



Primary Myxoid Liposarcoma of the Anterior Neck with Positive *FUS-CHOP* Translocation: A Case Report and Literature Review

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Abstract

Myxoid Liposarcoma is a variant of liposarcoma that usually occurs in the deep extremities and has a characteristic morphologic appearance. 95% of cases harbor a recurrent *FUS-CHOP* translocation. In this article we describe a challenging case of primary myxoid liposarcoma of the central compartment of the anterior neck, and present the first case of primary myxoid liposarcoma of the anterior neck with confirmation by *CHOP* fluorescence in situ hybridization, as well as a review of the literature.

Introduction

Myxoid Liposarcomas of the neck are rare, and most reported cases represent metastases from a primary tumor located in the deep extremities [1,2]. Very rare cases of primary myxoid liposarcoma of the neck have been reported in the thyroid, supraclavicular fossa, supraglottic larynx, retropharyngeal space, sinonasal tract, and mediastinum (with secondary involvement of the anterior neck) [3-10]. Because primary myxoid liposarcoma of the neck is so rare, diagnosis may be challenging, and there is limited data available to help guide treatment. In prior reported cases, the diagnosis was made based on morphologic features and no testing for the chromosome 12 (*CHOP*) translocation characteristic of myxoid liposarcoma was performed. Herein we report a case of primary myxoid liposarcoma of the anterior neck. While the case was initially a diagnostic challenge, a positive *CHOP* translocation by fluorescence in situ hybridization (FISH) test facilitated the appropriate diagnosis. To our knowledge, this is the first case report of a primary myxoid liposarcoma of the central compartment of the anterior neck that has been confirmed by a positive *CHOP* FISH test.

Case Report

The patient is a 43-year-old male who reported a 1.5 year history of an anterior, lower neck mass and several months of increasing dyspnea on exertion and a worsening cough with

sputum production. The patient also noted a 25-pound weight loss in recent months. Past history was significant for non-Hodgkin lymphoma in left lower extremity that was reportedly treated 10 years prior. An initial course of antibiotics was not helpful. A CT scan revealed a very large, lobulated mass (12x9x8 cm) in the central compartment of the anterior neck. The mass appeared to arise from within the anterior thyroid gland, displacing the sternocleidomastoid and platysma muscles, and extending from the level of the hyoid bone to the level of the aortic arch in the anterior mediastinum, with compression and displacement of the trachea (Figure 1). Fine needle aspiration reportedly showed atypical mononuclear cells, somewhat suspicious for a lymphoproliferative process. A PET scan showed the neck mass to be PET avid and also revealed a PET avid upper back subcutaneous mass. No other masses were identified. A core biopsy of the neck mass and a bone marrow biopsy was performed. The neck mass core biopsy showed a moderately cellular proliferation of bland spindled cells with myxoid stroma and scattered delicate arborizing vessels. FISH testing on the neck mass biopsy revealed a *CHOP* translocation. Given the classic morphology and the positive *CHOP* translocation, a diagnosis of primary myxoid liposarcoma was made. The bone marrow biopsy was unremarkable and flow cytometry analysis of the bone

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Figure 1 Computerized Tomography (CT) scan showing a 12 cm anterior neck mass with lateral displacement of the trachea..



marrow and neck mass were negative for a lymphoproliferative disorder.

The neck mass was then resected. While the imaging had suggested a thyroid origin, during the operation the mass appeared to expand the central neck compartment with extensive compression the thyroid, and anterior trachea, but without any invasion of the thyroid other neck structures. In addition, during the surgery a biopsy of the upper back subcutaneous mass was performed to rule out the possibility of a separate sarcoma which might have metastasized to or from the neck. Grossly, the neck mass measured 15 cm and showed an intact capsule with no evidence of invasion into surrounding tissues. Histologically the neck mass showed a vaguely nodular proliferation of bland oval-to-spindled cells in a myxoid background with scattered, branching, thin-walled vessels (Figure 2), scattered small lipoblasts (Figure 3), and occasional pools of extracellular mucin (Figure 4), characteristic of a myxoid liposarcoma. Focal areas of high grade, round cell component (Figure 5) were identified, comprising less than 2% of the tumor volume. No necrosis or mitotic activity was noted. The surgical margins were free of tumor. Sections from the upper back mass showed laminated keratin and inflammatory debris, consistent with contents of an epidermal inclusion cyst.

