Case Report

Osteosarcomatous Transformation in the Setting of Mazabraud’s Syndrome: A Case Report and Review of the Literature

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1. Introduction

Mazabraud’s Syndrome, named after the French physician Mazabraud in 1967 although first described by Henschen in 1926, is a rare disorder characterized by the presence of intramuscular myxoma(s) in association with monostotic or polyostotic fibrous dysplasia [1, 2]. With more than 100 reported cases of Mazabraud’s Syndrome, there are only six published cases of sarcomatous transformation of the fibrous dysplasia lesions in this specific setting [1–8]. Here, we report the development of an osteosarcoma arising from a fibrous dysplasia lesion in the femur of a 62-year-old female in the background of Mazabraud’s Syndrome.

2. Case Presentation

A 62-year-old otherwise healthy woman presented with three to four months of mechanical right groin pain radiating to the right buttock. She had a history of a benign soft-tissue mass in the right thigh that had been biopsied 10 years earlier, and the patient was told it was a myxoma. No other workup was done at the time, and no other lesions were clinically detectable. She had been very active and played tennis regularly. She was assessed with a hip ultrasound for her right groin pain and was prescribed physiotherapy. During physiotherapy, she felt a snap in her right groin and was no longer able to ambulate without a walker. Initial radiographs demonstrated a lucent intramedullary lesion within the subtrochanteric region—further characterized by a focally aggressive appearance with cortical destruction and lytic expansion of the lesser trochanter (Figures 1(a) and 1(b)). A ground-glass appearance, typical of fibrous dysplasia, was also noted in the mid-femoral shaft (Figure 1(c)).

Further workup included a Computed Tomography (CT) scan of the chest, abdomen, and pelvis which showed multiple hepatic and renal cysts but no evidence of a primary carcinoma or lung metastases. Bloodwork including serum protein electrophoresis was normal. A Total Body Bone Scan
(TBBS) revealed increased uptake in the right proximal femur and two areas of relatively mild uptake in the mid femur. Fat-suppressed T2 Magnetic Resonance Imaging (MRI) displayed an intermediate to high signal lesion within the medullary cavity of the proximal and mid right femoral shaft (Figure 2(a)). In line with the initial radiographs in which two benign sites of fibrous dysplasia were noted, in the third proximal lesion, there was cortical destruction with an extraosseous soft-tissue mass in the region of the lesser trochanter. Additionally, in keeping with the known myxoma, a soft-tissue T2 hyperintense mass within the medial distal thigh was also present (Figure 2(b)). On further review of the MRI images, five other myxomas were seen. The imaging features were consistent with Mazabraud’s Syndrome, with sarcomatous transformation of benign fibrous dysplasia in the proximal femur.

Due to the high risk of fracture, the patient was immediately placed on bedrest and a biopsy was not performed—as a preventative measure to reduce fracture risk. She was taken to the operating room and underwent wide resection of the proximal right femur with endoprosthetic reconstruction via a lateral approach. Along with bony specimens, one of the soft-tissue masses was also excised and sent to pathology for investigation (Figures 3(a) and 3(b)). Pathology later confirmed a high-grade osteosarcoma in the setting of fibrous dysplasia and a benign myxoma (Figures 4(a)–4(d)). There were no complications during the procedure.

Postoperatively, the patient stayed in the hospital for one week, with physiotherapy beginning on postoperative day one. Her postoperative course followed the normal trajectory of recovery with no major complaints or issues at her two-week follow-up. The patient declined adjuvant...
chemotherapy. The standard management of osteosarcoma at our center would include wide surgical excision with neo-adjuvant or adjuvant chemotherapy (methotrexate- and doxorubicin-based multidrug regimens). The patient is being followed to assess for complications and local or systemic relapse every three months with radiographs of the femur and chest. At one year postoperatively, there have been no complications or evidence of disease relapse.

3. Discussion

Fibrous dysplasia is typically a benign intramedullary fibroosseous lesion that is characterized by a disarrayed trabecula of woven bone separated by fibroconnective tissue [6, 7]. These lesions classically impact a single bone, with the femur being commonly involved. Malignant transformation of fibrous dysplasia is a rare event, with the most frequent sites of fibrous dysplasia and thus transformation being the craniofacial bones and proximal femur with secondary tumors inclusive of osteosarcoma, chondrosarcoma, and high-grade spindle cell sarcoma [7]. Myxomas are benign soft-tissue tumors defined by bland spindle- and stellate-shaped cells with a hypovascular, myxoid stroma [7]. To our knowledge, there have been no reported cases of malignant transformation of myxomas, although benign reoccurrences have been reported [7].
The association between fibrous dysplasia and intramuscular myxomas was first noted by Henschen in 1926, but the actual syndrome was self-named after Mazabraud in 1967 [1]. The general consensus of the recent literature is that both components of the syndrome are caused by the same postzygotic substitution mutation of \textit{GNAS1}—a gene that codes for an alpha subunit for a stimulatory G-protein involved with cell proliferation [4, 7]. The McCune-Albright Syndrome also shares fibrous dysplastic lesion due to a similar postzygotic mutation though likely not as penetrative into soft tissues as indicated by the lack of myxomas [2, 7].

