

Mazabraud Syndrome: A Rare Association of Fibrous Dysplasia and Intramuscular Myxomas

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Abstract

A 39-year-old female presented to our hospital with complaints of no specific low-grade pain and tenderness of left thigh and leg with small palpable swelling within the left upper thigh. On imaging, expansile bony lesions were noted in left femur and tibia suggestive of fibrous dysplasia with two small intramuscular soft tissue swellings in the upper and mid-thigh which proved to be myxomas on histopathological examination. The association of these two findings is known as Mazabraud syndrome.

Keywords: Mazabraud syndrome; Polyostotic fibrous dysplasia; Intramuscular myxomas

Introduction

Fibrous dysplasia (monostotic/polyostotic) in association with intramuscular myxomas is a rare musculoskeletal disorder known as Mazabraud's syndrome. Fibrous dysplasia is a benign congenital intramedullary disease process where normal bone is replaced by fibrous stroma and islands of immature woven bone. Soft tissue myxomas are benign mesenchymal tumors with the abundance of extracellular mucoid material [1].

The first case of Mazabraud's syndrome was described by Henschen [2], and the association between fibrous dysplasia and soft tissue myxomas was reported by Mazabraud et al. [3]. To our best knowledge, fewer than 100 cases of this rare association have been reported so far in the medical literature.

Case Report

A 39-year-old female presented to our hospital with pain and mild tenderness of the left thigh and leg of long duration with gradually increasing swelling in the medial aspect of the upper thigh. No history of weight loss or difficulty in walking or proximal muscle weakness was found. Local examination revealed small mobile soft tissue swelling in the medial aspect of upper thigh not attached to the underlying bone. On palpation, the swelling was mildly tender. Serum calcium, phosphate, and creatinine were within normal limits.

X-rays of left hip including femur and left tibia showed mildly expansile well-defined lucent lesions with hazy ground glass matrix surrounded by intact smooth sclerotic margins (Figures 1 and 2).



Figure 1: Frontal radiographs of the left hip including femur.



Figure 2: Frontal radiographs of the left hip including left tibia.

Non-contrast computed tomography evaluation of left lower limb showed large intramedullary well defined geographical map like mildly

expansile lesions with ground glass appearance in left femur and the proximal tibia having smooth cortical outline (Figures 3 and 4).



Figure 3: Coronal reformatted computed tomography images of left femur.



Figure 4: Coronal reformatted computed tomography images of left tibia.

MRI examination of left lower limb revealed polyostotic fibrous dysplasia involving left femur and proximal tibia showing low signal intensity on T1-weighted and mixed signal intensity on T2-weighted images with hypointense sclerotic rim and appear heterogeneously hyperintense on STIR sequence. In addition to bony lesions left proximal and mid-thigh shows two well-defined intramuscular soft tissue lesions appearing homogeneously hypointense on T1-weighted images and hyperintense on T2-weighted and STIR images (Figures 5-7). The bony lesions showed diffuse and the soft tissue lesions showed peripheral rim enhancement after intravenous gadolinium injection (Figure 8).

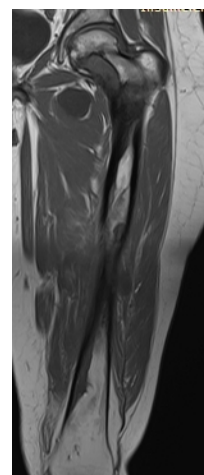


Figure 5: Stitched coronal T1-weighted.

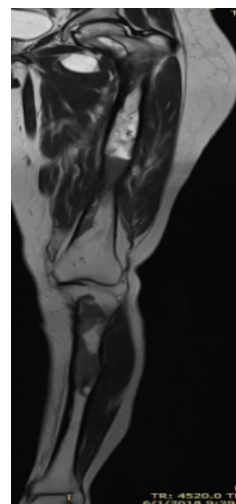


Figure 6: Stitched coronal T2-weighted.

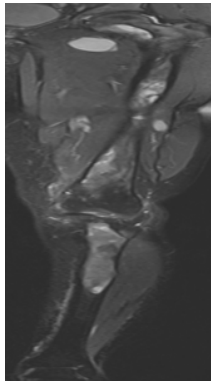


Figure 7: STIR images of left lower limb.

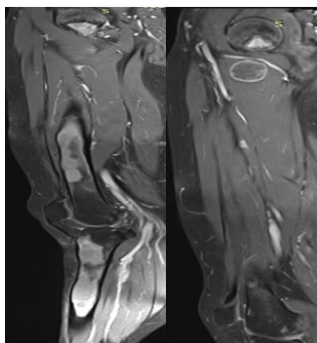


Figure 8: Coronal post-contrast T1-fat suppressed images of left lower limb.

Excision biopsy from the soft tissue lesion of left thigh showed myxoid areas on gross examination and microscopic examination showed an encapsulated tumor with extensive myxoid background and containing many interspersed stellate to spindle-shaped cells with ovoid to the elongated nucleus and scant to moderate amounts of cytoplasm confirmed as the intramuscular myxoma.

