Case Report

rare tumors

Rare Tumors
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Primary lung low-grade fibromyxoid sarcoma: A rare case with A diagnostic dilemma

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Abstract

Low-grade fibromyxoid sarcoma (LGFMS) is a rare, low-grade malignant soft tissue tumor that is often mistaken for benign or more rarely malignant tumor types. Commonly, this tumor affects young adults and typically arises in the deep proximal extremities or trunk with frequent recurrences and can metastasize to the lungs many years late. Visceral LGFMS is extremely rare. Only a few cases of primary LGFMS of the lung have been reported. Here, we present the clinical, gross, microscopic, and immunohistochemical characteristics of Evans tumor occurring in the lung with a review of the literature and discuss the differential diagnosis in this exceptional localization.

Keywords

Evans tumor, Muc 4, low-grade fibromyxoid sarcoma, lung soft tissue sarcomas

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Introduction

Low-grade fibromyxoid sarcoma (LGFMS) is a rare, low-grade malignant tumor that occurs most frequently in the proximal extremities and the trunk of children and young adults. This tumor was first described by Evans when he reported bland fibromyxoid neoplasms arising in the deep soft tissue of two young women and emphasized its deceptively benign appearance.[1] Lung involvement of LGFMS is extremely rare. Only 5 cases of primary lung LGFMS metastases in the lung have been reported[2–6] (Table 1). This *tumor is characterized by a benign spindle cell appearance but a malignant potential.*

We report herein the LGFMS arising from the lung parenchyma in a 21-year-old girl.

Case Report

A 21-year-old man with no smoking history and no significant past medical history presented with a persistent cough. Subsequent imaging revealed a lobular heterogeneous enhancing mass arising in the right lower. The physical exam was unremarkable. Computed tomography of the thorax as part of the preoperative evaluation showed the absence of other localization.

The mass was surgically removed. A lobectomy was performed for diagnostic and therapeutic purposes.

Grossly, the tumor was multinodular, firm, and surrounded by a thin, and fibrous pseudo-capsule. It measured up to 6 cm in greatest dimension, endobronchial with an

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Table 1. Cases of pulmonary low grade fibromyxoid sarcoma.

Authors	Age/sex	Pathology	Follow up (Months)
Magro et al[2]	20/F	LGFMS with rosette	Unknown
Kim et al[3]	50/F	LGFMS with rosettes	Unknown
Cuneyt et al[4]	16/F	LGFMS	No recurrences, no metastases (24)
Perez et al[5]	32/M	LGFMS	Unknown
Bartuma et al[6]	77/M	LGFMS with rosettes	Unknown

F: Female; M: Male. LGFMS: Low grade fibromyxoid sarcoma.

extension into the underlying lung parenchyma and no attachment to the visceral pleura. The cut surface had a whorled white tan appearance with focal myxoid and hemorrhage changes (Figure 1). The surgical margin was free of tumors.

Microscopically, the tumor was well-circumscribed and low to moderately cellular. It was composed of bland spindle cells arranged in crisscrossing fascicles within hyaline to myxoid stroma that tends to vary in different areas of the tumor (Figure 2). Tumor cells had scant wispy cytoplasm, uniform elongated nuclei with finely clumped chromatin and small inconspicuous nucleoli. The cells showed little mitotic activity. Epithelioid cells were present focally. There was a network of branching capillary-sized blood vessels. In some areas, the cellularity was increased, in a fibrous background. The transition between fibrous and myxoid areas was often abrupt. The pleura was free of tumors. Five pedicular lymph nodes were removed and they were reactive. Immunohistochemically, the neoplastic cells showed immunoreactivity for CD99 and MUC4 with a strong and diffuse expression of this antigen (Figure 3). They were negative for CK, SMA, EMA, H-caldesmon, Desmin, STAT6, MDM2, CD34, hormonal receptors, ALK (5A4, P80), and PS100. Cytogenetic and Molecular Genetic study was performed in France and showed the absence of SS18/SYT gene rearrangement.

Pathological diagnosis was made as "low-grade fibromyxoid sarcoma". Her postoperative course was uncomplicated and chemotherapy or radiotherapy wasn't given. She has remained well with no evidence of disease 6 months later.