As in the current case, Mazabraud’s Syndrome typically manifests as a polyostotic fibrous dysplasia with multiple intramuscular myxomas appearing close by [7]. The literature is indicative that the syndrome has a predisposition for females and often involves the long bones of the lower limbs bilaterally [4]. It is important to consider several differentials when approaching this presentation inclusive of the following: a primary bone malignancy, metastatic disease, multiple myeloma, lymphoma, and Paget’s disease. Radiographic findings of the fibrous dysplasia lesions classically include cortical thickening, cystic translucencies, and a ground-glass appearance [1]. Generally, these lesions prelude the appearance of the intramuscular myxomas [9]. Management of Mazabraud’s Syndrome is normally conservative unless there is functional impact.

With seven published cases, inclusive of the current case, the propensity for malignant transformation of a fibrous dysplastic lesion into a sarcomatous neoplasm in the setting of Mazabraud’s Syndrome remains a rare event (Table 1). A brief review of the reported cases notes that the average age of diagnosis of a sarcoma is 53 years of age, with a near equal predilection for gender. Patients usually present with an insidious onset of pain. Osteosarcoma was the most common malignant diagnosis followed by spindle cell sarcoma and chondrosarcoma. Transformations occurred in the femur (3 cases), tibia (2 cases), humerus (1 case), and radius (1 case). All previously reported cases underwent biopsy prior to definitive treatment. Unique to our case, we relied on a preliminary diagnosis based on imaging studies rather than biopsy to initiate management so as to reduce the risk of pathologic fracture.

### Table 1: Published studies of sarcomatous transformation of fibrous dysplasia in the setting of Mazabraud’s Syndrome specifically (McCune-Albright studies are excluded).

| Case | Author | Year | Title | Patient age | Gender | Diagnosis | Location | Presenting symptom |
|------|--------|------|-------|-------------|--------|-----------|----------|-------------------|
| 1    | Roze, R. et al. | 1967 | Fibrous dysplasia of bone and myxomas of the soft tissues. Localized sarcomatous degeneration [French] Osteogenic sarcoma and soft tissue myxoma in a patient with fibrous dysplasia and hemoglobin Mazabraud’s Syndrome with sarcomatous transformation: scintigraphic and radiologic imaging Osteosarcoma of the proximal part of the radius in Mazabraud syndrome. A case report Chondrosarcoma of the femur in Mazabraud’s syndrome: a first case study Mutational analysis of high-grade spindle cell sarcoma of the femur in Mazabraud’s syndrome Osteosarcomatous transformation in the setting of Mazabraud’s Syndrome: a case report and review of the literature | 72 | Female | Osteosarcoma | Right tibia (distal) | Pain |
| 2    | Witkin, G. et al. | 1986 | Osteogenic sarcoma and soft tissue myxoma in a patient with fibrous dysplasia and hemoglobin Mazabraud’s Syndrome with sarcomatous transformation: scintigraphic and radiologic imaging Osteosarcoma of the proximal part of the radius in Mazabraud syndrome. A case report Chondrosarcoma of the femur in Mazabraud’s syndrome: a first case study Mutational analysis of high-grade spindle cell sarcoma of the femur in Mazabraud’s syndrome Osteosarcomatous transformation in the setting of Mazabraud’s Syndrome: a case report and review of the literature | 41 | Male | Osteosarcoma | Left tibia | Asymptomatic |
| 3    | Nyguen, B. et al. | 2005 | Mazabraud’s Syndrome with sarcomatous transformation: scintigraphic and radiologic imaging | 48 | Male | Spindle cell sarcoma | Right humerus (proximal) | Pain |
| 4    | Crawford, E. et al. | 2009 | Mazabraud’s Syndrome with sarcomatous transformation: scintigraphic and radiologic imaging | 63 | Male | Osteosarcoma | Right radius (proximal) | Pain |
| 5    | Szymanski, C. et al. | 2015 | Mazabraud’s Syndrome with sarcomatous transformation: scintigraphic and radiologic imaging | 51 | Female | Chondrosarcoma | Left femur | Pain and swelling |
| 6    | Calleja, M. et al. | 2018 | Mazabraud’s Syndrome with sarcomatous transformation: scintigraphic and radiologic imaging | 36 | Female | Spindle cell sarcoma | Right femur | Pain |
| 7    | Ghert, M. et al. | 2018 | Mazabraud’s Syndrome with sarcomatous transformation: scintigraphic and radiologic imaging | 62 | Female | Osteosarcoma | Right femur (proximal) | Pain |

### 4. Conclusion

In summary, we present a case of an otherwise healthy 62-year-old female, with a known history of an untreated myxoma, diagnosed with a high-grade osteosarcoma secondary to Mazabraud’s Syndrome. With only six previously published cases, this malignant transformation of an otherwise relatively benign syndrome clearly adds further weight to the previously reported cases. Although malignant transformation...
remains a rare event, close monitoring of asymptomatic patients with this condition for radiographic changes in their lesions and/or clinical symptoms is recommended.

Consent

The patient has given informed consent to have her case published.

Conflicts of Interest

The authors declare that they have no competing interests.

Authors’ Contributions

IM and MG wrote and completed the major revisions for this paper. SP provided the gross anatomy and histology review and descriptions. NP provided the radiological review and descriptions. All authors have read, reviewed, and approved the final manuscript.

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