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CASE REPORT

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Polyostotic fibrous dysplasia associated with intramuscular myxomas: Mazabraud's syndrome

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Abstract Mazabraud's syndrome, though uncommon, is reported increasingly frequently. It represents an entity readily recognisable radiologically on MR imaging. Awareness of the syndrome, particularly when the myxoma is solitary, can prevent misdiagnosis of intramuscular myxomas (especially when large) as malignant mesenchymal tumors containing myxoid tissue. We review the 34 cases previously reported in the literature and include a recent case from our center.

Key words Fibrous dysplasia · Soft tissue tumor · Intramuscular myxoma · MRI · Mazabraud's syndrome

Introduction

Intramuscular myxomas are uncommon benign solitary tumors of large muscle groups, occurring predominantly in the lower limbs. Very much less common are the myxomas that may be associated with fibrous dysplasia (usually polyostotic), which are frequently multiple.

This association is now known as the Mazabraud syndrome. We report the case of a patient from our center, which is only the 35th in the literature.

Case report

A 44-year-old white man, a native of Rio de Janeiro, had noted a slowly growing painless mass in his right thigh for 15 years. Since it did not bother him, and it did not interfere with his work as a truck driver, he never consulted a physician. When he sought to change his occupation, he underwent a pre-employment physical. The large thigh mass was noted, and also a bony mass in relation to his upper ribs. Enlarged nodes were also present in his right supraclavicular fossa. He was referred to a local hospital, where he underwent several biopsies. He was then sent to our center for further evaluation.

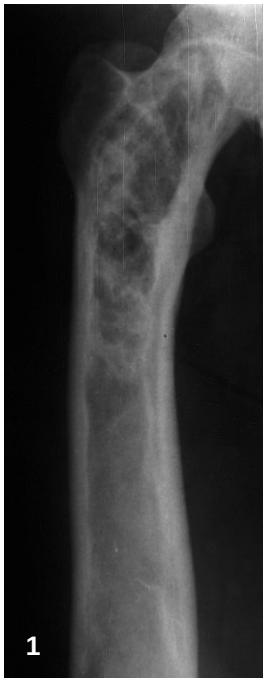
On examination he was found to be in good general health and showed no evidence of recent weight loss. The chest showed a large scar posteriorly, where the third and fourth ribs had been resected, and also a scar in his right supraclavicular area, where excisional biopsy of several nodes had been performed. The right thigh showed a non-tender rubbery mass measuring approximately 25×12 cm in the antero-medial aspect of the thigh, with a biopsy scar.

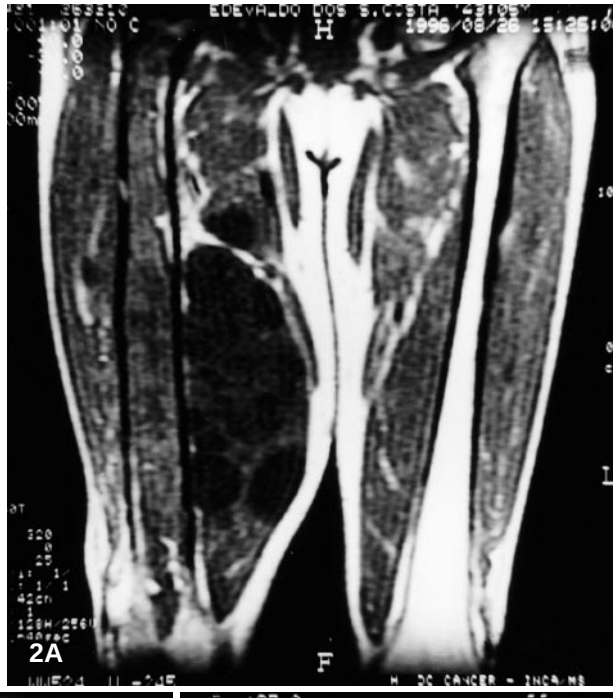
The patient underwent bone scintigraphy with technetium MDP, which this revealed multiple areas of increased uptake limited to the right half of the body – skull, upper ribs, pelvis, femur, and tibia. Chest radiographs and CT scans showed partial resection of two ribs and also characteristic expansion of several ribs, typical of fibrous dysplasia. A soft tissue plain film of the thigh showed a very large soft tissue mass and the typical findings of fibrous dysplasia – expansion of the femur with patchy areas of sclerosis and lucency (Fig. 1).

