



Case report

Mazabraud's syndrome: Report of its first incidence in the Middle East and a literature review



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H I G H L I G H T S

- This is the first case report of Mazabraud's Syndrome from Middle East.
- Providing a literature review of the disease and its presentation.
- Discussing GNAS1 gene involvement in fibrous dysplasia as well as other diseases.
- Documenting the management plan done for the patient and the result of the follow up.

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Introduction: Mazabraud's syndrome, a rare benign disease with indolent course, is best described as an association between soft tissue myxoma and fibrous dysplasia of the bones. In this report, we describe the first case of this syndrome from Saudi Arabia.

Case presentation: A 24-year-old male in overall good health status, presented with progressive left knee swelling over 6 years with no other associated symptoms. The swelling measured 5 cm in diameter, with smooth surface, and soft palpable texture. Radiological examination followed by histopathological examination of the excised mass confirmed our diagnosis of Mazabraud's syndrome. The patient was closely followed up with systematic examination with no recurrence.

Discussion: Fibrous dysplasia, soft tissue myxoma and multiple endocrinological diseases like McCune-Albright syndrome characterize Mazabraud's syndrome. Furthermore, fibrous dysplasia is found to be associated with GNAS1 gene mutation. Many patients can have asymptomatic course of the disease but may present with pathological fractures, pain, and limitation of movement when the myxoma is near the joints or just simple cosmetically disturbing swelling like in our case.

Conclusion: Patients with such presentation need to be investigated thoroughly to rule out associated diseases and to evaluate the extent of such pathology. The improvement of radiological modalities can help in narrowing the differential diagnosis and following the patient to early detect the recurrence or any malignant transformation of the condition.

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1. Introduction

Henschen first reported Mazabraud's Syndrome in 1926 [1]. The classic description of benign soft tissue myxomas associated with

fibrous dysplasia of bone was later on detailed by Mazabraud et al. [2] To date, less than 100 cases of Mazabraud's Syndrome have been described in the literature [3,4] with more of female predominance [5].

Herein, and as to the best of our knowledge, we present the first case of this syndrome from Saudi Arabia and Middle East, with a brief review of the literature related to such presentation.

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2. Case presentation

A 24-year-old male patient who denies any past medical or surgical history with an overall general well being, presented to Plastic surgery outpatient clinic with a complaint of persistent swelling over the left knee that started 6 years prior to his presentation. The swelling was slowly progressive in size and not associated with pain. The patient denies any history of trauma to the site or history of other masses in the body. There was no history of discharges from the mass. It does not affect his gait or daily activity. Family history was unremarkable together with in-depth systematic review.

On physical examination, this was a young male patient with good body built. No skin lesions or obvious deformity were noticed. Chest, cardiovascular, and abdominal examination were within normal.

On local examination, a round swelling over the anterior aspect of the proximal tibia, 5 cm in diameter, No scars or punctum were seen and the overlying skin was intact. A smooth, non-tender, soft tissue mass was felt. It was not attached to the overlying skin, nor tethered to the underlying tibia. Left knee range of motion was full. Trans-illumination test together with Doppler signals were negative.

The patient was admitted to the hospital for further investigations and possible excisional biopsy, which was discussed with the patient. Routine labs were within normal limits.

In radiological assessment, X-ray of the left leg showed mild

increased bone density, subtle irregular lucency and mild expansion with thickening of the cortices involving the proximal metaphysis and diaphysis of left tibia. No periosteal reaction was seen. There was a large antero-medial soft tissue swelling at the level of tibial tuberosity (Fig. 1). The team elected to further investigate the patient with MRI of the left knee, tibia and fibula that showed intramedullary abnormal signal changes involving the proximal tibial metaphysis and diaphysis. A lesion with well-defined borders and endosteal scalloping without cortical break through or periosteal reaction was found. The lesion had intermediate intensity on T2-weighted cuts and low signal intensity on T1-weighted images with patchy enhancement on the images post contrast. The most likely findings represent fibrous dysplasia. There were multiple small patchy areas within the tibial and femoral epiphysis, which showed patchy enhancement, likely representing polystotic fibrous dysplasia. There was a subcutaneous multi-loculated multi-septated cystic lesion seen within the most superior part of the anterior medial aspect of the left leg measuring $6.6 \times 5.5 \times 7.4$ cm with pressure effect on the proximal tibia without direct invasion. It showed septation and capsular enhancement. It was either representing ganglion cyst or soft tissue myxoma. There was no evidence of joint pathology. The visualized muscle was grossly unremarkable (Fig. 2).