Discussion

Liposarcomas are among the most common soft tissue sarcomas in adults, accounting for approximately 12% of all sarcomas [11]. The most common liposarcoma variants include well differentiated liposarcoma/atypical lipomatous tumors. These tumors comprise 40-45% of liposarcomas and are usually found in the retroperitoneum, and extremities. Myxoid liposarcomas make up approximately 10-15% of liposarcomas, and usually occur in the deep soft tissues of the extremities, with two thirds of cases developing in the thigh. A typical myxoid liposarcoma shows uniform round to oval cells, small signet-ring

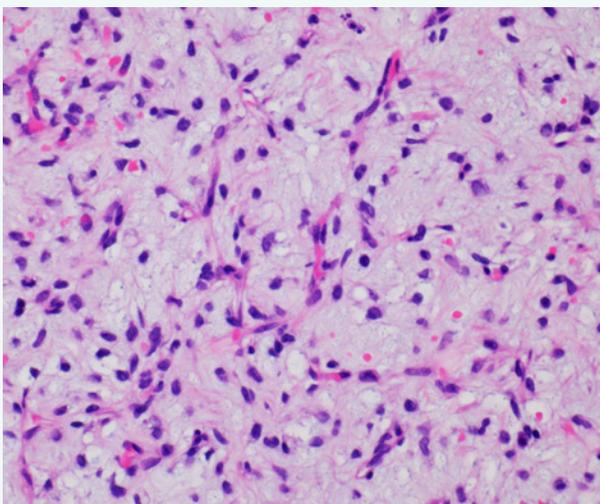


Figure 2 Bland oval-to-spindled cells in a myxoid background with scattered branching thin-walled "chicken wire" vessels.

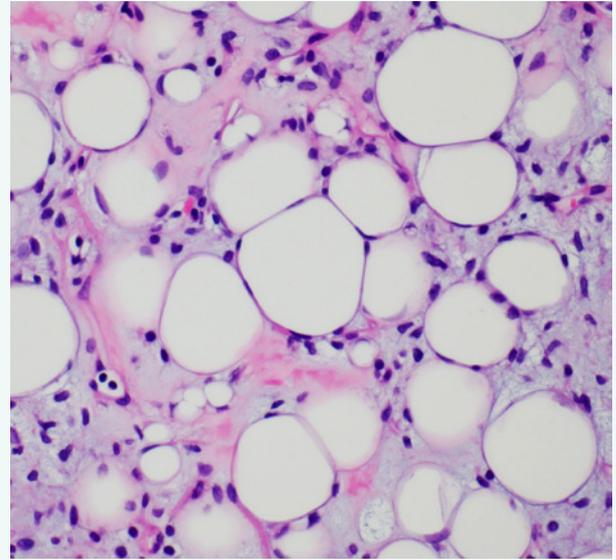


Figure 3 Scattered adipocytic components with a few small lipoblasts showing multiple cytoplasmic vacuoles which indent the nuclei.

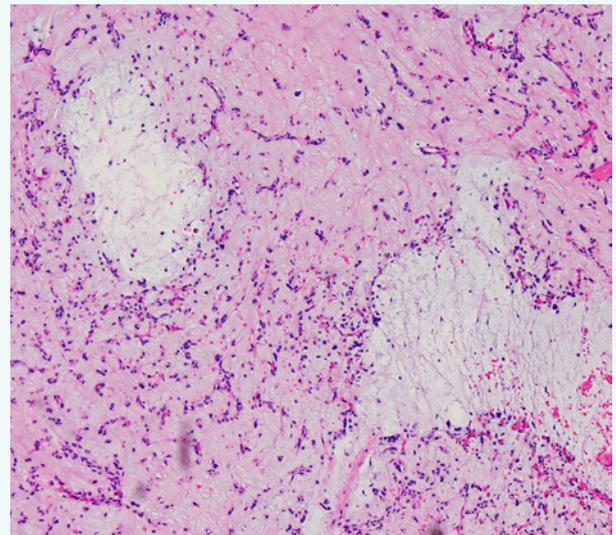


Figure 4 Pulmonary edema-like areas showing pools of extracellular mucin material.

