Human Pathology (2013) 44, 2614–2618

ELSEVIER

Human PATHOLOGY

www.elsevier.com/locate/humpath

Case study

Phosphaturic mesenchymal tumor, nonphosphaturic variant, causing fatal pulmonary metastasis

Kazuyoshi Uchihashi MD, PhD[a,*], Aki Nishijima-Matsunobu MD, PhD[a], Atsuji Matsuyama MD, PhD[b], Fumio Yamasaki MD, PhD[c], Tsuyoshi Tanabe MD[d], Tetsuji Uemura MD, PhD[d], Naoko Aragane MD, PhD[e], Mai Yakushiji MD[a], Mihoko Yamamoto MD[a], Shigehisa Aoki MD, PhD[a], Shuji Toda MD, PhD[a]

[a]*Department of Pathology & Microbiology, Faculty of Medicine, Saga University, Saga 849-8501, Japan*
[b]*Department of Pathology & Oncology, School of Medicine, University of Occupational and Environmental Health, Kitakyushu, 807-8555, Japan*
[c]*Department of Pathology, Saga Social Insurance Hospital, Saga 849-8522, Japan*
[d]*Division of Plastic & Reconstructive Surgery, Department of Surgery, Faculty of Medicine, Saga University, Saga 849-8501, Japan*
[e]*Division of Pulmonary Diseases, Department of Internal Medicine, Faculty of Medicine, Saga University, Saga 849-8501, Japan*

Received 1 February 2013; revised 8 April 2013; accepted 11 April 2013

Keywords:
FGF23;
Giant cells;
Phosphaturic mesenchymal tumors of the mixed connective tissue type;
Pulmonary metastasis

Summary Phosphaturic mesenchymal tumors of the mixed connective tissue type (PMT-MCTs) are rare neoplasms, most of which are benign and cause tumor-induced osteomalacia because of overproduction of a phosphaturic hormone, fibroblast growth factor 23 (FGF23). This entity may have been unrecognized or misdiagnosed as other mesenchymal tumors, such as giant cell tumor, hemangiopericytoma, and osteosarcoma. Ten percent of these tumors, without phosphaturia, were diagnosed only by their histologic features. We report here the first case of malignant PMT-MCT, nonphosphaturic variant, resulting in fatal multiple lung metastases. Chondromyxoid matrix with "grungy" calcification, multinucleated giant cell proliferation, and expression of FGF23 mRNA (reverse transcription–polymerase chain reaction) and fibroblast growth factor 23 protein (immunohistochemistry) were seen in the primary and recurrent tumors of the right foot. The lung metastases showed flocculent calcification and FGF23 protein expression as well as giant cell proliferation. This unique case highlights the need for careful histologic assessment of PMT-MCTs, especially the nonphosphaturic variant, and the need for recognition of its rare malignant behavior.

1. Introduction

Phosphaturic mesenchymal tumors of the mixed connective tissue type (PMT-MCTs) are rare and histologically distinctive neoplasms, most of which cause tumor-induced osteomalacia (TIO) through the elaboration of a phosphaturic hormone, fibroblast growth factor 23 (FGF23). The tumor typically follows a benign clinical course, and the symptoms of osteomalacia regress after its removal. Histologically, PMT-MCTs are composed of proliferated spindle cells with low nuclear grade and low mitotic activity embedded in a distinctive myxoid to chondromyxoid matrix with "grungy" or flocculent calcification. Other

* Corresponding author. Nabeshima 5-1-1, Saga 849-8501, Japan.
E-mail address: uchihash@cc.saga-u.ac.jp (K. Uchihashi).

0046-8177/$ – see front matter
http://dx.doi.org/10.1016/j.humpath.2013.04.027

features of PMT-MCT may include osteoclast-like giant cells, mature fat cells, osteoid-like matrix, and woven bone. This entity was suggested in the early 1970s by Evans and Azzopardi [1] and Olefsky et al [2]. The concept was further codified by Weidner and Santa Cruz [3], who coined the term *PMT-MCT* to describe the morphologic features of 17 TIO-associated mesenchymal tumors. More recently, Folpe et al [4] advanced the novel concept of histologically identical tumors not accompanied by TIO, which they called nonphosphaturic variants.

Here, we present the first case of malignant PMT-MCT, resulting in multiple lung metastases. We were able to follow the histologic features from primary to recurrent lesions of the foot to pulmonary metastasis.

