Mazabraud's syndrome: a case report

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Summary

Fibrous dysplasia of bone (FD) is a benign bone disease, rare, not hereditary, and characterized by an abnormal proliferation of fibroblasts and deficient differentiation of osteoblasts, leading to the replacement of trabecular bone tissue by fibrous connective tissue. In some cases, the bone lesions are presented together with various extra-skeletal manifestations constituting specific syndromes. Mazabraud's syndrome represents the infrequent combination of one or more intramuscular myxomas and fibrous dysplasia. The acknowledgment would make it possible to differentiate myxomas, which are benign tumors, from malignant mesenchymal tumors with myxoid material, and in this way reduce the need for unnecessary biopsies and/or surgeries.

KEY WORDS: fibrous dysplasia of bone; myxomas; Mazabraud's syndrome.

Introduction

Fibrous dysplasia of bone (FD) is a rare and benign skeletal bone disorder with a broad spectrum of clinical presentation ranging from asymptomatic radiological findings to severe bone abnormalities of severe and disabling nature (1, 2). It is produced by an activating somatic mutation of the GNAS1 gene (3) and is characterized by an abnormal proliferation of fibroblasts and deficient osteoblast differentiation that leads to a replacement of trabecular bone tissue by fibrous connective tissue. There are monostotic, poliostotic, panostotic and craniofacial forms (4). Rarely, it can be associated with muscular myxomas. This association is called Mazabraud's syndrome (MS) (5).

We present the clinical case of a 51-year-old patient with a previous diagnosis of FD who consulted for the appearance of painless tumors in the right lower limb.

Case report

A 51-year-old patient with a history of left breast cancer, hypothyroidism, iron deficiency anemia and polyostotic fibrous dysplasia consulted for the appearance of a palpable and painless tumor in the anterior region of the right thigh of 5 months of evolution associated with right coxalgia.
Physical examination revealed a slight facial asymmetry with left exophthalmos. *Café-au-lait* spots on the trunk were evident, at the level of the left mid-axillary line and abdomen (right flank). On the right brachial biceps, a 5 cm long tumor with a hard-elastic consistency, painless and not adhered to deep planes was palpated. At the level of the anterior aspect of the right quadriceps, two 7 and 6 cm lesions with similar characteristics were palpated with respect to the one described in the right arm.
Initially, a soft tissue ultrasound was performed, which revealed the presence of two muscle tumors in the right quadriceps muscle. One of them, with heterogeneous hypoechoic material inside, measured 51 by 40 mm; the second measured 61 by 31 mm and presented an anechoic fluid surrounded by smooth walls. They presented peripheral vascularization with an arterial spectral pattern.
The laboratory tests are shown in Table 1.
An imaging magnetic resonance imaging (MRI) with gadolinium was performed, which revealed the presence of bone lesions in the proximal third of the right femoral shaft and femoral neck, isointense to muscle planes in T1 sequence and hyperintense in inversion-recovery sequence (IR), of hypointense edges, without involvement of cortical bone, of 10 cm in length and 2.4 cm in transverse diameter. A level of the anterior aspect of the proximal third of the right thigh showed the presence of two focal lesions, lobed, hypointense in T1 and hyperintense in T2 of 7 and 5 cm in length and 5 mm in transverse plane, with involvement of the crural muscle, with peripheral enhancement after administration of contrast. The bone lesions were compatible with bone dysplasia and the coexistence of intramuscular soft tissue lesions, interpreted as muscular myxomas, suggested the diagnosis of Mazabraud's syndrome (Figure 1).
The ^{99}mTc bone scintigraphy showed an abnormal concentration of the tracer in left calvaria and facial bones, right humeral diaphysis, bilateral anterior and left posterior costal arches, sternum, iliac crests, both hips, pubic symphysis, both proximal thirds of the femoral diaphysis and both tibial diaphysis, predominantly right.
Due to the extension and distribution of bone lesions and pain refractory to non-steroidal anti-inflammatory drugs, treatment with pamidronate (180 mg every 6 months intra-

Table 1 - Laboratory tests.

	Results	Reference ranges
Hematocrit (%)	28	36-44
Hemoglobin (g/dl)	8.3	12-16
Glucose (mg/dl)	76	70-110
Urea nitrogen (mg/dl)	14	10-50
Creatinine (mg/dl)	0.7	0.5-0.9
Sodium (mEq/l)	136	135-145
Potassium (mEq/l)	4.5	3.5-5.0
Calcium (mg/dl)	8.9	8.5-10.5
Phosphate (mg/dl)	2.9	2.7-4.5
Alkaline phosphatase (mUI/ml)	393	35-105
24-hour urine calcium (mg)	234	100-320
Urine deoxypyridinoline/urine creatinine ratio (μmol/mM)	8.97	3-7.4
PTH (pg/ml)	51.4	15-65
25(OH) vitamin D (ng/ml)	23.4	>30
Blood protein electrophoresis	Normal	Normal

