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Case study

Cytogenetically confirmed low-grade fibromyxoid sarcoma arising from the tibia ☆

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Summary Low-grade fibromyxoid sarcoma is a rare soft tissue tumor with a benign histologic appearance but comparatively aggressive clinical course. These discrepant features make it extremely important to diagnose early so that appropriate management can be initiated. This diagnosis often hinges on the presence of the hallmark cytogenetic aberration, a balanced 7;16 translocation resulting in a *FUS-CREB3L2* fusion gene. Although this neoplasm most commonly arises in the deep soft tissue of the lower extremities, it has been reported to arise from a wide variety of sites including intraabdominal and intracranial locations. Only 1 previous study has described low-grade fibromyxoid sarcoma as arising from a bony site; however, cytogenetic and immunohistochemical confirmation was not available at that time. Herein, we describe the first ever cytogenetically confirmed case of low-grade fibromyxoid sarcoma arising as a primary bone tumor in the tibia of a 35-year-old woman.

1. Introduction

First described by Evans in 1987, low-grade fibromyxoid sarcoma (LGFMS) is a rare soft tissue tumor that typically arises in the deep soft tissues of the lower extremities in young adults [1,2]. The diagnosis can be difficult to make and often relies on confirmatory cytogenetics to detect the balanced 7;16 translocation that is the hallmark of this entity [3,4]. Furthermore, although these tumors classically arise in the deep soft tissues of the groin and lower extremity, rare cases have been reported in subcutaneous [5], mesenteric [2], and even intracranial [6] locations. To date, however, only 1 case report of a tumor arising in the talus has suggested LGFMS arising as a primary bone tumor [7]. Confirmatory cytogenetic studies were not available in that report. In this case, we report the first ever cytogenetically confirmed case of an LGFMS arising in the tibia of a young woman.

2. Case report

2.1. Clinical features

A 35-year-old woman presented to an orthopedic clinic after noting pain and swelling over her left anterior proximal leg. Radiographs of the left tibia and fibula at that time showed a multiloculated expansile lytic lesion located eccentrically on the medial aspect of the proximal tibia extending beyond the normal cortical contour with a thin sclerotic rim and distorted internal architecture (Fig. 1A).

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The patient was referred for follow-up with an orthopedic clinic but was noncompliant with follow-up.

She subsequently presented to an emergency department 5 years later with increasing left leg pain and difficulty with ambulation. Physical examination revealed a proximal anterior fullness over the left tibia without deformity, erythema, or tenderness. Range of motion, sensation, and strength were intact. Radiographs of the left tibia and fibula (Fig. 1B) revealed interval progression of the multiloculated, expansile lesion in the proximal tibial diaphysis. The lesion measured 6 × 7 × 13.5 cm and demonstrated an exophytic extraosseous extension posteriomedially. A magnetic resonance imaging was performed (Fig. 1C and D) and showed a marrow-replacing lesion that extended through the medial cortex of the tibia with a large posteromedial soft tissue component involving the posterior tibialis and flexor digitorum muscles with associated compression of the tibial nerve.

2.2. Histologic, immunohistochemical, and cytogenetic features

A biopsy performed at another institution showed a low-grade spindle cell neoplasm in an extensively collagenized background (Fig. 2A). The nuclei were bland with dispersed chromatin and inconspicuous nucleoli without mitoses or pleomorphism. Immunohistochemistry showed the tumor to be focally positive for smooth muscle actin and epithelial membrane antigen (EMA) while being negative for CD99, AE1/AE3, S-100, CD57, CD68, and CD34. No further classification was given at that time. The lesion was, however, favored to be a nerve sheath tumor.

A computed tomography–guided fine needle aspiration and core biopsy were performed. Cytologic examination of the fine needle aspirate revealed spindle cells with plump but bland nuclei in a background of myxoid matrix material (Fig. 2B). Histology on the core needle biopsy revealed a moderately cellular tumor composed of cytologically bland spindle cells arranged in short fascicles with other areas showing a more storiform arrangement (Fig. 2C). Palisading could be noted in a few areas as well as focal myxoid change. Necrosis and mitoses were absent. Immunohistochemical staining revealed the tumor to be strongly positive for MUC4 (Fig. 2D) with weak patchy positivity for EMA. Some cytoplasmic staining for STAT6 and β-catenin was noted, but no nuclear staining was present. The tumor was also negative for MDM2, TLE, Desmin, smooth muscle actin, S-100, AE1/3, and CD34.

Fluorescence in situ hybridization (FISH) was then performed using dual-color break-apart probes flanking the common breakpoint site in the *FUS* gene. Positive break-apart signals were found in the majority of the tumor cells, and a diagnosis of low-grade fibromyxoid sarcoma was rendered (Fig. 3).

3. Discussion

LGFMS is typically a rare soft tissue tumor representing less than 1% of soft tissue sarcomas, with an estimated incidence of 0.18 per million [8]. The diagnosis, however, is an extremely important one to make, as, despite its "benign" histologic appearance, LGFMS has a relatively malignant clinical course. It is commonly unencapsulated and infiltrating, making complete excision difficult without a wide resection. Local recurrence is estimated to occur in up to 64% of cases [2]. Different from a low-grade soft tissue sarcoma,

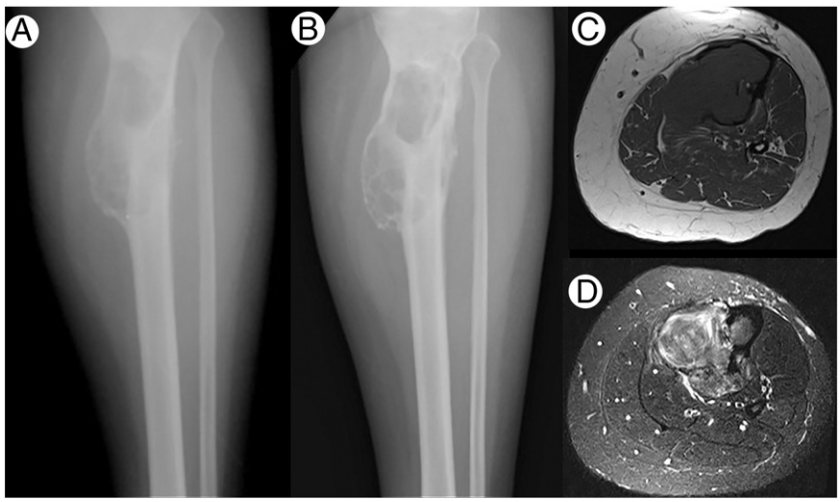

Fig. 1 A, Anteroposterior radiograph of the left tibia at initial presentation showing a multiloculated lytic lesion emanating from the proximal tibia. B, Anteroposterior radiograph of the left tibia at follow-up presentation (5 years later) showing interval growth of the multiloculated lytic lesion. C and D, Magnetic resonance imaging studies. On T1 hypointense/isointense (C) and short-T1 inversion recovery heterogeneous (D) lesion extending from the proximal tibia is noted to have a large soft tissue component involving the posterior tibialis and flexor digitorum muscles and compression of the tibial nerve.