Based on the findings described above, Mazabraud's syndrome was considered as working diagnosis till definitive diagnosis can be achieved with excisional biopsy and histopathological assessment. Intra-operatively the mass was found to have dense attachment to

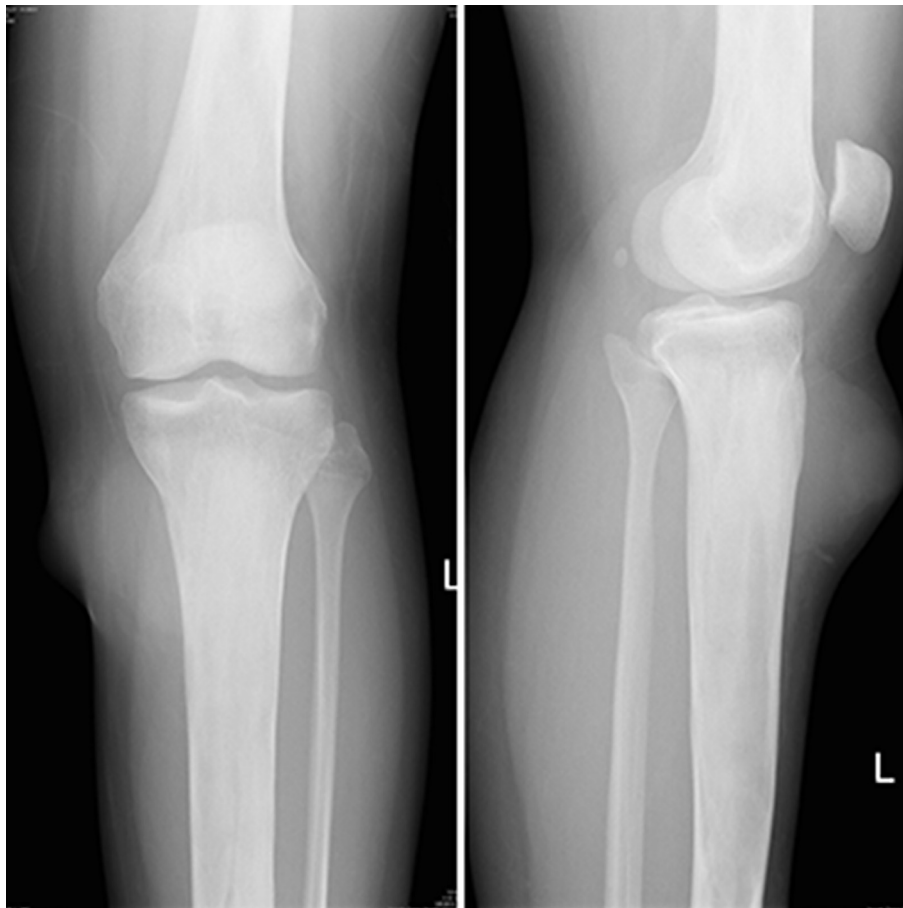


Fig. 1. X-ray of the left leg showed non-specific mild increased bone density, subtle irregular lucency and mild expansion with thickening of the cortices.

