Mazabraud Syndrome: Case Report with Review of Imaging

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Abstract: Mazabraud's syndrome is the rare combination of soft tissue myxomas with fibrous dysplasia. The recognition of co-existent soft tissue and osseous abnormalities is the key to diagnosis, allowing differentiation from other malignant myxoid lesions, and instituting appropriate management and avoiding debilitating therapy. Of the cross-sectional imaging modalities, MR imaging is preferred due to its high correlation with the histological character of the myxoma. Although biopsy is needed in equivocal cases, MR imaging can indicate the likely diagnosis and assist in pre-biopsy and pre-operative planning. Given the few reports of sarcomatous degeneration in the fibrous dysplasia component, clinical follow-up is advisable. Cognizance of the fact that myxoma is histologically a solid lesion with fluid-like radiological characteristics, is the fundamental principle essential to comprehend the varied and often counter-intuitive imaging appearances.
Key words: Mazabraud's syndrome, fibrous dysplasia, myxomas, imaging, MR

MAZABRAUD-SYNDROMA: ESETISMERTETÉS ÉS A KÉPALKOTÓ VIZSGÁLATOK LELETEINEK ÁTTEKINTÉSE

A Mazabraud-syndroma a lágyrész-myxoma és a fibrosus dysplasia ritka kombinációja. Kórismézésének előfeltétele az egyidejűleg fennálló csont- és lágyrész-rendellenességek felismerése. Csakis ezáltal különíthető el más, rosszindulatú myxoid elváltozásoktól, továbbá kezelhető szakszerűen, illetve kerülhető el a csonkító onkológiai terápia. A keresztmetszeti képet alkotó eljárások közül az MRI a legmegfelelőbb, ugyanis a mágnesrezonanciás kép és a myxoma szövettani sajátosságai között szoros a korreláció. Bár kétes esetben biopszia szükséges, a MRI-kép alapján valószínűsíthető a helyes kórisme és a lelet megkönnyíti a biopszia, ill. a műtét tervezését. Szórványosan beszámoltak a fibrosus dysplasiás összetevő sarcomás elfajulásáról, ezért ajánlatos nyomon követni a folyamat klinikai kórlefolyását. Nem szabad feledni, hogy a myxoma szövettani értelemben parenchymás elváltozás, ugyanakkor radiológiai jellemzői a folyadékokéhoz hasonlóak. Ezt a kettősséget szem előtt tartva helyesen értelmezhetjük a kivizsgálás során készített felvételeken ábrázolódó változatos és az intuitív értékelést gyakran kizáró küllemét.
Kulcsszavak: Mazabraud-syndroma, fibrosus dysplasia, myxomák, képalkotó vizsgálat, MRI

Although Henschen in 1926 [1] first reported the association of intramuscular myxomas with skeletal fibrous dysplasia, the syndrome is largely known after Mazabraud who emphasized its importance in the French literature in 1967 [2]. Wirth brought it to the attention of the English literature in 1971 [3]. Supposedly of uncommon occurrence with a recent paper quoting 44 reported cases till 2002 [4], current literature search reveals many more cases, probably because of increased clinical awareness and advancement in imag-