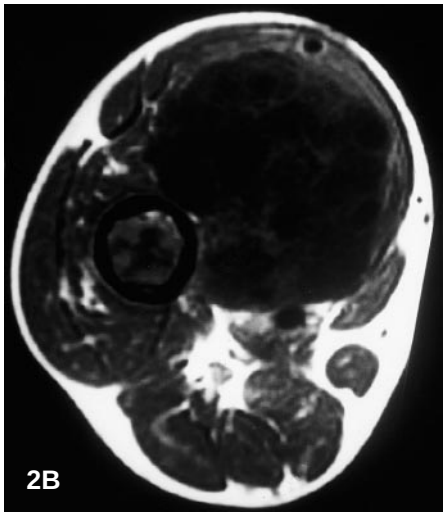
Fig. 1 Anteroposterior plain film of right femur, showing expansion of medullary cavity with cortical thickening and patchy sclerosis, typical of fibrous dysplasia

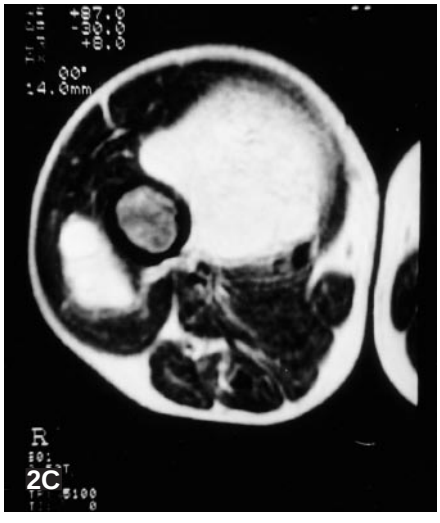
Fig. 2 **A** Coronal T1-weighted MR image (TR 320; TE 25). Multiple well-defined masses (hypointense) are demonstrated in the right thigh. **B** Axial T1-weighted MR image (TR 580; TE 23) shows bulky mass in the region of the vastus intermedius. **C** Axial T2-weighted MR image (TR 5100; TE 125) reveals marked hyperintensity of the largest mass and a mass on the lateral aspect as well

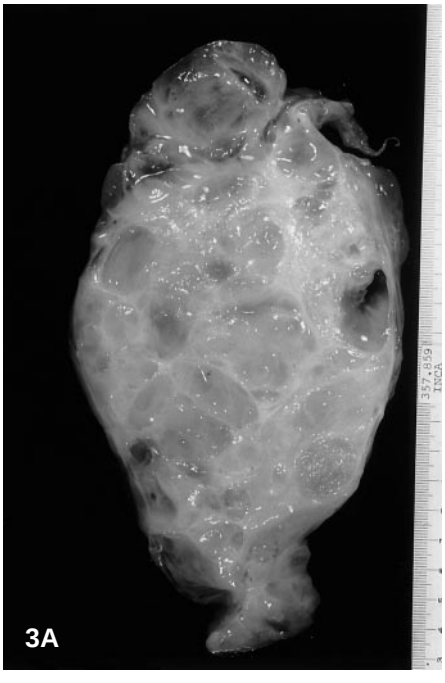
Fig. 3 **A** The cut surface of two masses show the typical glistening slimy surface of a myxoma. The masses were well encapsulated and showed small fluid-filled cystic spaces. **B** High-power section showed the tumor to be composed of small numbers of inconspicuous cells. There was a loose network of reticulin fibers. The small cells were hyperchromatic with pyknotic nuclei and scanty cytoplasm

