Human Pathology (2015) **46**, 461–466

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Human PATHOLOGY

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Case study

# Pediatric low-grade fibromyxoid sarcoma mimicking ossifying fibromyxoid tumor: adding to the diagnostic spectrum of soft tissue tumors with a bony shell☆

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Received 18 August 2014; revised 5 November 2014; accepted 12 November 2014

**Keywords:**
Bone;
Low-grade fibromyxoid sarcoma;
Ossification;
Ossifying fibromyxoid tumor;
Superficial;
Subcutaneous;
Pediatric

**Summary** We describe a case of superficial low-grade fibromyxoid sarcoma (LGFMS) in a 12-year-old boy, confirmed by the detection of *FUS-CREB3L2* fusion transcripts by reverse-transcription polymerase chain reaction and *FUS* rearrangement with fluorescence in situ hybridization, which had morphological features similar to ossifying fibromyxoid tumor (OFMT), including an almost complete rim of mature, metaplastic bone. LGFMS and OFMT can appear morphologically similar, with bland ovoid cells within a fibrous to myxoid matrix. Both can occur superficially; and whereas MUC4 immunoreactivity is characteristic of LGFMS, this can also be seen in some OFMTs. As the morphological spectrum of LGFMS is wide, we highlight the potential for diagnostic confusion with OFMT, which is clinically pertinent as most OFMTs behave in a benign manner whereas LGFMS is a malignant neoplasm with a propensity for local recurrence and a significant metastatic rate.


## 1. Introduction

Low-grade fibromyxoid sarcoma (LGFMS) is a fibroblastic soft tissue neoplasm most frequently occurring in the deep soft tissues of adults, which is characterized by its classically bland histological features of spindle cells in a variably collagenous and myxoid matrix. Despite its bland morphology, it can behave aggressively, with multiple local recurrences and distant metastases, predominantly to lungs. LGFMS is more rarely encountered in pediatric patients; superficial forms may affect children more often than those occurring deeply and appear prognostically better than deep LGFMS [1]. We describe an unusual case occurring in the subcutaneous tissues of the back in a 12-year-old boy, with an almost complete rim of metaplastic bone and which had morphological features similar to ossifying fibromyxoid tumor (OFMT). These 2 distinct neoplasms can show significant morphologic overlap not only in small biopsy

☆ Disclosures: The authors have no conflicts of interest or funding to disclose.

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http://dx.doi.org/10.1016/j.humpath.2014.11.004
0046-8177/

specimens but even in excision material. Both can occur at superficial sites; and whereas MUC4 expression is characteristic of LGFMS, it can also be seen in some OFMTs. As the histological spectrum of LGFMS is wide and remains to be fully characterized, particularly in the pediatric population, we highlight the potential for diagnostic confusion with OFMT. This is clinically significant because most OFMTs behave in a benign manner whereas LGFMS is a malignant neoplasm with a propensity for local recurrence and a significant rate of metastasis.

## 2. Case history

A 12-year-old white male presented with recent enlargement of a mass in the central lumbar region, which had been present for 7 years, having enlarged gradually over the past 3 years and more rapidly over the last 3 months. It was uncomfortable when leaning back in a chair but was otherwise asymptomatic. The patient had been seen by several local physicians over the preceding years, and the mass had been thought to represent either a lipoma or a cyst. He was otherwise well with no other lesions, and there was no previous medical history. Clinical examination showed a firm, mobile, well-defined, nontender, approximately 3-cm diameter mass in the superficial subcutaneous tissues of the lumbar back. Magnetic resonance imaging scan showed a 2.3-cm lobulated mass in the subcutaneous tissues overlying the lumbosacral spine, slightly to the right of the midline. The lesion had internal septations with increased signal on T1-weighted and short tau inversion recovery sequences. Radiologically, its nature was uncertain; but there were no obvious aggressive or invasive features. Chest computed tomography scan showed no pulmonary metastases. A biopsy of the mass was performed, and it was then widely excised. Surgically, it was noted to appear purely subcutaneous, but the surgical resection was extended to the interspinous ligaments. The patient made an uneventful postoperative recovery and is well 6 months after surgery.

