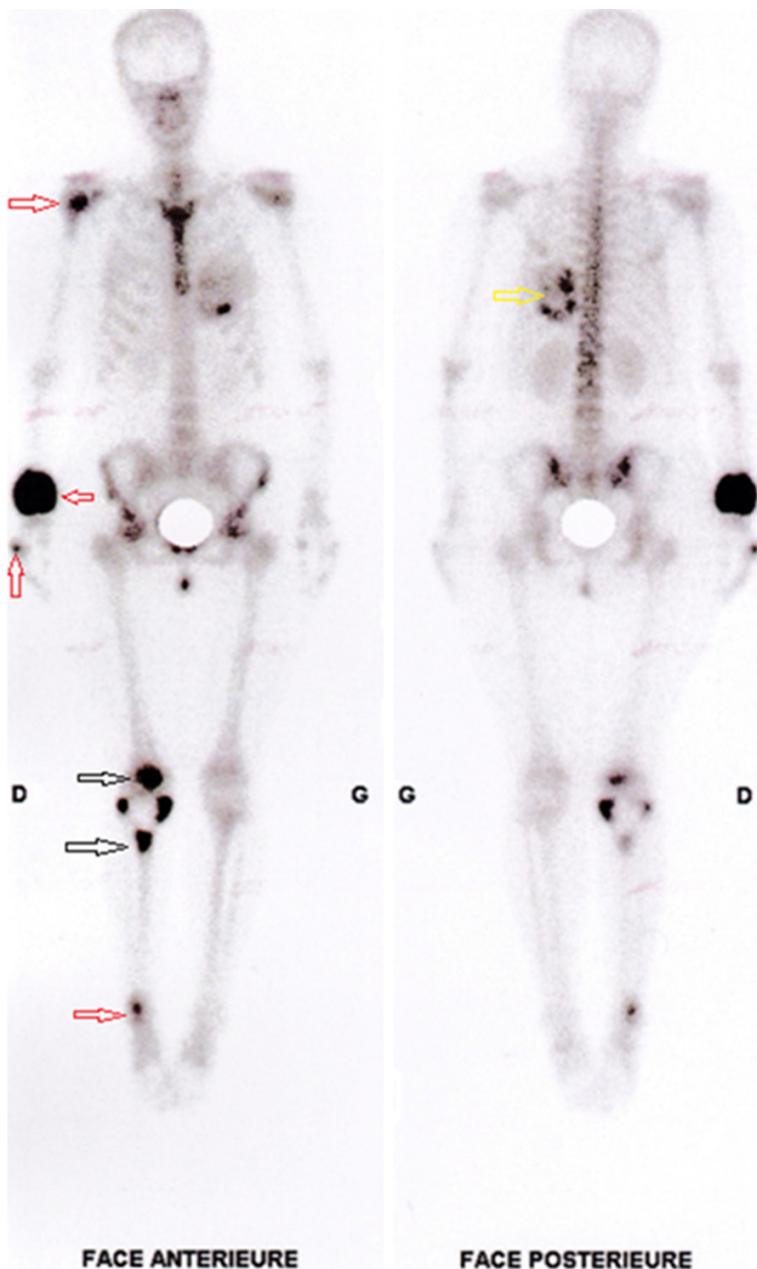


Figure 3. Radiobiphosphonates bone scintigraphy showing multiple uptakes at the right patella and the upper end of the right tibia (recurrent lesions with black arrows), at the lower end of the right tibia, the right hand, the right wrist and right humeral head (metachronous lesions with red arrows). Note intense extra-osseous uptakes next to the left inferior pulmonary area (yellow arrow).

showed intense uptake on the right wrist, the right humeral head, the right hand, the right patella and the upper and the lower end of the right tibia (metastatic recurrences) with extra-bone uptake next to the left pulmonary area (**Figure 3**). (As reference, quantification of uptake in the right wrist was compared with L2;

with respectively: 708.390 cts/sec Vs 5796 cts/sec). A complement SPECT-CT centered on the thorax was carried out, showing a lytic lesion with perilesional condensation fixing radiobiphosphonates at the right humeral, with multiple calcifications in a residual pulmonary cavity (**Figure 4**). A chest CT with contrast injection allowed a better characterization of the residual character of calcifications.

The patient has received medical treatment based on Denosumab as a target therapy. Six months later, bone scintigraphy evaluation for our patient showed a slight decrease of lesions uptake especially in wrist and right shoulder attesting a slight regression of disease (**Figure 5**). Notified that our patient has received for monitoring bone scan the same injection dose (680MBq of ^{99m}Tc -HMDP) in the left elbow and we do respect the same time delay, the same scale bar and quantification in the right wrist was also compared with L2 (504.195 cts/sec Vs 6782 cts/sec).

Discussion

Bone giant cell tumors are typically rare benign tumors that represent about 5 to 10% of bone primary tumors [1]. They have aggressive character and possibility of malignant transformation.