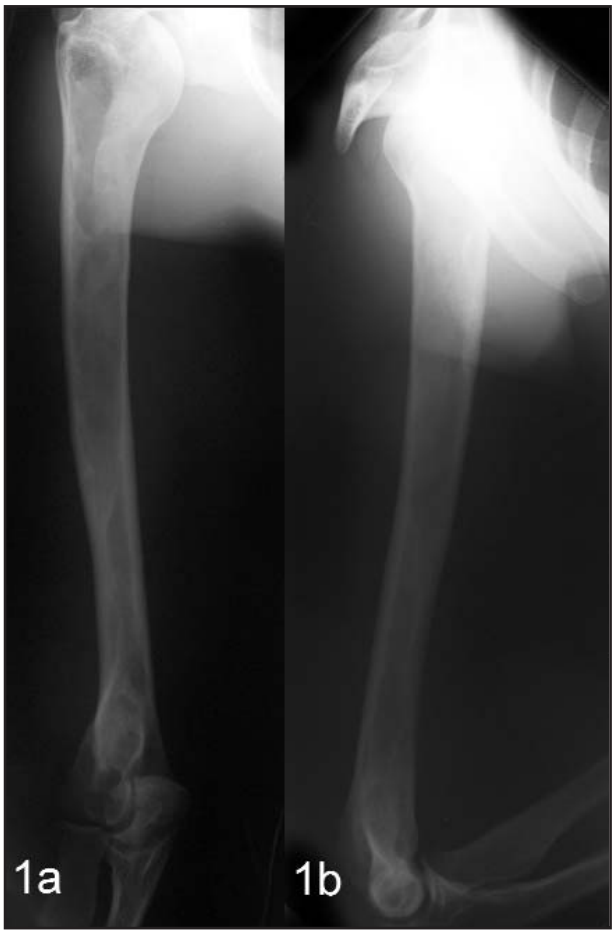

Fig 1. Plain radiographs anteroposterior (a) and lateral (b) demonstrating the polyostotic fibrous dysplasia predominantly affecting the entire length of the humeral diaphysis, with further involvement in the proximal radius.

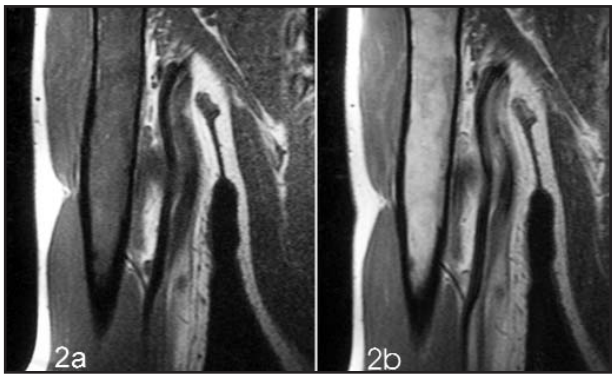

Fig 2. The fibrous dysplasia on coronal T1-weighted sequences shows a heterogeneous signal intensity similar to muscle on the pre-contrast sequence (a) and heterogeneous enhancement on the post-contrast sequence (b).

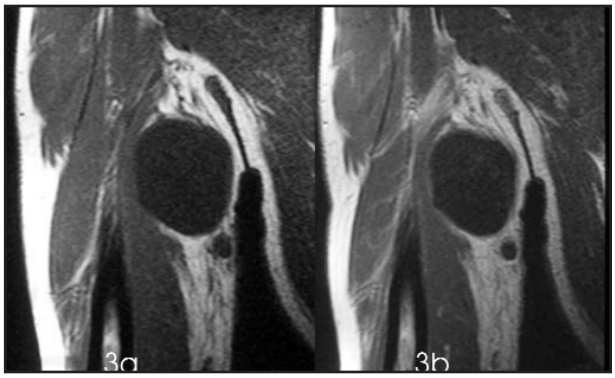

Fig 3. Sagittal T1-weighted pre- (a) and post-contrast (b) sequences demonstrating two of the well defined, oval, low signal intensity myxomas having thin internal septa, and moderate peripheral and septal enhancement. The peritumoural fat rind and fat caps are well demonstrated.

ing techniques. Many cases likely go unrecognised as both the osseous and soft tissue components of this syndrome are relatively asymptomatic and the myxomas usually appear years after initial occurence of fibrous dysplasia. We report a case at our institution along with a review of clinico-pathological and radiological features, differential diagnosis, and the importance of its awareness among radiologists.

CASE REPORT

A 37 year old right hand dominant baker presented to a neighbouring district general hospital with a six month history of painless swelling to the medial aspect of the right arm. Radiographs of the right arm at that time did not demonstrate any soft tissue abnormality, although on retrospect, polyostotic fibrous dysplasia was manifest in the humerus and proximal radius (Fig. 1). He re-presented two years later with gradual increase in the size of the mass and paraesthesia in the distribution of the ulnar

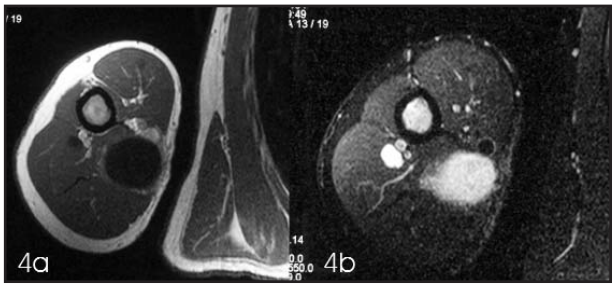

Fig 4. Axial post-contrast T1-weighted (a) and STIR (b) demonstrating apparent 'cystic' characteristics on MR imaging of the histologically solid nature of the lesions, seen in an intramuscular location.

nerve. Without performing cross-sectional imaging, an attempted surgical excision under local anaesthesia was abandoned, as intra-operatively there appeared to be nerve involvement. A fine needle aspiration performed on the operation table was subsequently reported as non-diagnostic. The post procedure MR imaging (coronal and axial STIR, pre and post gadolinium-DTPA contrast T1-

weighted sagittal and axial sequences) was interpreted as demonstrating a 4 cms mass in the posterior compartment of the arm with two further smaller masses in the vicinity, and the bone lesion was considered dysplastic in nature (Fig. 2). With a provisional diagnosis of neurofibromatosis, he was referred to our tertiary orthopaedic hospital for further management.