## 3. Materials and methods

The histopathological features were noted, and immunohistochemistry was performed on formalin-fixed, paraffin-embedded (FFPE) material using the following commercial antibodies: AE1/AE3 (Zymed Laboratories, San Francisco, CA; 1:50), epithelial membrane antigen (EMA) (Dako, Glostrup, Denmark; 1:400), desmin, h-caldesmon, CD68 (Dako; 1:50), smooth muscle actin (SMA), glial fibrillary acidic protein (GFAP), neurofilament (Dako; 1:200), chromogranin (Dako; 1:300), myogenin, CD99, synaptophysin, MIB1 (Dako; 1:100), S100 protein (Dako; 1:1500), CD34, CD23 (Novocastra Laboratories, Newcastle-upon-Tyne, UK; 1:30), MyoD1 (Novocastra; 1:50), CD35 (Dako; 1:20), CD56 (Invitrogen, Camarillo, CA, USA; 1:50), CD117 (Dako; 1:500), claudin-1 (Zymed; 1:25), STAT6 (Sigma-Aldrich, Gillingham, UK; 1:1500), MUC4 (Santa Cruz Biotechnology, Heidelberg, Germany; 1:50), and INI1 (Becton Dickinson, Plymouth, UK; 1:100). Molecular genetic and molecular cytogenetic analyses were performed on FFPE material for *FUS* and *EWSR1* rearrangements by fluorescence in situ hybridization (FISH) and for specific fusion transcripts by reverse-transcription polymerase chain reaction (RT-PCR). For FISH, 1-$\mu$m–thick FFPE sections were dewaxed overnight at 60°C, treated with hot buffer wash at 80°C (2-3 hours) then proteolytic enzyme treatment at 37°C, and washed in distilled water then an alcohol series before addition of *FUS* or *EWSR1* DNA probes (Abbott Laboratories Ltd, Maidenhead, UK). Hybridization was performed overnight according to manufacturer's protocols. RT-PCR was performed to assess for *FUS-CREB3L2* fusion transcripts according to standard methods.

## 4. Results

### 4.1. Histopathological findings

Gross examination of the main specimen showed an ellipse of skin with a central 2.5 × 2.5 × 1.4–cm subcutaneous nodular tumor, with a homogeneous beige cut surface (Fig. 1A). No hemorrhage or necrosis was present. Core biopsy and excision specimens showed similar histologic features of a subcutaneous lobulated, moderately cellular neoplasm that was surrounded by a thin fibrous pseudocapsule. Almost completely surrounding the lesion, in the area of the fibrous pseudocapsule was a thin shell of mature, metaplastic-type bone (Fig. 1A-D). The tumor was composed of cells mostly with rounded or ovoid vesicular

**Fig. 1** A, LGFMS. Grossly, this is a subcutaneous, maximally 2.5-cm nodular tumor, with a firm, homogeneous beige cut surface. B, The excision specimen shows a rounded lesion within the subcutis, which is surrounded by a fibrous pseudocapsule. There is a peripheral shell of mature bone almost completely surrounding the neoplasm, in the region of the pseudocapsule (hematoxylin and eosin, ×1). C, The lesion has a collagenous to hyalinized stroma, in which small cells are embedded in patternless distributions. Note the absence of discernible morphology of LGFMS (hematoxylin and eosin, ×40). D and E, The tumor is largely composed of uniform, bland, rounded to ovoid cells with indiscernible cytoplasm, sometimes with a reticular pattern (E) (hematoxylin and eosin, ×40 [D] and ×200 [E]). F, The rounded and ovoid vesicular nuclei have even chromatin. They lack the cytology of typical LGFMS, in which the nuclei have a flattened, slightly angulated appearance (hematoxylin and eosin, ×200). G, In some areas, the neoplasm is more cellular, with sheets of moderately pleomorphic ovoid cells with nuclear hyperchromasia (hematoxylin and eosin, ×200). H, The tumor shows diffuse cytoplasmic expression of MUC4, characteristic of LGFMS. This is also seen in some OFMTs, although this is usually in a focal distribution (×100).