Discussion

Fibrous dysplasia is a pathological osseous condition characterized by replacement of normal bone with fibrous tissue in mono-ostotic or polyostotic forms. Pathogenesis of fibrous dysplasia is explained by the gene mutation (GNAS1) located on 20q13.2eq13.3 chromosome responsible for encoding of Gs(a) protein. In patients with fibrous dysplasia abnormally increase GNAS1 activity and cellular proliferation rate contribute to failed differentiation and maturation of the developing bones [4]. Fibrous dysplasia weakens the bone and predisposes the patient to deformity and pathological fractures. This disease is not curable and inherits from one to another generation. Fibrous dysplasia is associated with McCune-Albright syndrome, various endocrinopathies, and intramuscular myxomas. Differential diagnosis of mono-ostotic forms is simple or aneurysmal bone cysts, medullary bone infarct, enchondroma, low-grade osteosarcoma or chondrosarcoma, non-ossifying fibroma.

Intramuscular myxomas are described as benign soft tissue neoplasm that commonly seen in middle-aged women. They have the tendency to grow slowly in large muscles of limbs especially thighs and gluteal region. Intramuscular myxomas are usually painless and asymptomatic with a very low recurrence rate after surgical excision. Symptomatic individuals are having myxomas around joints limiting mobility and at times due to adjacent muscle infiltration. Differential diagnosis of Intramuscular myxomas are ranging from benign to malignant types of soft tissue lipomas, neurogenic tumors and fibrous neoplasm of the predominant myxoid component on histopathology.

Mazabraud syndrome is a rare association of fibrous dysplasia with intramuscular myxomas and few cases reported in the literature so far [5]. The disease is more frequent in middle age women than men and patients are often asymptomatic. However, complications such as skeletal deformities, fractures and pain can occur [1,6,7]. The etiology of Mazabraud's syndrome is unknown and believed to be caused by a basic metabolic error of both soft and bone tissues during the initial growth period by somatic gene mutation GNAS1 responsible for abnormal cell proliferation and expressed in both lesions [8-10].

Mazabraud syndrome is characterized by the presence of multiple intramuscular myxomas that tend to be located in the lower extremities in the vicinity of the fibrous dysplasia [6]. The syndrome is more commonly present with the polyostotic fibrous dysplasia; however, association with monostotic form has been reported as well. The development of fibrous dysplasia occurs before the formation of the intra-muscular myxomas, and the soft-tissue lesions become apparent years later [5]. Malignant transformation of fibrous dysplasia can also occur as part of Mazabraud syndrome but it is very uncommon [8]. Most common varieties of sarcomatous dedifferentiation are osteosarcoma, fibrosarcoma, malignant fibrous histiocytoma, and rarely chondrosarcoma with preference to polyostotic form.

Role of various imaging modalities has been described for evaluation of bone and soft tissue lesion that includes X-ray, Ultrasonography, CT, MRI and FDG PET-CT.

Fibrous dysplasia imaging appearance is dependent on amount of fibrous matrix and on conventional radiography they appear as well-defined, slightly expansile, geographical pattern lucent lesions with ground glass matrix and peripheral smooth cortical rim, these lesions tend to grow slowly over a period of years and may involve single or multiple bones (mono-ostotic or polyostotic forms). Computed tomography findings are similar to x-ray with evidence of intramedullary well defined expansile lesions having ground glass appearance, the role of CT is limited to evaluate the extent of the lesion and any deformity. MRI examination of polyostotic fibrous dysplasia shows low signal intensity on T1-weighted and mixed signal intensity on T2-weighted images with the hypointense sclerotic rim. After intravenous gadolinium injection, bony lesions show variable patchy to diffuse enhancement. Fibrous dysplasia shows increased tracer uptake on Tc99 bone scans [11].

Intramuscular myxomas are seen as well-defined hypoechoic lesions on ultrasound and appear cystic on MRI imaging with T2W bright signals and peripheral rim enhancement after intravenous gadolinium injection.

Fibrous dysplasia demonstrates abundant fibrous matrix with poorly mineralized bone and sparse areas of immature trabeculae on histopathology. Presence of Cartilaginous islands is the helpful differentiating feature from chondrosarcoma and lack of osteoblast rim

from cemento-ossifying fibroma. Myxomas show gray-white or pearly appearance on gross examination with abundant hypocellular mucoid matrix and no cellular atypia or mitotic figures suggesting benign feature.

Treatment of fibrous dysplasia and myxomas is usually conservative considering the benign nature. Surgical excision of myxoma is considered in patients with symptoms arising from the limitation of movement due to swelling and any localized pain due to muscle infiltration. Fibrous dysplasia tends to stable after skeletal maturity and recently the role of bisphosphonates has been described to reduce pain, prevent deformities or fractures, partial resolution of the lesions and promote bone formation [12,13].

Mazabraud's syndrome was commonly misdiagnosed as neurofibromatosis in the pre-MRI era. Role of imaging remains important in differentiating it from malignant bone lesions and malignant transformation of pre-existing low-grade benign bone lesions [13] or soft tissue malignant neoplasm with an abundance of the myxoid component.

DiCaprio and Enneking recommended a standard radio imaging-clinical work-up including endocrinological evaluation in patients of Mazabraud's syndrome with regular interval follow up assessment considering the increased risk (8.3% instead of 1%) of malignant transformation of the fibrous dysplasia lesions [14]. So far no case report is published suggesting the malignant transformation of the myxomas [15].

In conclusion, radiologists and clinicians need to be aware of Mazabraud's syndrome as an association of fibrous dysplasia and soft tissue myxomas in order to prevent misdiagnosis as a malignant condition and avoid unnecessary intervention or surgical procedures considering them benign lesions with very low potential of malignancy.

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