2. Case presentation

The patient was a Japanese woman in her early 30s. She presented with a mass in the right foot sole. She had noticed the mass 10 years before her first visit to the hospital and felt it had been increasing in volume recently. She denied any trauma to the area. She had no history of osteomalacia or fracture, and the serum concentrations of

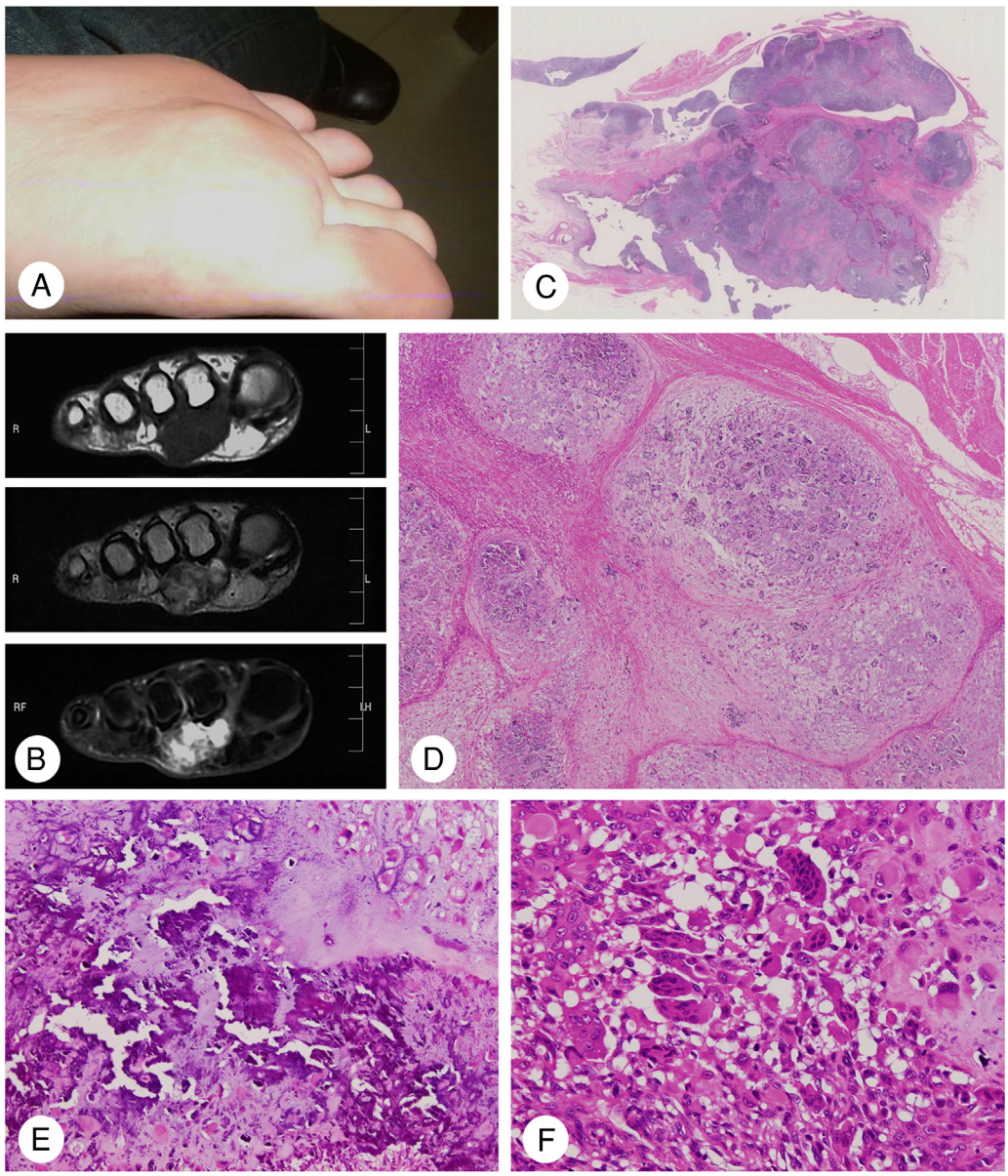

Fig. 1 A, Firm immobile nodule is seen in subcutaneous tissue of sole of foot. B, MRI shows soft tissue mass measuring 2.3 × 2.3 × 1.5 cm that is enhanced by gadolinium (Gd). C-E, Tumor is poorly circumscribed and composed of multiple cartilaginous nodules with "grungy" calcification imparted by fibrous septa. F, Multinucleated giant cells and histiocytoid mononuclear cells are seen at the periphery of the nodules. Abbreviations: T_1WI, T1-weighted image, T_2WI, T2-weighted image.