CASE REPORT

Mazabraud’s syndrome. A case with multiple myxomas

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Summary Mazabraud’s syndrome is defined as the combination of one or more intramuscular myxomas and fibrous dysplasia of bone. The diagnosis is important given the increased risk of malignant transformation of the bone lesions. We report a case in a 56-year-old patient with a 14-year follow-up during which multiple surgical procedures were required to remove myxomas (present at more than 15 sites). The resected myxomas were large and progressive. Unique features in this case include the long follow-up and the number of myxomas considerably above the average for this disease. Eighty other cases of Mazabraud’s syndrome have been reported. The condition predominantly affects middle-aged women (mean age, 44 years). The bone lesions may be monostotic or polyostotic. Mazabraud’s syndrome may be difficult to distinguish from soft-tissue sarcoma or neurofibromatosis. Identification of the underlying genetic abnormality provides diagnostic confirmation, as shown in our patient. The management consists in surgery to remove the myxomas and magnetic resonance imaging at regular intervals to monitor the lesions.

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Mazabraud’s syndrome is defined as the combination of benign intramuscular myxomas and fibrous dysplasia of bone. The first descriptions were written by Henschen in 1926 [1] and by Mazabraud in 1957 and 1967 [2—5]. Both fibrous dysplasia and myxoma are non-malignant lesions that are common in isolation but rarely occur in combination. In 2009, Zoccali at al. reported a case and found 67 additional cases in the literature [6]. To our knowledge, 12 other cases have been reported since then [7—17]. Here, we report what is probably the 81st case.

Case-report

This 56-year-old man with multiple soft-tissue masses had undergone surgical resection of two masses in the right groin in 1997, one mass in the left groin in 1998, one mass in the left calf in 1999, and one mass in the left vastus lateralis muscle in 2001. The pathological diagnoses were lipofibroma or benign neurofibroma.

When he presented at our department in 2005, computed tomography (CT) findings were as follows (Fig. 1):

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Computed tomography of the abdomen and pelvis showing multiple, slightly hypodense masses in the soft tissues.

- three masses on the left side, one in the vastus lateralis muscle, another in the proximal thigh adhering to the inferior pubic ramus, and the third in the iliacus muscle anterior to the femoral head;
- five masses on the right side, consisting of a small mass in the groin, a mass posterior to the vastus medialis muscle, another mass located more distally in the vastus medialis muscle, and two masses in the psoas muscle;
- a pleural nodule with a cortical reaction in the adjacent right ninth rib having the appearance of a bony spur, and a subpleural nodule measuring a few millimetres in size and located in the posterolateral part of the lower right lobe;
- and bony images in both femurs corresponding to typical radiographic images of fibrous dysplasia (Fig. 2).

Magnetic resonance imaging (MRI) confirmed the presence of multiple intramuscular masses in the proximal parts of both lower limbs, five located on the left side and two on the right side. The largest mass measured 100 by 70 mm and was located in the left obturator externus muscle, where it displaced the pelvirochanteric muscles. The masses were well defined and strictly intramuscular. They generated a signal of fluid intensity (low intensity on T1 images and high intensity on T2 and STIR images) and exhibited weak post-gadolinium enhancement producing

Figure 1 Computed tomography of the abdomen and pelvis showing multiple, slightly hypodense masses in the soft tissues.

Figure 2 Anteroposterior radiographs of both femurs: typical signs of dysplasia including medullary bone remodelling in the diaphysis, rim sclerosis, and thinning and expansion of the cortices with no invasion or periosteal reaction. Note the high-density zones producing a ground-glass appearance.
a heterogeneous appearance with predominantly central uptake. The femoral bone lesions were typical for fibrous dysplasia, with low signal on T1 images and moderately high signal on T2 images (Fig. 3).

In November 2005, the two masses in the proximal left thigh were removed, both to relieve patient discomfort and to obtain pathological confirmation of the diagnosis. Upon gross examination, both masses were off-white in colour, with a slippery surface. The pathological examination identified a fibrous pseudocapsule, which had a translucent gelatinous appearance and a slippery consistency resembling a wet cake of soap, with whitish septae that adhered to the knife blade. Microscopically, there was a low-density cellular proliferation consisting of spindle-shaped cells, each containing fibrillar cytoplasm on either side of a small regular oval-shaped nucleus having one or more nucleoles. The extracellular matrix was myxoid, stained by Alcian blue, and faintly lobulated by thin fibrous septae. The diagnosis was multifocal myxoma arising as a feature of polyostotic Mazabraud’s syndrome with fibrous dysplasia lesions in both femurs.

Enlargement of the masses in the proximal right thigh prompted surgical excision in 2006 and 2007. The histological findings were identical to those obtained
previously. Serial MRI scans were obtained between 2008 and 2010 to monitor the lesions, which increased gradually in size, leading the patient to present again at our clinic in 2011. He had noticed a large mass in the lateral left thigh and reported left femoral neuralgia, which was ascribed to a large myxoma in the psoas muscle with a substantial anterior extension medial to the iliac wing (Fig. 4). The gross appearance is shown in Fig. 5. Microscopically, the lesions were myxomas with no atypical cells. The R201H mutation in the GNAS gene was found in the operative specimens. This mutation has been reported in fibrous dysplasia of bone, McCune Albright syndrome, and other endocrine tumours [6,18–22].