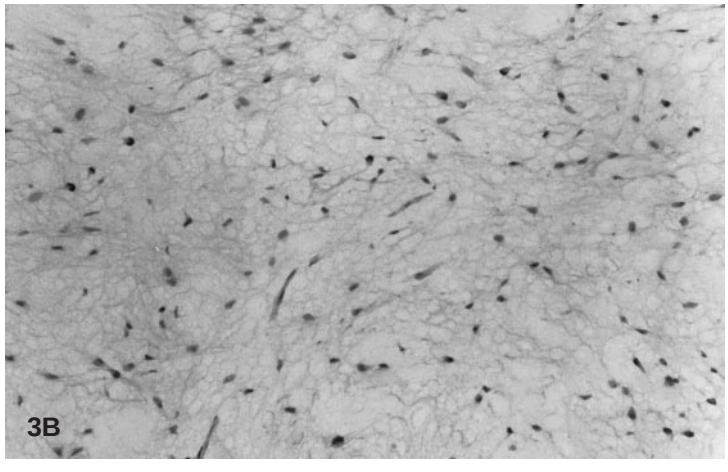












MR scans (Fig. 2), including axial and coronal T1-weighted and T2-weighted images, were obtained. These studies revealed multiple masses in the right thigh. The largest, in relation to the vastus intermedius, measured 20 cm. The masses were hypointense to muscle on T1 weighting but were markedly intense on T2 weighting. The underlying femur was expanded and showed hypointensity on T1 weighting and hyperintensity on T2 weighting.

The findings were characteristic of myxoma, and the grossly abnormal femur made this a very typical case of Mazabraud's syndrome. Review of all the submitted material confirmed the fibrous dysplasia in the resected ribs without evidence of malignancy. (A frozen section of the ribs performed elsewhere had been thought to reveal a low-grade osteosarcoma in addition to the fibrous dysplasia.) The supraclavicular nodes showed simple reactive changes. The biopsy of the soft tissue mass was thought to be a simple myxoma.

The patient underwent excision of the two masses on the medial aspect of the thigh. The multiple masses on the opposite side of the thigh were not resected.

The surgical specimen revealed two masses (Fig. 3A). The very large one measured 20.0 cm. The smaller one measured 5.0 cm. The tumors were both encapsulated, and on section were glistening and slimy and revealed a whitish gray appearance with small fluid-filled cystic spaces. Histologically (Fig. 3B) the specimen showed a tumor that was composed of relatively small numbers of inconspicuous cells, abundant mucoid material, and a loose network of reticulin fibers. The cells were small with hyperchromatic pyknotic nuclei and scanty cytoplasm. There was no cellular pleomorphism, mitosis, or multinucleated giant cells.

Mature collagen fibers were seen occasionally. At the periphery, the tumor merged into surrounding muscle, fat cells and atrophic muscle fibers. Immunohistochemistry revealed that the cells stained with vimentin but not with desmin or S100 protein and desmin.

About 9 months after surgery the patient returned for follow-up. The masses on the lateral aspect of the thigh, which had not been removed, were unchanged and no new masses were found. MR confirmed the clinical findings.

Discussion

Although first described by Henschen [1] in 1926, it was Mazabraud [2] who, in reporting his second case in 1967, emphasized that despite there being only nine cases to date, the association was not fortuitous but represented a real entity and an association with fibrous dysplasia of bone. Earlier authors had believed that the finding was related to neurofibromatosis. In fact the patient reported in 1967 had been referred to Mazabraud as a case of neurofibromatosis. Mazabraud emphasised that the myxoma was not related to neurofibromatosis. There is no familial incidence and it is not inherited.

All the early reports were in the European literature, with the first report in English being by Wirth et al. [3] in 1971. Awareness of the entity is important because the myxoma may be quite large, and differentiating this completely benign lesion from malignant mesenchymal tumors with large amounts of myxomatous material, particularly liposarcoma, may be difficult. Although in some cases of this syndrome, malignancy, especially liposarcoma, was reported (or suspected) no amputations were performed, but there were several cases with extensive resections. No malignancy has ever been reported in the myxoma of Mazabraud's syndrome. An extensive review of reported cases is tabulated in Table 1 [4–19]. (Not included in this review is a case mentioned in Mietenen and co-workers' paper [20], for which no clinical details were provided.)

Intramuscular myxoma grows slowly and is usually quite painless. However, in seven patients pain was a significant symptom. It is a disease of adults and has never been reported in children, the youngest patient being 17 [3]. It is approximately twice as common in women than men (23 vs 12). The mean age was 46 years. The tumors are not usually very large, the largest being 25 cm (case no. 18) [7]. The average size was 5 cm. The most common single site was the right thigh (63%). The remainder of the cases were distributed between right and left thighs, buttocks, arms, shoulders, and chest wall.

The myxomas tend to develop in groups or clusters. In the majority of cases they are multiple (see Table), but in ten cases the myxoma, at the time of reporting, was solitary. It is easy to overlook small myxomas and, since many cases were reported prior to the availability of MRI, small myxomas may have been missed. Recurrences are uncommon and occurred in only two patients (16, 27) [5, 14]. Differentiating recurrent tumors from new tumors in the same anatomical area may be difficult.