These tumors affect especially young adults between 20 and 40 years old, with a slight female predominance [2, 3]. Bone giant cell tumors have mostly histological diagnosis and they specially affect epiphyseometaphyseal regions of long bones of members, meadows the knee (50% of cases) away of the elbow (9% of cases) bringing in some

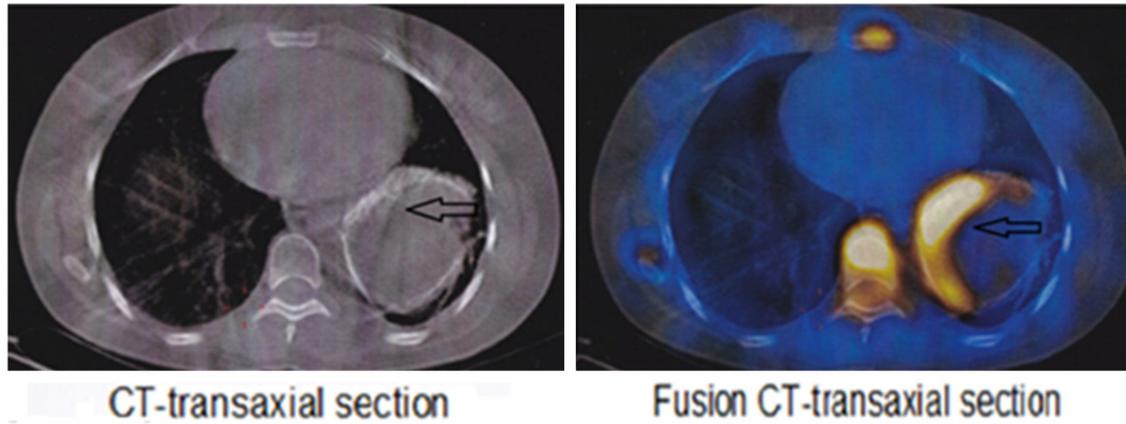


Figure 4. SPECT/CT centered on the chest in transaxial sections showing intense uptakes in a residual cavity of the left inferior pulmonary area: dystrophic calcifications (arrows).

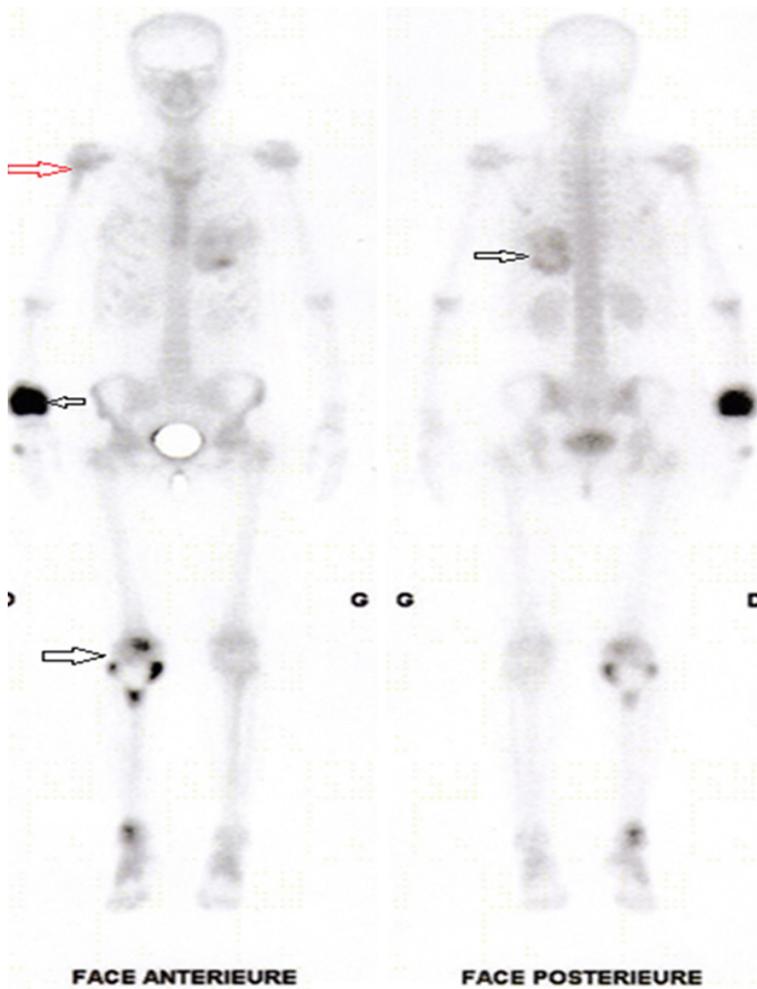


Figure 5. Radiobiphosphonates bone scan control showing in addition of the extinction of uptake in the right shoulder (red arrow) with a slight decrease of uptake previously described in the left lung cavity, the right wrist and knee (black arrows) attesting a slight scintigraphic improvement.

cases to articular sacrifice [1, 4, 5]. Other rare localizations of lumbar spine and pelvis (sacroiliac and coxo-femoral joints) can be seen and pose a problem of differential diagnosis [4-6]. Noted that the evolution can be marked by the occurrence of unique or multiple benign lung metastases, bilateral in the majority of cases, resectable or not, testifying to initial tumor aggressiveness. However, cases revealing lung metastases were procedures in 1 to 2 % of cases [7].