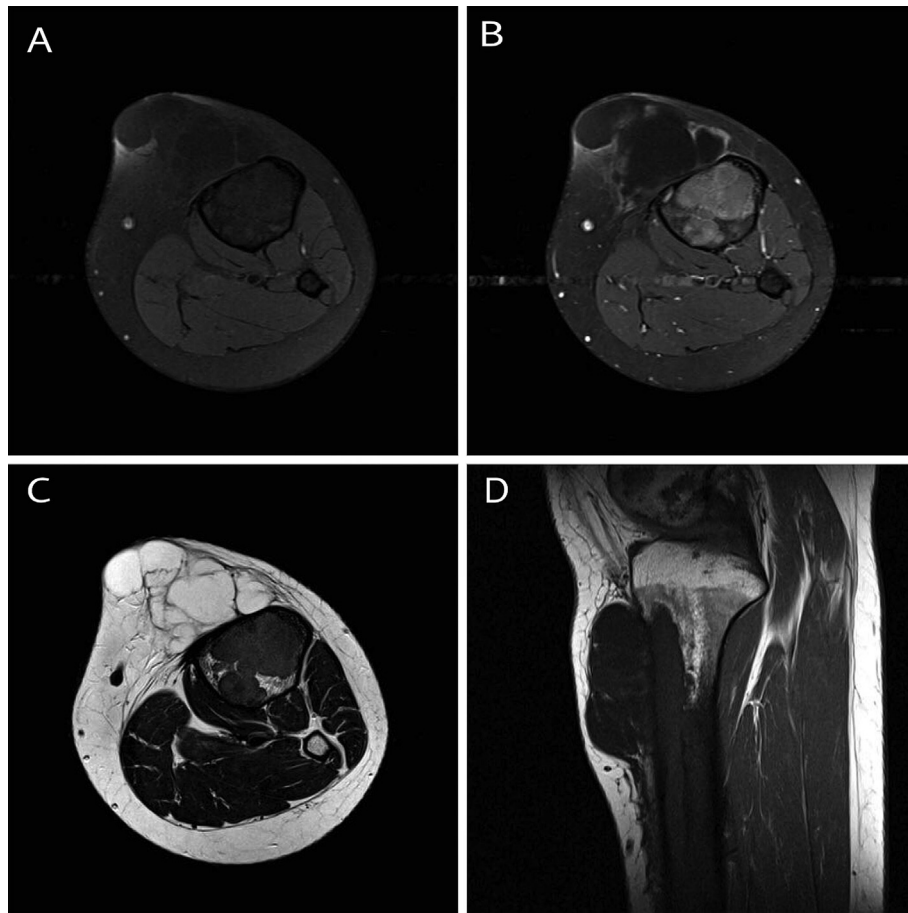


Fig. 2. MRI of the left knee, tibia, and fibula (A) T1 axial fat saturated cut without contrast (B) T1 axial fat saturated cut with contrast (C) T2 axial without contrast (D) T2 sagittal cut without contrast. Showed intramedullary abnormal signal changes involving the proximal tibial metaphysis and diaphysis. A lesion with well-defined borders and endosteal scalloping without cortical break or periosteal reaction is suggestive of fibrous dysplasia. A subcutaneous multi-loculated multi-septated cystic lesion was seen within the most superior part of the anterior medial aspect of the left leg with pressure effect on the proximal tibia without direct invasion. It shows septation and capsular enhancement representing soft tissue myxoma.

the anterior tibial surface with an overall jelly-like material. The periosteum was elevated and lifted with the mass. The mass was totally excised and sent to the histopathology lab (Fig. 3). Tru-cut biopsy was taken from the tibia surface and also sent for examination. Standard wound closure and dressing was done. Patient was discharged the next day with strict follow-ups.

The pathologic specimen was $8.0 \times 7.0 \times 5.0$ cm in size that was partially encapsulated. Cut surface showed a nodular architecture and overall gelatinous matter. Microscopic examination of the mass showed large hypo-cellular nodules separated by irregular fibro-collagenous bands. The nodules were formed of bland stellate and spindle cells lying in myxoid background that was poor in blood vessels. Mitotic activity was practically absent (Fig. 4a, b, and c). Immuno-histo-chemical studies showed that these cells were negative for desmin, smooth muscle actin, and for S100 protein. CD34 showed focal positivity. Another biopsy from a lytic bone lesion at the upper end of tibia consisted of a needle core measuring $2.0 \times 0.3 \times 0.3$ cm. Under the microscope, the lesion consisted of haphazardly arranged trabeculae of woven bone lying in cellular fibrous stroma. No osteoblastic rimming of these bone trabeculae present and diagnosed as fibrous dysplasia (Fig. 4d).

The patient was later on followed regularly in the clinic with no signs of local or distant recurrence. Written, explained and informed consent was taken from the patient for the purpose of publication of this report and any accompanying photographs.

3. Discussion

Fibrous dysplasia is a benign disease characterized by non-ossifying areas of bone that might be mono-ostotic or poly-ostotic. It was linked to certain mutation of the GNAS1 gene, on 20q13.2–q13.3 chromosome, that is encoding for a Gs(α) protein. Patients with fibrous dysplasia have an increase in GNAS1 activity and later on cellular proliferation rate together with some failure of differentiation and maturation of the developing bones in relation to soft tissue [6,7].