Discussion

LGFMS, formerly called Evans tumor, is a low-grade sarcoma of the deep soft tissue of the proximal extremities or trunk in young adults. It is very rare in the viscera as a primary site, with only a few cases reported in the literature. Here, we present a case of Evans tumor occurring in an unusual and rarely reported location; an intra-thoracic mass arising within the lung.

In this location, common symptoms include persistent cough, chest pain, dyspnea on exertion, and pleural effusion.[5] To confirm the lung as a primary site, metastasis from an extrathoracic site needs to be excluded.

Although typically grossly well-circumscribed, there is often extensive microscopic infiltration into the surrounding lung tissues. On a cut section, the tumor often has a yellow-white appearance. Sometimes, focal areas with a glistening appearance secondary to the accumulation of myxoid ground substance are observed and some tumors exhibit cystic degeneration.

Histologically, LGFMS is of low or moderate cellularity and is composed of bland spindle-shaped cells with small hyperchromatic oval nuclei. The cells have indistinct pale eosinophilic cytoplasm and show only mild nuclear pleomorphism with little mitotic activity.[7–9] The cells are deposited in a fibrous and myxoid stroma that tends to vary in different areas of the tumor. The vasculature is prominent as a network of curvilinear and branching capillary-sized blood vessels more distinguishable in the myxoid zones.

Hyalinizing spindle cell tumor with giant rosettes is an unusual fibrous tumor first delineated in 1997 by Lane et al in a series of 19 cases.[10] Although originally considered distinctive entities, LGFMS and hyalinizing spindle cell tumors with giant rosettes are now regarded as part of a histologic spectrum.

Several arguments confirm this: similarity in age and location, the virtual identity of the spindled stroma including the occasional presence of intermediate-grade fibrosarcoma, and the presence of the same characteristic translocation [t(7;16)].

Despite its deceptively bland histologic appearance, LGFMS has a high rate of local and repeated recurrence as well as pulmonary metastases in a significant percentage of cases. In our case, the tumor arises within the lung as a primary site.

Immunohistochemically, the neoplastic cells in LGFMS show consistent immunoreactivity for MUC4, a transmembrane glycoprotein that plays a role in cell growth signaling pathways.[11] These tumor cells may show focal immunoreactivity for muscle markers, including smooth muscle actin, muscle-specific actin, and desmin, but most cases are negative for these antigens. Other markers that are usually negative include CD34, S-100 protein, and cytokeratins.[12,13] Our case presents strong and diffuse positivity for MUC4 and was negative for muscle markers and cytokeratins. Cytogenetically, this tumor is