The fibrous dysplasia was multiple in most cases, but in seven patients it was solitary (see Table). Albright's syndrome and formes frustes were found in ten patients. Fibrous dysplasia usually develops in childhood or early adult life, and therefore clearly precedes the development of myxoma by years or even decades. Patients, however, may be unaware that they have this bony disease and may only be diagnosed at the time they present with myxoma. This occurred in seven patients. The polyostotic lesions may be distributed among multiple bones bilaterally (27 patients), but were unilateral in 16 patients. In only two patients (cases 20 and 25) were the fibrous dysplasia and the myxoma solitary [9, 12].

The most serious complication of fibrous dysplasia is osteosarcoma,

Table 1 Mazabraud's syndrome: reported cases

	Author	Year	Fibrous dysplasia polyostotic?	Myxoma multiple?	Age (years)
1	Henschen [1]	1926	Yes	Yes	66
2	Krogius	1928	Yes	Yes	26
3	Uelinger	1940	Yes	Yes	67
4	Braunwarth et al	1953	No	Yes	55
5	Mazabraud and Girata	1957	Yes	No	54
6	Heineman	1958	Yes	Yes	82
7	La Porte et al	1961	Yes	Yes	24
8	Lick and Viehweger	1962	Yes	Yes	59
9	Mazabraud et al [2]	1967	Yes	Yes	NR
10	Wirth et al [3]	1971	Yes	Yes	17
11	Wirth et al	1971	Yes	Yes	33
12	Le Jeune et al	1972	Yes	Yes	42
13	Ireland et al [4]	1973	No	Yes	49
14	Ireland et al	1973	Yes	Yes	61
15	Ireland et al	1973	Yes	Yes	28
16	Logel [5]	1976	Yes	Yes	41
17	Berkhoff et al [6]	1981	No	Yes	36
18	Sedmak et al [7]	1983	Yes	Yes	50
19	Lever and Pettingale [8]	1983	Yes	No	52
20	Segev and Reiner [9]	1983	No	No	74
21	Witkin et al [10]	1986	Yes	No	41
22	Blasier et al	1986	Yes	Yes	57
23	Biagini et al [11]	1987	Yes	Yes	42
24	Glass-Royal et al	1989	Yes	No	33
25	Sundaram et al [12]	1989	No	No	31
26	Glanoutsos et al [13]	1990	No	Yes	53
27	Gober/Nicholas [14]	1993	No	Yes	37
28	Prayson and Lesson	1993	Yes	No	36
29	Aoki et al [15]	1995	Yes	Yes	46
30	Aoki	1995	Yes	No	70
31	Fujii et al [16]	1996	Yes	Yes	53
32	Limouzy et al [17]	1996	Yes	No	45
33	Court-Payen et al [18]	1997	Yes	Yes	50
34	Chyu and Sundaram	1997	Yes	No	34
35	Present case	1998	Yes	Yes	44

which occurred in two patients with the syndrome (cases 9 and 21). Both involved the tibia [2,10]. Osteosarcoma is a rare complication of fibrous dysplasia and usually occurs in under 1% of cases [21]. The two cases represent close to 6%, and this may be more than simply fortuitous.

One patient (15) had developed a fibrosarcoma of the breast 26 years prior to Mazabraud's syndrome [4] and another (17) had developed cancer of the colon [6] 3 years prior to developing the syndrome.

These two cases are probably not related to the syndrome. Of interest is case 19 [8] who, in addition to Mazabraud's syndrome, had Albright's syndrome and hypophosphatemic osteomalacia. Removal of the solitary myxoma had no effect on the osteomalacia. The nature of the myxoma has been much discussed in the literature. Since a true capsule has been reported to be absent in many cases, this process may be reactive rather than neoplastic. Many believe that the myxoma is an extraosseous manifestation of fibrous dysplasia, which may not be apparent for many years.

The myxomas tend to be congregated in relation to the bone most extensively involved, and a local mechanical factor may play a part in the etiology. Since the myxomas are benign, conservative management is indicated. If pain is significant or the tumor very large then the myxoma(s) should be removed. As in this case, the smaller lesions are safely left and observed.

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