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Original Article

Fibrous dysplasia mimicking bone metastasis in nasopharyngeal carcinoma: a case report and literature review

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Abstract: Fibrous dysplasia of bone (FDB) is a rare bone disease that may be misdiagnosed as bone metastasis in terms of some symptoms and imaging features. Therefore, the differential diagnosis between FDB and bone metastasis may be a challenge. To our knowledge, there are no reports in the literature to date regarding concomitant nasopharyngeal carcinoma (NPC) with FDB. The aim of this study was to report the case of a NPC patient with FDB, to highlight correct diagnosis and treatment. A 28-year-old young woman was investigated for accidental nasal bleeding. A mass on the right neck and local pain on right femur, and she was submitted to a standard imaging examination suggesting the presence of a solitary right femur metastasis from NPC. Then the patient was submitted to four cycles of chemotherapy, with a partial response (PR) for the mass in neck but no change in the bone metastasis. Because the bone lesion was single, pathologic biopsy was taken to confirm diagnosis. Surprisingly, it was a FDB instead of tumor. At five-year follow-up, she is free of recurrent disease. In this case, we believe that although NPC with FDB is rare, it should not be omitted when bone metastasis is suspected, especially when the metastasis is solitary, because it is crucial for diagnostic staging and treatment choice.

Keywords: Nasopharyngeal carcinoma, bone metastasis, fibrous dysplasia, diagnosis, pathology

Introduction

Nasopharyngeal carcinoma (NPC) is one of the most common tumors in Southeast Asia, and bone is most common distant metastatic lesion [1]. Although multiple metastases to the bone are clearly established, it is quite rare to see a solitary distant bone metastasis in NPC. MRI, whole-body bone scan, and FDG PET/CT scan are sensitive for detecting bone metastasis [2]. Fibrous dysplasia of bone (FDB) is a disorder in which parts of bone are replaced by fibrous connective tissue and trabecular bone of poor quality. Its incidence is difficult to estimate and may involve a single bone (60%) or polyosteosis (40%), often in ribs, pelvis, and long bones [3]. Furthermore, several studies have shown that FDB is associated with false-positive bone scan and FDG PET/CT [4], which can be interpreted as metastatic lesions. Therefore, distinguishing FDB and distant bone metastasis is very important considering that it may mimic radiologic examinations of bone metastasis [5]. As far as we know, there has been no literature report on NPC associated with FDB so far. In this paper, we report a case of NPC with an oligo right femur metastasis confirmed by whole-body bone scan and MRI scan, but the final pathologic biopsy of the bone lesion was fibrous dysplasia (FD).

Case presentation

A 28-year-old woman presented with a sudden onset of nasal bleeding in June 2014, without fever, nasal congestion, dizziness, headache, cough, or other symptoms. Since the nosebleed relieved itself, she did not pay much attention to it. Then she presented with a 2.0 cm×3.0 cm mass on the right neck in January 2015. When physical examination was performed, the right neck mass was 2.0 cm×3.0 cm, with a normal temperature in skin and a tenderness in the mass. The laboratory results showed no abnormalities.

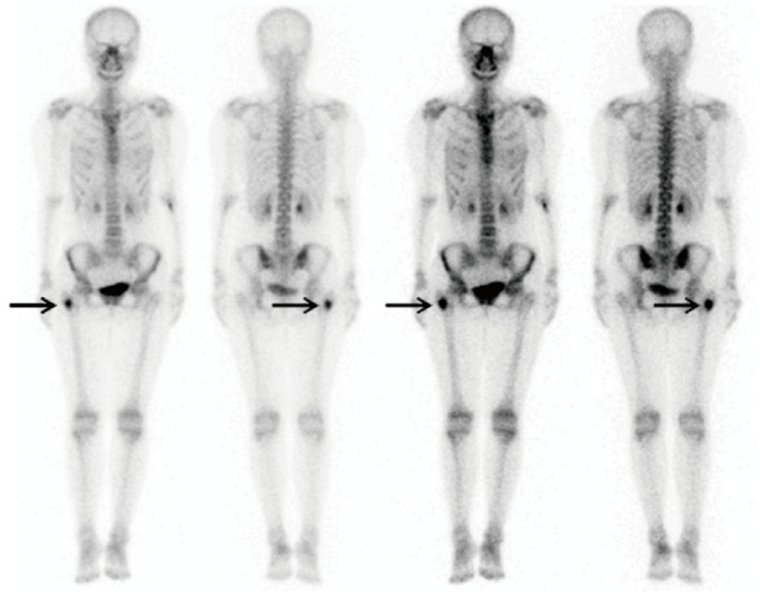

Figure 1. Whole-body bone scan showed an active focus of abnormal bone metabolism in the upper right side of the femoral bone.