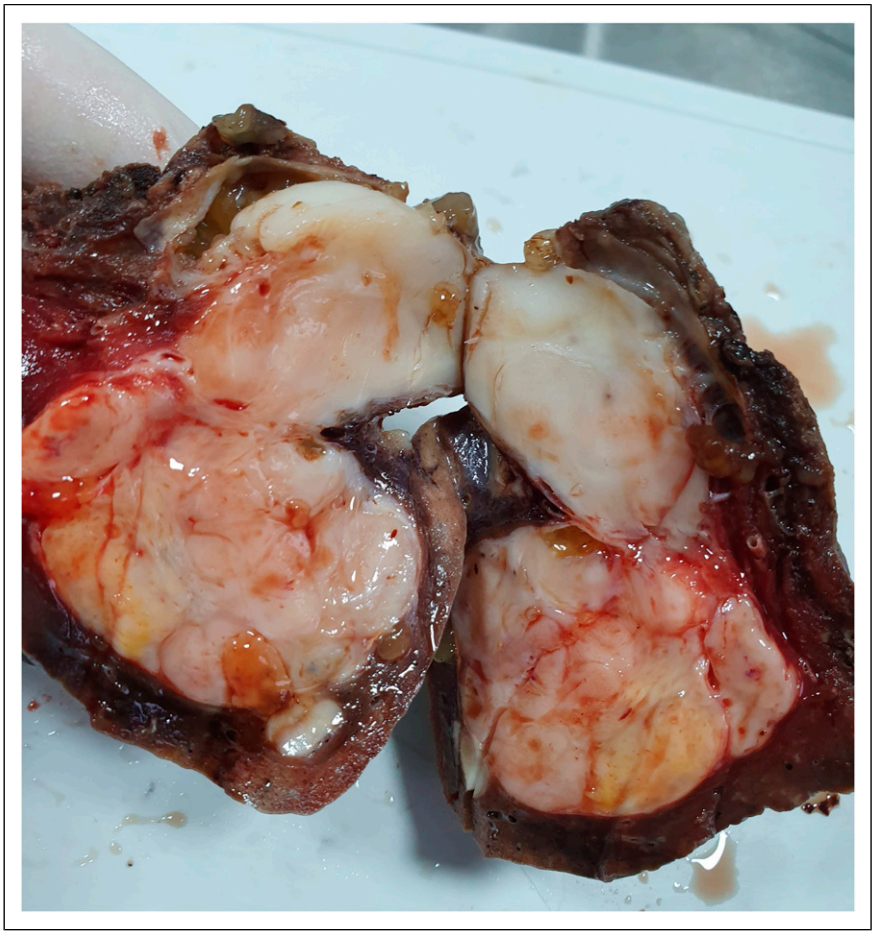

Figure 1. The tumor was endobronchial with an extension into the surrounding lung parenchyma and no attachment to the visceral pleura. The cut surface had a whorled white tan appearance with focal myxoid and hemorrhage changes.

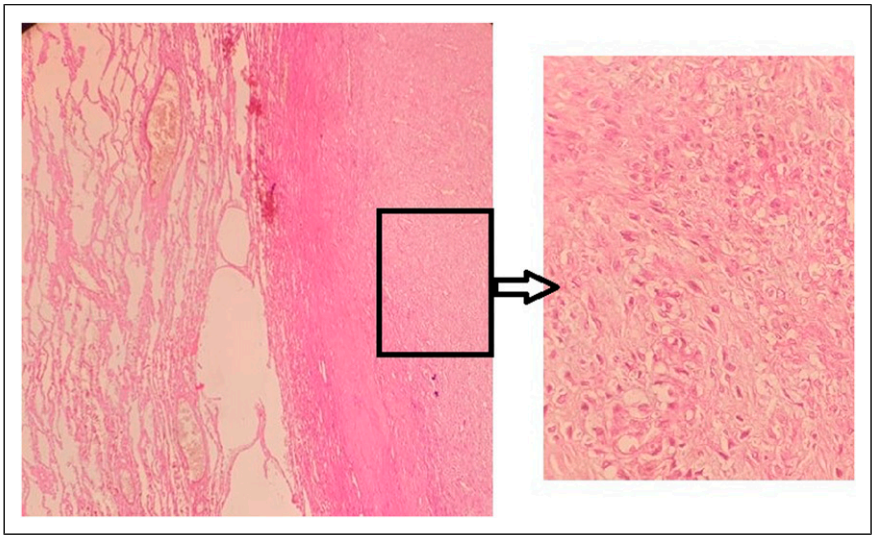

Figure 2. Crisscrossing fascicles of bland spindle tumor cells within hyaline to myxoid stroma that tends to vary in different areas of the tumor.