Such a condition can be associated with different endocrine pathologies as in McCune-Albright syndrome in which patients present with precocious puberty, goiter, and diabetes mellitus together with distinctive irregular cutaneous patched “café au lait spots”. When it is associated with soft tissue intramuscular myxoma, it is diagnosed as Mazabraud's Syndrome [8,9].

In the vast majority of Mazabraud's Syndrome patients, the fibrous dysplasia is poly-ostotic as in our patient, with multiple intra-muscular myxomas. The myxomas are benign mesenchymal tumors with hypovascular nature, and no epithelial lining. Myxomas in general have low incidence of recurrence [10]. Asymptomatic to painful mass of intramuscular myxomas that is progressively enlarging and causing some degree of limitation especially when near joints was noticed. This usually precedes the development of fibrous dysplasia that is also asymptomatic in its

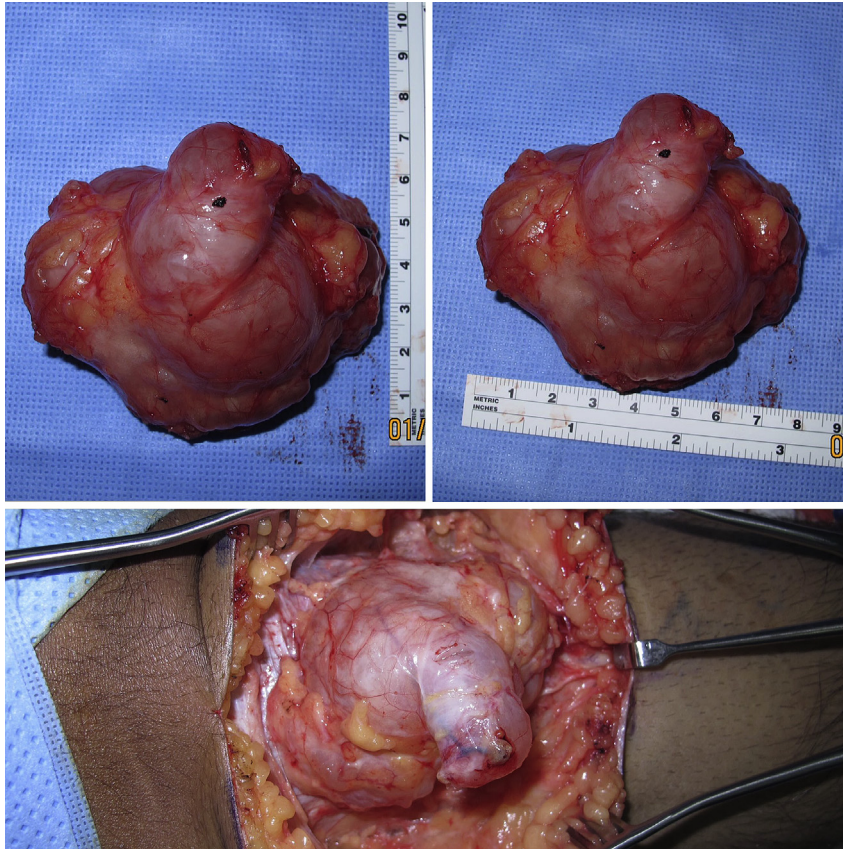


Fig. 3. Intraoperative pictures before and after excision.