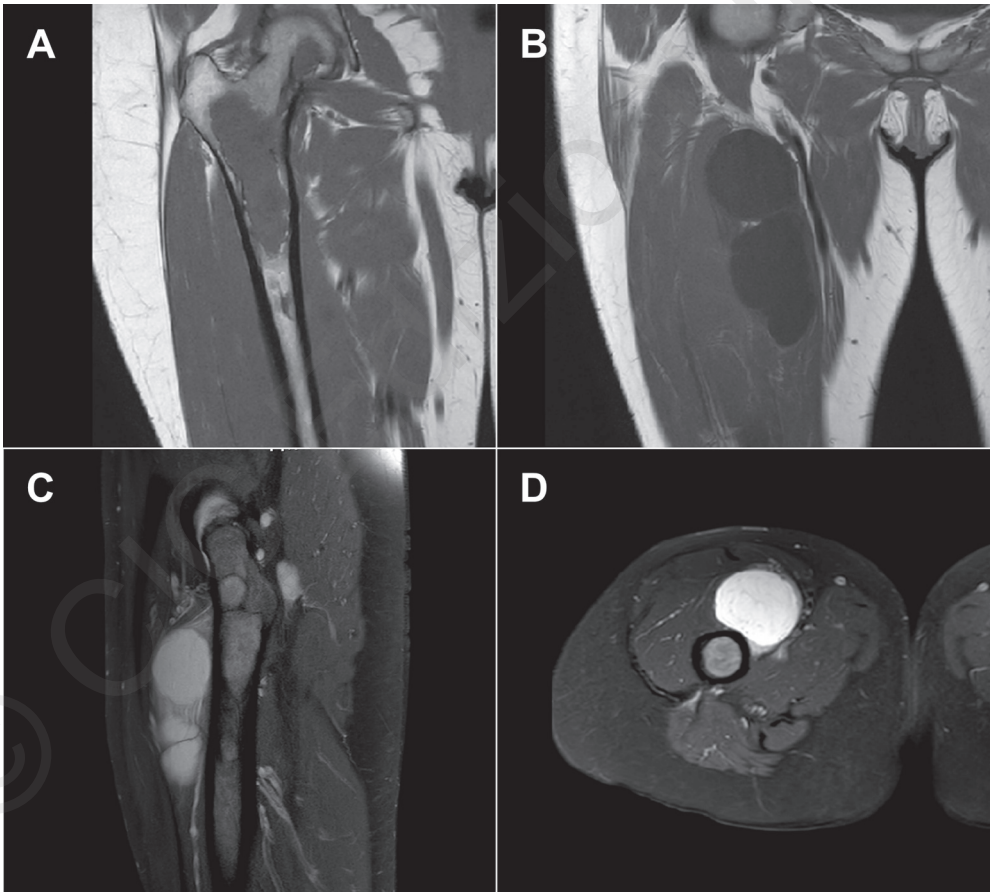

Figure 1 - RMI of right thigh and hip. A) T1 coronal: bone lesions in the proximal third of the right femoral shaft and femoral neck, isointense to the muscular planes. B) T1 coronal: two focal lesions, lobulated, hypointense in T1 of 7 and 5 cm in length. C) T2 sagittal: both lesions are hyperintense in T2 and do not involve cortical bone. D) T2 axial: hyperintense lesion in T2 that compromises right crural muscle.

venously) and vitamin D was conducted. Conservative management of muscle injuries was adopted.

Discussion

Fibrous dysplasia is an infrequent and benign condition caused by a mutation in the GNAS gene located on chromosome 20q13.2-q13.3 and which codes for the alpha subunit of the activating G protein (Gsα). Mutations inhibit the intrinsic Gsα GTPase activity leading to an overproduction of cyclic AMP (3).

The presence of FD, one or more endocrinopathies and café-au-lait spots may indicate a condition called McCune-Albright syndrome (6). When the FD is associated with muscular myxomas, it is known as Mazabraud syndrome.

MS was initially described in the German literature by Henschen in 1926. Subsequently, Mazabraud et al. presented the association between FD and soft tissue myxomas in 1967 (7). Myxomas are benign, single or multiple neoplasms. In MS, myxomas are often multiple. They are slow-growing, painless and close to the bones most affected by FD but without evidence of continuity between the lesions. Women are affected twice more and the average age at diagnosis is 44 years (8). The FD is often polyostotic and the femur, the bone most commonly affected, while the quadriceps is the most affected by myxomas. However, any site is possible. The FD can precede the development of the myxoma by years or even decades (9). When a myxoma is identified, careful examination can reveal the presence of more tumors, since 70% are multiple, as was the case with our patient.

Several hypotheses have been proposed to explain the Mazabraud´s syndrome including a common histological origin during embryonic development or alterations in the early growth of bones and soft tissues. Recently mutations have been identified in several genes involved in cell proliferation, including the GNAS gene (10).

The most important step in the diagnosis is the exclusion of malignant tumors, such as soft tissue sarcoma, low-grade osteosarcoma that complicates a preexisting bone lesion, liposarcoma or malignant tumors with myxoid component (myxoid chondrosarcoma, myxoid liposarcoma and myxoid fibrous histocytoma) (11). MRI is the most useful imaging technique for differential diagnosis. Myxomas are lesions with well-defined contours. The MRI images of the myxoid material show the intensity of the fluid signal (low signal intensity in T1-weighted images, high signal intensity in T2 and no change in T1 images after contrast). After administration of intravenous contrast they present heterogeneous enhancement to peripheral predominance. This pattern of enhancement is useful to distinguish myxomas from avascular lesions such as intramuscular synovial cysts, hematomas or abscesses. Occasionally they may present a ring of perilesional fat and edema of adjacent muscles (12).

The treatment of myxomas consists in the follow-up of lesions or local resection when they are symptomatic or growing lesions. Although it has been suggested that myxomas do not recur after surgical resection (13), Szendroi et al. reported a high recurrence rate, locally or in adjacent muscles, with a recurrence time of several years (more than 10 years), suggesting the need for follow-up long-term (14). In our patient, expectant behavior was adopted.

Conclusion

Mazabraud's syndrome is an infrequent entity that should be considered in patients with intramuscular tumors and fibrous dysplasia. Its recognition could be useful for an adequate preoperative diagnosis, reducing the need for biopsies or unnecessary surgeries.

Conflicts of interest

The Authors declare no conflicts of interest.

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