Discussion

Fibrous dysplasia in Mazabraud’s syndrome may be monostotic or polyostotic. The myxomas typically arise near the affected bones, although there is no evidence of continuity between the two lesions [23,24]. Mean age at diagnosis is 44 years and women are affected twice as often as men [6]. The youngest patient was 17 years of age at the time of the diagnosis [25]. The number of reported cases has increased over the years: Cabral et al. identified 35 cases in 1998 [26], Endo et al., 56 cases in 2007 [27], and Zoccali et al., 68 cases in 2009 [6]. The most common sites of myxoma are the thighs, shoulders, buttocks, and forearms. The fibrous dysplasia lesions predominantly affect the femurs, tibias, ribs, pelvis, and skull. Polyostotic forms often occur as part of McCune Albright syndrome, which manifests as endocrine abnormalities with precocious puberty or thyroid dysfunction (or more rarely Cushing’s syndrome, diabetes, acromegaly, or hyperparathyroidism [28]) and as skin pigmentation alterations with café-au-lait spots [6,27,29–31].

Several hypotheses have been put forward, including a shared histological origin of myxomas and fibrous dysplasia during embryonic development [2–5,32], a metabolic abnormality during early growth of bone and soft tissues [25], defective tissue development, and a genetic susceptibility [24]. More recently, genetic and immunohistochemical studies identified mutations in several genes including the GNAS gene (20q13.2–13.3) involved in cell proliferation [20]. Dysplastic changes develop in all the cells that express the mutation. This mutation has been reported in fibrous dysplasia of bone, McCune Albright syndrome, and a number of endocrine tumours. It was first described in McCune Albright syndrome in 1991 [33], and its association with fibrous dysplasia of bone was confirmed in 1999 by Bianco and Robley [18]. A 2001 report describes the presence of the GNAS mutation in myxomas [21].

Before the introduction of MRI, Mazabraud’s syndrome had to be differentiated from a long list of diagnoses [12,23,26,27]. Historically, neurofibromatosis was the most common mistaken diagnosis. The most important step is elimination of malignant tumours such as soft-tissue sarcoma, low-grade osteosarcoma complicating a pre-existing bone lesion [9], liposarcoma, or any other malignant tumour having a myxoid component. According to Mc Laughlin et al. [14], a number of features can be used to support the diagnosis, including epidemiological characteristics (predominance in women with a mean age of 44 years), clinical features (intramuscular masses, with or without pain, in patients with known fibrous dysplasia of bone), and radiological findings (features typical for myxoma and fibrous dysplasia on radiographs, CT scans, and MRI scans). Fibrous dysplasia lesions exhibit increased radionuclide uptake during scintigraphy and a heterogeneous appearance by ultrasonography [34]. Recently introduced imaging techniques such as positron-emission tomography have been used to evaluate patients with Mazabraud’s syndrome [15] but are not warranted in everyday practice when standard imaging methods are used to monitor the lesions [16].

It has been suggested that myxomas do not recur after surgical excision [27]. In contrast, Szendroi et al. reported a high rate of recurrence, either locally or in the adjacent muscles, with time to recurrence of several years (up to more than 10 years) indicating a need for long-term follow-up [35]. Similarly, our patient required multiple surgical procedures (five, to remove seven myxomas) over more than 14 years.

Fibrous dysplasia is a non-malignant lesion of bone that is usually asymptomatic and solitary. Pain may occur, however, as well as deformities such as scoliosis and shepherd’s crook deformity of the proximal femur (marked coxa vara producing apparent widening of the hips) or pathological fractures [20]. DiCaprio and Enneking [20] have suggested that patients with Mazabraud’s syndrome may require a diagnostic work-up including evaluation by an endocrinologist, radiographs, and whole-body scintigraphy or CT; followed by radiographs at 6-month intervals given the increased risk of malignant transformation of the fibrous dysplasia lesions to osteosarcoma [6,20,36], of 8.3% instead of 1% [20]. To date, six cases of osteosarcoma have been reported [5,10,36–39]. All the osteosarcomas developed at unusual sites: there were two cases each at the radius, tibia, and humerus. In the case with the longest follow-up (16 years for the myxomas and 31 years for the fibrous dysplasia), malignant transformation did not occur [35]. No case of malignant transformation of the myxomas has been reported [26].
Conclusion

Unique features in this clinical case are the prolonged follow-up, which is among the longest reported to date, and the very large number of myxomas (more than 15) compared to earlier studies, in which the number rarely exceeded five or was not specified. Despite the enlargement of the lesions over time and the development of isolated clinical symptoms, we found no evidence of malignant transformation. Thus, having a large number of myxomas may not constitute a risk factor for malignant transformation. Nevertheless, careful long-term monitoring by imaging studies is mandatory, and we believe that whole-body MRI is the best option at present. This is one of the rare cases in which the genetic diagnosis was obtained (GNAS gene mutation in the fibrous dysplasia and myxoma cells).

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References