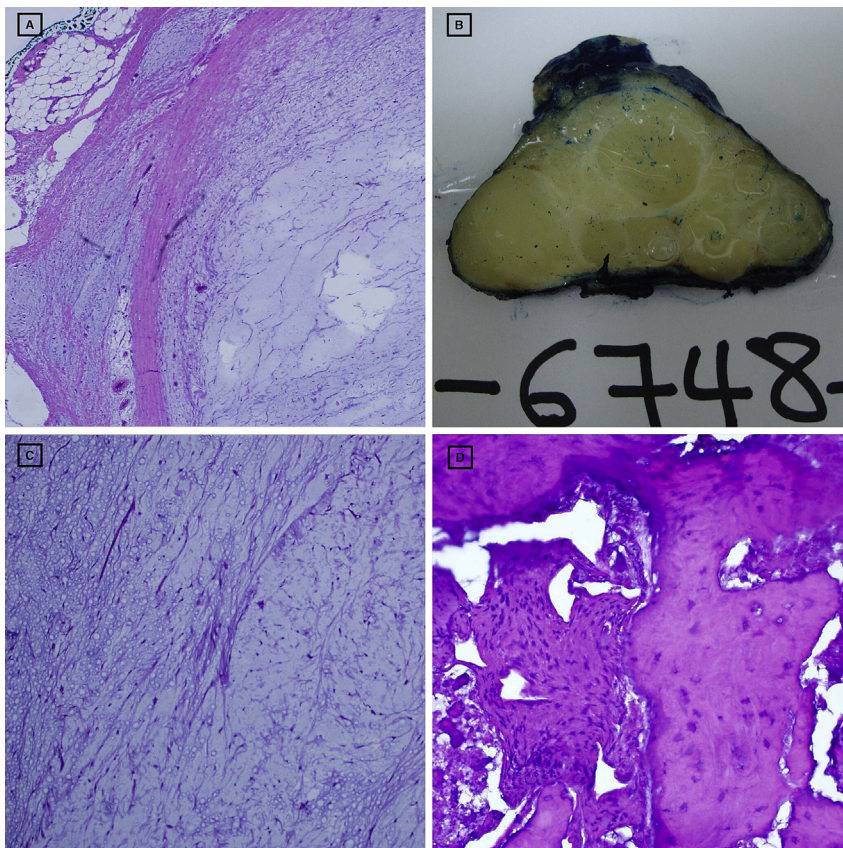


Fig. 4. (A) Low magnification showing hypocellular nodules separated by fibrocollagenous bands. (B) Gross appearance of the soft tissue mass with nodular and gelatinous surface. (C) High-power view highlights the lack of atypia and myxoid background. (D) Woven bone trabeculae with no osteoblastic rimming separated by cellular fibrous stroma.

course with some incidence of pathological fractures [11]. The utilization of various diagnostic modalities is of great importance when dealing with such case in which the characteristic radiological findings of plain X-ray showing non-specific increased bone density with thickening of the cortices. Magnetic resonant imaging showing cystic mass that is paralleled with meticulous pathological analysis as shown in this case might guide the diagnostic workup of such disease entity [10].

The management of such condition is based on the underlying pathology. Myxomas were noticed to follow a conservative course whereas surgical excision is indicated wherever symptoms like pain or pressure presents and/or as a tool to obtain histological diagnosis. Fibrous dysplasia as well follows a slowly progressive course. Conservative management is warranted with an aim to prevent pathological fracture and associated deformities in which surgical management is indicated [3,10]. Medical trial with Bisphosphonates has been mentioned in the literature with an aim to improve the associated pain with fibrous dysplasia and to improve the deformed bony architecture [12,13].

Close patient follow up is warranted although fibrous dysplasia is mostly benign, malignant transformation into osteogenic sarcomas was found. Mazabraud's Syndrome patients are at increased tendency with unclear mechanism [14]. For myxomas, malignant transformation has never been reported but an increased risk of recurrence was found either locally or at distant location especially with incomplete excision [5,14].

Deferential diagnosis involves multiple conditions that is based on radiological assessment and includes but not limited to myxoid neurofibroma, myxolipoma, myxoid liposarcoma, and myxoid chondrosarcoma together with several condition for the case of myxoma whereas simple bone cyst, enchondroma, non-ossifying fibroma, chondrosarcoma, and osteosarcoma for fibrous dysplasia [3].

4. Conclusion

Mazabraud's Syndrome is a rare disease with slow and indolent course. Knowledge of such disease process together with the radiological features of associated fibrous dysplasia and soft tissue intramuscular myxoma will help in guiding the diagnostic workup of such patients. Screening of other associated endocrinological disturbances is indicated in specific conditions. Frequent patient follow up is very important in detecting recurrent myxomas and preventing further deformities and monitoring for possible malignant transformation.

Ethical Approval

Informed consent was taken and signed by the patient for treatment and another one for publication.

Author contribution

All of the authors were involved in searching the literature, writing and editing this manuscript.

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Conflicts of interest

No conflicts.

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