Clinically, the localized pain and periarticular tumefaction are the master symptoms, but the pathological fractures can be revealing in 5 to 10% of cases [5-8] bringing initially to realize a standard radiography centered on the painful or fracture website. Typically, it is oval or rounded epiphyse-metaphyseal pure lytic lesion, standard geographical lacuna with discret soufflure of the bone, sometimes limited by condensed edging [9, 10]. Enneking and Campanacci [11, 12] distinguish three clin-

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ical radio-stages independently of any histological and evolutionary aspect. They describe a quiet form (net limits, underlined by condensation with trabeculations: honeycomb aspect), an active form (imprecise limits and blown cortical, by far the most frequent form) and an aggressive form (fuzzy boundaries, broken cortical, soft tissue invasion with or without fracture).

For active or aggressive form, CT shows better the cortical rupture as well as the extension in sub-chondral area or the extension in the soft neighborhood parts. Computed tomography is also recommended in case of recurrently tumors [10, 13, 14]. MRI is more performing when extension of the tumor in soft parts and neighborhood structures is suspected. It guides better surgical acting in most cases [15-18].

The solitary form is most frequent, but the multiple bone localizations can be seen. Remains forms are very rare (less than 1%) and they translate most often aggressiveness from of the initial tumor [19, 20]: case of our patient. These multiple localizations occur in the majority of cases without owner pathologies but some cases associated with Paget disease and aneurismal cyst were described in the literature [5, 17, 21, 22]. They qualified those benign localizations by synchronous or metachronous lesions. Our patient saw appear of metachronous secondary lesions during a period of 10 years.

Bone scintigraphy with radiobiphosphonates has plays a major role in detecting synchronous or metachronous localizations. Typically, Bone scan showed increased uptake in the most vast majority of GCT [23-26]. Increased uptake peripherally with central photopenia (doughnut sign) was seen in 57% of cases reported by Levine and al [24]. Blood pool imaging, dynamic bone scintigraphy, and imaging with gallium-67 also reveal a typical increased radionuclide uptake, compared usually to a lesser degree than delayed (static) bone scintigraphy [23, 24]. Increased uptake of the radiotracer in bone across an articulation and in adjacent joints is common (62% of cases) and should not be mistaken with tumor extension [23, 24]. This phenomenon, referred to as "contiguous bone activity" or "extended pattern of uptake", is related to increased blood flow and disuse osteoporosis [24, 27]. Numerous data have

already been published showing the impact of hybrid imaging in the oncology indications (positron emission tomography (PET) and single-photon emission computed tomography (SPECT)/CT): SPECT-CT demonstrates always a gain in sensitivity and specificity comparing with planer bone scintigraphy detection and allows an accurate anatomical identification for these uptakes [28]. For our patient, bone scan with radiobiphosphonates showed extra-osseous uptakes next to the left pulmonary area. SPECT-CT centered on the thorax highlighted calcifications uptakes in a residual cavity. We qualified these hot spots by dystrophic calcifications. They are mostly occur within damaged tissues outside any hypercalcemia associated and they are also attached to a direct infringement of the cell membrane with large influx of ionized calcium realizing crystals of hydroxapatite [29]. CT with contrast injection showed no pathological enhancement in favor of residual calcifications.

The treatment of bone giant cell tumors is mostly surgical, ranging from a simple resection to curettage with filling by the surgical cement. Amputation or disarticulation still quite rare for very aggressive articular forms invading the soft parts [30]. Recidivism, even after radical treatment, is frequent and occurs in 30% of cases [31]. Radiotherapy which can induce a malignant transformation still not indicated for the majority of teams.

When the surgical treatment could be difficult especially in front of multiple bone and lung metastases, medical treatment is conceivable. Chemotherapy based on adriamycin, dacarbazine, vincristine, cytoxan, actinomycin, bleomycin can be administrated [7, 32, 33]. Recently an additive targeted therapy, based on Denosumab, with intense anti osteoclastic activity, can reduce the frequency and the aggressiveness of distant metastases [34]. For our young patient the result for such medical treatment was partially favorable by showing a slight decrease uptake in metastatic lesions previously described. This shows the interest of bone scintigraphy with radiobiphosphonates in monitoring of such pathology under an uncoded therapy.

Disclosure of conflict of interest

None.

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Address correspondence to: Salah Nabih Oueriagli, Department of Nuclear Medicine, IBN-SINA Hospital Center, University Med V-Rabat, Morocco. E-mail: salah.nabihoueriagli@gmail.com

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