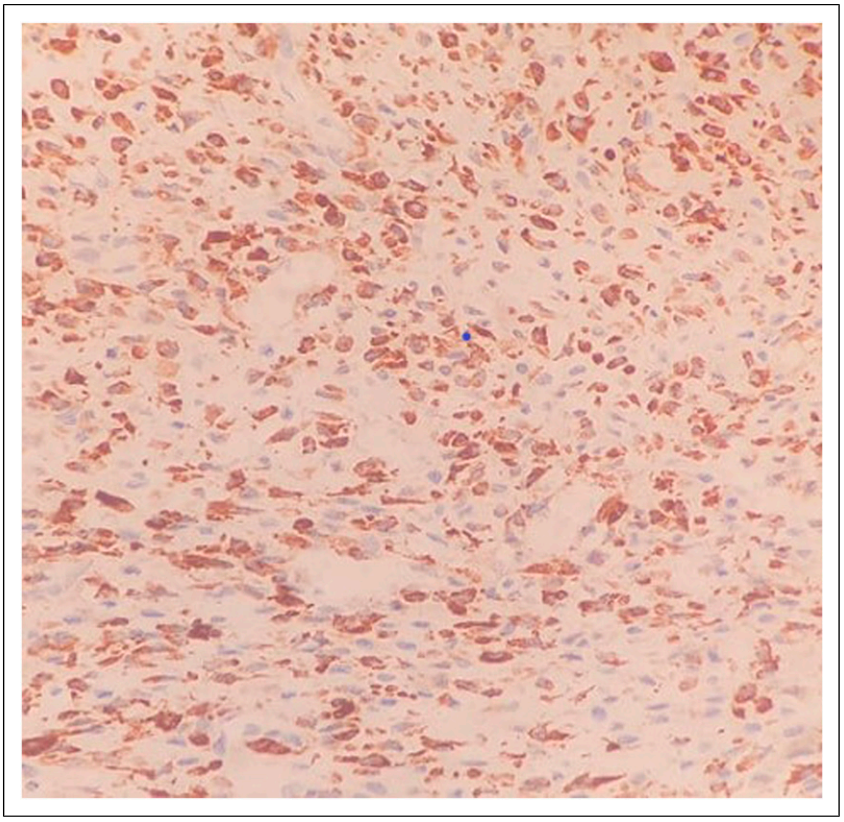

Figure 3. The neoplastic cells showed strong nuclear immunoreactivity for MUC4.

characterized by the presence of a characteristic translocation involving the FUS gene on chromosome seven and the CREB3L2 gene on chromosome 16.[14–17] Although not entirely specific, MUC4 has changed the diagnostic approach of these tumors and restricted the use of molecular testing to cases with atypical morphology, on a small specimen, or when MUC4 is negative.

Diagnosis of LGFMS is still difficult because of its bland-looking histologic features that can potentially be confused with other benign or low-grade spindle cell proliferations with myxoid morphologies.

Malignant peripheral nerve sheath tumors can contain myxoid foci, however, tumor cells arranged in an irregular fascicular growth pattern, are more elongated and their nuclei are wavy. They are reactive for S-100 protein in up to 60% of cases. In our case S-100 protein was negative. *Spindle cell liposarcoma* always contains an atypical lipomatous component that includes the presence of lip blasts. The myxoid zones of LGFMS may also resemble *myxoid liposarcoma*, particularly the cases with a well-developed plexiform vascular pattern. However, LGFMS lacks lipoblasts, and adequate sampling always reveals fibrous areas. No lipoblast was seen in our case and MDM2 was also negative. Besides alternating fibrous and myxoid zones were observed.

LGFMS may be confused with *myxofibrosarcoma*. The latter is uniformly myxoid, lacks alternating fibrous zones, and always has a greater degree of nuclear pleomorphism and hyperchromasia.

A *solitary fibrous tumor* (SFT) was also considered. SFTs are usually cytologically bland, and negativity for STAT6 immunohistochemical stain is the most sensitive method to rule it out. This was the case and STAT6 was negative. Spindle cell morphology and the lung location yielded suspicion of *synovial sarcoma*. Molecular testing for the SYT gene breaks apart by FISH, a highly specific test that is positive in about 95% of synovial sarcomas, was performed and was negative thus ruling it out. Since this case, the wide availability of a monoclonal antibody targeting the fusion gene SS18-SSX has made molecular testing less useful.

Others differential diagnoses can be evocated such as fibrosarcoma. It is characterized by a herringbone fascicular pattern and the absence of myxoid component. It is a diagnosis of exclusion that should be made with much hesitation.[17] A myxoid neurofibroma present a background of thick collagen bundles. Tumor cells have Wavy nuclei that expess p100.

Desmoid type fibromatosis usually lacks myxoid areas (sometimes can be myxoid, though), fibrous cells are aligned

in broad sweeping fascicles, straighter. Tumor cells appear more like reactive fibroblasts. Distinct ectatic vessels are present. On immunohistochemistry, diffuse or occasionally focal nuclear beta catenin staining is observed.[18]

In conclusion, primary lung LGFMS is a rare entity with a moderate to high rate of recurrence and metastasis that challenge pathologists. It should be considered in the differential diagnosis of lung or more generally in visceral soft tissue tumors.

Author contributions

AA conceived the project. AA TA contributed by providing the data. YH analyzed the data. YH wrote the manuscript. AA, CM, and HR revised the manuscript critically for important intellectual content, and Supervision., Validation: AA, BH,FL

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Ethical statement

Ethical approval

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

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