At our oncology multidisciplinary team meeting, review of MR images noted the 4 cms mass located in the peripheral anteromedial aspect of the triceps muscle, adjacent to the deep fascia separating it from the anterior compartment and the neurovascular bundle. It was longitudinally oval with a mild lobulated contour, having signal intensity lower than muscle on T1-weighted sequences (Fig. 3) and similar to fluid on the STIR sequences (Fig. 4). The T1-weighted sagittal sequence demonstrated a thin margin of adipose tissue surrounding the mass, with a fat cap at the cranial and caudal aspects of the mass. There were thin internal septae within the otherwise relatively homogeneous lesion. Post contrast T1-weighted sequences demonstrated moderate peripheral enhancement with mild internal irregular septal enhancement. The other two separate masses, measuring 1 cm each, also demonstrated similar imaging characteristics. One was located at the same axial level, in the lateral belly of the triceps muscle adjacent to the deep fascia separating it from the anterior compartment; and the second was situated in the subcutaneous fat, superficial to the deep fascia of the arm, medial to the basilic vein. The expansile bony abnormality along the extent of the visualised humerus diaphysis had a signal intensity similar to muscle on the T1-weighted sequences, heterogeneous intermediate to high signal intensity on the STIR sequences, and moderate heterogeneous enhancement post gadolinium contrast. Intraosseously, the margins separating the lesion from the fatty bone marrow was well defined, but lacked a low signal intensity rim on both sequences. The endosteal aspect of the cortex was smoothly scalloped. Review of the previous plain radiograph confirmed the impression of fibrous dysplasia with mild expansile modelling abnormality of the humerus, ground glass matrix and endosteal scalloping. A further focus was noted in the proximal radius in the same radiographs. The soft tissue lesions were indicated as likely soft tissue myxomas and Mazabraud's syndrome was the suggested diagnosis. Excision of the 4 cm intramuscular mass under general anaesthesia was subsequently done and histologically confirmed as intramuscular myxoma of typical appearance. Post operatively, there was a small area of residual numbness to the medial aspect of the elbow with no other neurological deficit.

Discussion

Fibrous dysplasia is a non-inherited bone abnormality in which abnormal differentiation of osteoblasts leads to replacement of normal marrow and cancellous bone by immature bone and fibrous stroma [5]. The monostotic form comprises approximately 80% of cases. The polyostotic form is often unilateral, and usually shows a monomelic pattern. McCune-Albright syndrome is the commoner of the two known syndromes associated with fibrous dysplasia, and often occurs in girls as a triad of precocious puberty, polyostotic fibrous dysplasia and cutaneous hyperpigmentation. Mazabroud's syndrome is the rarer occurrence of soft tissue myxomas with fibrous dysplasia.

Myxoma, so termed by Virchow in 1863 to describe a tumour histologically resembling the Wharton's jelly of foetal umbilical cord, was established by Stout as a distinct lesion, and defined as a mesenchymal neoplasm composed of undifferentiated stellate cells in a myxoid stroma [6]. Most commonly noted in the heart, non-cardiac myxomas can involve subcutaneous tissue, skeletal muscle, aponeurotic tissue, bone, genito-urinary system and skin [7]. Approximately 17% of myxomas are intramuscular in origin, most commonly occurring in the thigh [8]. The relationship between fibrous dysplasia and soft tissue myxomas remains unclear. The initial postulations of a common histiogenetic origin [2] or basic inborn error of tissue metabolism of both tissues [3] continue to prevail.