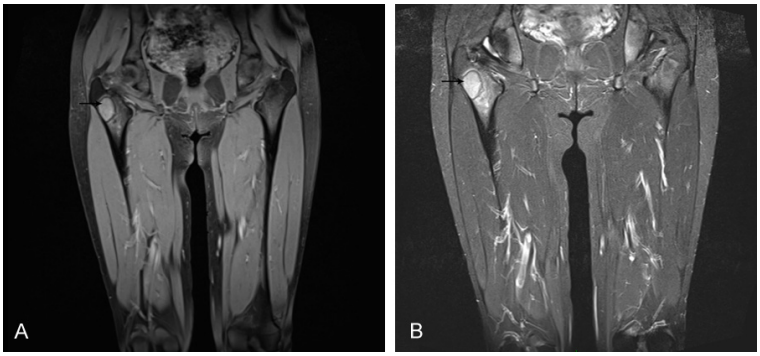

Figure 2. Thigh MRI scan revealed a low intensity in the T1 sequences (A) and at high intensity in the T2 sequences (B) with a size of about 2.2×2.2×3.2 cm (the superior and inferior diameter of left and right X) and irregular flakes around the focus. Contrast-enhanced scan showed that the above lesions had no obvious enhancement.

The nasopharyngoscopy examination and biopsy established a diagnosis of undifferentiated squamous cell carcinoma of nasopharynx. MRI scan of nasopharynx and neck showed NPC with lymph node metastasis. No tumor lesions were found on chest CT or abdominal B-ultrasound. Whole-body bone scan (**Figure 1**) showed an increased isotope uptake in the upper right side of the femoral bone, which was considered bone metastasis. Thigh MRI scan (**Figure 2**) revealed an abnormal signal of the right side of the proximal femur, a metastatic tumor to be diagnosed. This patient's initial TNM stage was cT2N1M1 (AJCC, 7th edition). Then she was treated with chemotherapy consisting of paclitaxel (135 mg/m^2, day 1), cisplatin (75 mg/m^2, day 1), and 5-Fu (750 mg/m^2, CIV 22 h, day 1 to day 5) delivered every 3 weeks for 4 cycles.

After that, the MRI scan of nasopharyngeal cavity and neck suggested that the lymph nodes significantly shrank. However, MRI scan of the right femur revealed no changes. Radiotherapy was the final chance for the young lady to survive from cancer. If there was no bone lesion, this possibility could be as high as 90%. Selection of the dose delivered to head and neck is critical. Then on April 10, 2015, we performed a puncture biopsy of right upper femur tumor, and the final pathologic finding was fibrous dysplasia of bone (FDB) (**Figure 3**). The patient was treated by radical intensity-modulated radiation therapy (IMRT) (total dose of 70 Gy, 2.12 Gy/F). After radiotherapy, MRI indicated that the nasopharyngeal lesions and the right neck lymph node had disappeared consistent with complete remission (CR) after concurrent chemoradiotherapy (CCRT). Then she was followed-up every 3 months for the first 2 years, every 6 months between the third to fifth year, and annually thereafter. A complete physical examination was performed every time. Currently the patient is healthy with no tumor recurrence or distant metastasis for more than 5 years.

Discussion

FDB is a slowly progressive bone disorder of unknown origin, characterized by excessive proliferation of cellular fibrous tissue and irregular trabeculae instead of normal bone and bone marrow. It is estimated that FDB accounts for 5-7% of benign bone tumors, and it is a

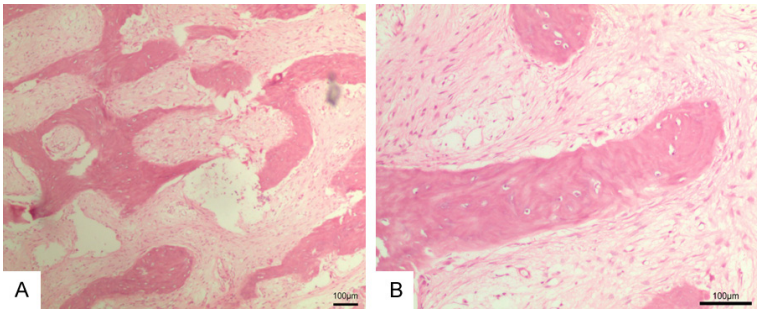

Figure 3. A puncture biopsy of right upper femur tumor shows a bundle of tissue between small trabecular structures, fibroblasts; and no osteoblasts were arranged around the trabecular bone (A. H&E magnification ×100; B. H&E magnification ×200), Bar = 100 μm, which indicated a fibrous dysplasia of bone (FDB).

diagnosis frequently discussed in differentiating tumor lesions [6]. The disease is caused by a mutation in the GNAS1, leading to excess cell lineage resulting in increased proliferation and differentiation of osteoblasts [7]. When FDB occurs, it may be a single bone (monostotic FDB) or multiple bones (polyostotic FDB), with a slow and relatively subtle progression. The majority of the monostotic patients are asymptomatic, but when the bone damage expands and deforms, it may cause pain, swelling, bone deformities, or pathologic fractures, which are similar to bone metastasis [8].