Patients with Mazabraud's syndrome usually present with slow growing and painless masses of myxomas, although pain and rapid enlargement can occasionally be the main symptoms [9, 10], or mass effect on neighbouring structures, such as the ulnar nerve in our patient. Apart from presentation with complications, the fibrous dysplasia component is usually asymptomatic and, as in our case, may be incidentally discovered at the time of investigation of the soft tissue myxoma [9, 11]. The myxomas in Mazabraud's syndrome are most commonly associated with the polyostotic form, but are also described in association with the monostotic, McCune-Albright and forme fruste variants [9]. Similarly, myxomas, which are usually solitary, are noted as multiple masses in 81% of Mazabraud's patients, occurring in clusters [9,11]. Fibrous dysplasia is usually diagnosed in the first three decades of life, whereas myxomas tend to present later in the fourth and fifth decades [9, 10]. Although solitary myxomas have only a 1.4:1 ratio preponderance in females [10], females are affected twice as commonly as males in Mazabraud's syndrome [9]. The myxomas occur in the vicinity of the most severely affected bone, usually in the lower extremities, with a predilection for the right side [12].The masses average 4-6 cms in size, although some can be as large as 25 cms [4, 9]. Although malignant transformation in non-Mazabraud polyostotic fibrous dysplasia is estimated at 0.4% to 0.5% [13], incidence of malignant transformation of fibrous dysplasia to osteogenic sarcoma in Mazabraud's syndrome is probably higher. There are three described cases of sarcoma among the total 50 odd reported Mazabraud patients [2, 14, 15]. Malignancy in

the soft tissue myxoma component of Mazabraud's syndrome has not been reported.

Histologically, intramuscular myxoma is a pauci-cellular lesion composed of a mucoid basophilic matrix rich in mucopolysaccharide [16]. Characteristically, they lack a true capsule, and 59% have a circumscribed margin, while 41% are infiltrative [10]. Partial pseudocapsule is present in 52%, this feature permitting the mucoid matrix from the lesion to extend into the adjacent skeletal muscle, leading to peri-lesional muscle atrophy and reactive fat deposition (70%), and oedema (84%) [10,16,17]. Fluid filled spaces, described as intra-lesional cysts in the literature, are observed in 22 to 62% of myxomas [9, 10, 18]. The cysts are usually small, but may occasionally be large obscuring the more solid component [19].

Imaging of myxomas is largely a reflection of the histological nature. While conventional radiography is diagnostic for fibrous dysplasia, only 45% of myxomas are noted as a soft tissue fullness or mass, with no evidence of calcification or contiguous involvement of the adjacent bone by the myxoma [10]. Delayed radionuclide bone imaging may occasionally show mild homogeneous tracer uptake [10]. In keeping with the poor vascularity, angiography demonstrates only a mass effect by displacement of adjacent vessels or draping of the mass by the vessels, with the lesion per se being avascular or hypovascular [10].

Cross-sectional imaging appearances are dependent on the predominant fluid-like nature of the solid lesion, given the high mucin and low collagen content [10]. Sonographically, the masses appear well defined and hypoechoic with posterior acoustic enhancement [10,20], these features being akin to the ultrasound definition of a cyst. As intramuscular cysts are relatively uncommon, identification of a fluid-like lesion on ultrasound examination of a solid mass should raise possibility of a myxoma and prompt radiological investigation for possible co-existing fibrous dysplasia. Anechoic foci and pseudocapsule may be occasionally demonstrable [10, 20].

Computed tomography (CT) depicts a well defined, usually unencapsulated and homogeneous low attenuation mass (Hounsfield range from 10-60), occasionally demonstrating peri-lesional fat around the margin [10, 21]. Post contrast, enhancement occurs in 50% of masses, equally divided between heterogeneously diffuse and thick, peripheral, septal with nodular pattern [10].

MR imaging best mirrors the histological nature of the lesion, given its superior contrast range as compared to other modalities. The soft tissue myxoma is a well defined ovoid lesion, having low signal intensity on T1-weighted sequences and high signal intensity on fluid-weighted T2W or STIR sequences [17]. Imaging in the longitudinal plane of the lesion is most useful to detail margin borders and appreciate signal differences between the myxomas and adjacent muscle [17]. The margins are usually well defined with partial or absent capsule in 70% [10]. Although the 'split fat' sign is usually noted in association with an intermuscular mass, in the cases of intramuscular myxomas, a prominent cap of fat at the superior and inferior aspect of the lesion has been noted in 64% [10]. Post gadolinium-DTPA injection contrast, the enhancement pattern is variable. It can range from diffuse heterogeneous enhancement (57%) to a nodular and thick peripheral and septal pattern (43%) [10]. The predominantly myxoid rich spaces in the myxomas can be of similar intensity to the solid cellular areas on the fluid-weighted sequences. Post contrast MR imaging is not altogether effective in differentiating between the two, as the enhancement pattern of the solid cellular areas is unpredictable. The two characteristics reported as being strongly suggestive of myxoma and reliable in differentiation from other myxoid tumours, are the presence of a peritumoral fat rind (65% to 71% of myxomas) on T1-weighted sequence and increased signal in the adjacent muscle (55% to 79% of myxomas) on the fluid-weighted sequences [10, 17].

Table 1.

Differential Diagnosis of Soft Tissue Myxoma on Cross-sectional Imaging

A) CYSTIC LESIONS
- a) Synovial cyst
- b) Bursa
- c) Ganglia
- d) Abscess

B) NEUROGENIC LESIONS
- a) Neurofibroma
- b) Neurilemomma
- c) Malignant peripheral nerve sheath tumour

C) BENIGN MYXOID LESIONS
- a) Desmoid with myxoid degeneration
- b) Nerve sheath myxoma
- c) Myxolipoma
- d) Myxochondroma

D) MALIGNANT MYXOID LESIONS
- a) Myxoid liposarcoma
- b) Myxofibrosarcoma (myxoid MFH)
- c) Low-grade fibromyxoid sarcoma
- d) Extraskeletal myxoid chondrosarcoma
- e) Botryoid type rhabdomyosarcoma

The differential diagnosis of myxoma on imaging can be considered in four broad groups [4, 10, 17, 22, 23] (Table 1). Soft tissue myxomas are usually intramuscular, occurring in clusters, whereas cystic lesions are rarely intramuscular in location. Ultrasound is often used in the investigation of a soft tissue mass for its ability to differentiate between a solid versus cystic mass. However, when dealing with myxomas, this characteristic is not reliable given the similar sonographic characteristics of cystic lesions and solid myxomas. The location of the abnormality is more helpful in differentiation rather than ultrasound features. In 50% of myxomas, contrast enhanced CT and MR imaging may demonstrate the het-

erogeneous enhancement pattern, whereas cystic lesions often show only thin rim enhancement and delicate septa. Unlike soft tissue myxomas, neurogenic tumours are usually intermuscular, demonstrating an entering and exiting nerve, and the target sign on fluid-sensitive sequences [24]. Malignant myxoid lesions are the ones to be wary of, especially myxoid liposarcoma and myxofibrosarcoma (myxoid MFH). Myxoid liposarcoma is predominantly intermuscular and often shows a little intralesional fat in 42% to 92% cases [25]. Myxofibrosarcomas are more heterogeneous lesions with areas of haemorrhage and solid nodules which may enhance avidly [26].

The key to the diagnostic dilemma of an intramuscular soft tissue mass is the recognition of co-existing osseous abnormalities [27]. However, other lesions may also have both osseous and soft tissue abnormalities [27] such as Maffucci syndrome (enchondromatosis with soft tissue haemangiomas), neurofibromatosis, multiple myeloma and malignant melanoma, with metastases and lymphoma being rarer. These conditions can usually be differentiated on the basis of clinical presentation and imaging features. It is poignant to note that the patient in Mazabraud's report and our patient were both referred for management with a provisional diagnosis of neurofibromatosis.

Given the benign nature of myxomas, conservative management is usually adopted, with excision done if the mass is large or painful. Clinical and radiological awareness is paramount if the patient is to be spared the reported misadventures of extensive surgery, irradiation, or biopsy of further evolving myxoma masses [4]. Detection of myxoma should prompt a search for fibrous dysplasia, of assistance in differentiating from the more worrisome malignant myxoid tumours. Imaging characteristics, particularly on MR, can be helpful in prospectively diagnosing myxoma, but does not always obviate tissue diagnosis. Biopsy is the preferred mode, as fine needle aspiration can be non-diagnostic. Given the occasional reports of malignant transformation in the osseous fibrous dysplasia component of Mazabraud's syndrome, it is prudent to clinically follow-up the patient and be alert for any sudden change in symptomatology.

Myxoma is one of the most fascinating lesions encountered in radiology. It is histologically and behaviourly a solid mass, but the same histological composition of a predominant mucoid matrix is primarily responsible for the fluid-like characteristics on imaging. When dealing with an intramuscular mass seemingly with fluid-like characteristics, myxomas should be the strongest contender in the differential diagnosis, as true intramuscular cysts are far rarer. Recognition of myxomas should alert to the possibility of associated fibrous dysplasia and hence Mazabraud's syndrome, a relatively benign lesion in comparison to the confounding differential lesions including malignant myxoid sarcomas. Comprehension of these principles would enable the radiologist to avoid misdiagnosis and thereby mismanagement.

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