In this case, we reported a patient who had a space-occupying lesion on her right femur by imaging examination, diagnosed with NPC at stage cT2N1M1 (bone metastasis). Distant metastasis is prone to appear among NPC cases, of which bone metastasis is the most common type. To our knowledge, few case reports about concomitant cancer and FDB, or other rare primitive bone diseases, have been reported, especially in NPC. Due to similar symptoms, non-specific imaging features and lack of professional knowledge of FDB, the difficulty for physicians to diagnose accurately is greatly increased. Therefore, a correct understanding and differential diagnosis between FDB and bone metastasis is particularly important, for accurate staging and an appropriate treatment plan.

Currently, the diagnosis of FDB is mainly based on imaging studies, such as CT, MRI, whole-body bone, and FDG PET/CT scan. Reviewing this case and previous literatures, we assessed the main points of differential diagnosis of FDB and bone metastases in imaging (**Table 1**). As far as we know, MRI characteristics in patients with proven FDB are not consistent in the current literature. Kinnunen et al. [9] summarized data of all published studies describing MRI characteristics in patients with histopathologically confirmed FDB and found that the signal is usually at low intensity in the T1 sequences and at high intensity in the T2 sequences, which is consistent with Kushchayeva et al. [10] and the results in our case. However, Cho et al. concluded that signal intensity on T1 and T2 weighted images and the degree of contrast enhancement on T1 weighted images may help to differentiate fibrous dysplasia from metastasis [11]. For bone metastasis, MRI is also connected with low T1 sequences and contour or mixed high T2 signal [12], which is similar to FDB and our result. Therefore, the differential diagnosis of FDB with MRI only is still challenging. Furthermore, FDB was reported to be false-positive in a bone scan and FDG PET/CT scan, so the radiologic features of FD in cancer patients could lead to a misperception in the assessment of tumor staging, and there have been several reports of FD mimicking malignancy radiologically. Kao et al. [13] reported a colon cancer patient whose FDG activity increased in temporal bone by bone scan and FDG PET/CT scan but biopsy proved FDB finally. Lapietra et al. [14] report a case of FD radiographically mimicking a metastatic process. On the other hand, Shigesawa et al. [15] showed that FDG PET/CT is useful for differentiating bone metastasis from FDB in patients with a malignancy. Therefore, benign bone lesions such as FDB are associated with false positive imaging and need to be considered in a differential diagnosis of bone metastasis.

It is worth pointing out that CT scan is the best technique for demonstrating the radiographic characteristics of FDB. Kimitsuki et al. [16] demonstrated the most common pattern, which is characterized by a ground-glass appearance on CT imaging. Strobel et al. [17] reported that dedicated CT interpretation led to the correct diagnosis of a benign lesion. However, bone destruction and sclerotic deposits on CT

Table 1. Review of relevant literature regarding the differential diagnosis of FDB and bone metastases

Demographics	Symptom	Location	Diagnosis	Therapy	Prognosis	Ref.
20 man	Headache	Head	FDB (operation)	No	Not mentioned	[5]
43 man	Pain	Right 8th-rib bone	FDB (biopsy)	Not known	Remission	[8]
46 woman	Pain	Limb	FDB (operation)	Radiotherapy	Progress	[11]
57 woman	Asymptomatic	pelvis, trochanters, and scapula	FDB (biopsy)	No	Remission	[13]
58 man	Pain	Bilateral ribs and iliac bones	FDB (biopsy)	Chemotherapy	Remission	[14]
53 woman	Asymptomatic	Left fourth rib	Bone metastasis (imaging scans)	Radiotherapy	Remission	[16]
62 man	Syncope and headache	Head	FDB (imaging scans)	Not known	Remission	[17]

Abbreviation: FDB: fibrous dysplasia of bone.

imaging are usually clearly shown in bone metastases with a sensitivity that ranges from 71-100% [18]. Unfortunately, this patient did not get a CT scan, which might be a significant point of identification in this case. Also, radionuclide-guided bone biopsy is a reliable, well-tolerated technique to determine the diagnosis of these lesions with a sensitivity of 97% and specificity of 100% [19]. The histopathologic hallmark of FD is fibrous tissue and spindle-shaped, fibroblast-like cells within the bone marrow [20], which fortunately is consistent with our findings in this case. Especially when diagnosing the isolated and suspicious asymptomatic bone metastasis, a CT scan may be appropriate but biopsy diagnosis is the gold standard.

Conclusions

How to formulate an accurate diagnosis between FDB and bone metastasis is critical for clinical treatment. This case is instructive for a careful analysis of all the clinical data before changing the cancer treatment plan from curative intent to palliative. If misdiagnosis happens, it may lead to overtreatment, and cause psychological stress to patients, or even contributes to an irreparable loss to the family or the patient. Therefore, in some suspected bone metastases, for NPC patients, a characteristic ground-glass appearance on CT could be an auxiliary diagnosis. A core needle biopsy is necessary for a definitive diagnosis, so as to make the most accurate TNM staging and appropriate treatment.

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Written consent was obtained from the enrolled patient.

Disclosure of conflict of interest

None.

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