lipoblasts, and a myxoid background with prominent, arborizing, thin-walled, "chicken wire" vessels. Mitotic activity in myxoid liposarcomas is usually rare or completely absent. The tumor may have variable numbers of interspersed fat cells, signet ring cells and multivacuolated lipoblasts. A subset of cases show round cell morphology, which is associated with a worse prognosis. These areas show hypercellular, back-to-back, primitive round cells with increased nuclear-to-cytoplasmic ratios.

The differential diagnosis of myxoid liposarcoma includes: myxoid undifferentiated pleomorphic sarcoma (myxofibrosaroma), extraskeletal myxoid chondrosarcoma, myxoma, or myxoid variants of other tumors. Compared

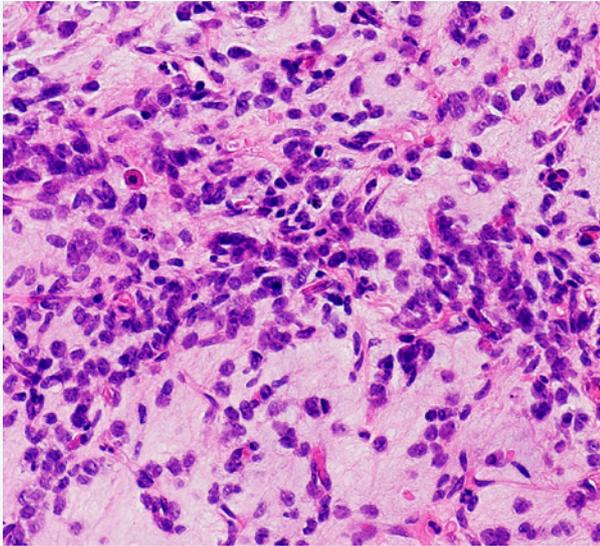


Figure 5 Areas of transition to round cell morphology, showing somewhat enlarged, back to back cells with increased nuclear to cytoplasmic ratios.

with myxoid liposarcoma, myxofibrosarcoma shows a higher degree of nuclear atypia, coarser vasculature and brisk mitotic activity. Pleomorphic vacuolated cells (psdudolipoblasts) found in myxofibrosarcoma may also mimic lipoblasts leading to a misdiagnosis of myxoid liposarcoma. Extraskeletal myxoid chondrosarcoma shows small clusters or cords of eosinophilic spindled cells, unlike the single-cell appearance of a myxoid liposarcoma. Myxomas show a characteristic paucity of vessels compared with the prominent thin walled vasculature seen in myxoid liposarcoma. If a purely round cell component were biopsied, the differential diagnosis may even include a lymphoma. Finding an area of classic myxoid liposarcoma can help make this distinction.

Myxoid liposarcoma is characterized by a recurrent translocation $t(12;16)(q13;p11)$ in over 95% of cases, leading to a fusion of the amino terminal domain of *FUS* (a.k.a. *TLS*) to *CHOP* (a.k.a. *DDIT3* or *GADD153*). An alternative translocation $(12;22)(q13;q12)$ is found in rare cases leading to a fusion of *EWS* to *CHOP* [12]. Antonescu et al. systematically studied numerous cases of liposarcoma, including its histologic mimics, and found that the *FUS-CHOP* translocation is completely specific and highly sensitive for myxoid liposarcoma [13]. Suzuki et al. retrospectively analyzed a single case of well-differentiated liposarcoma and 3 cases of dedifferentiated liposarcoma with histologic features of pleomorphic sarcoma, pleomorphic malignant fibrous histiocytoma, and monophasic synovial sarcoma respectively, and reclassified them as myxoid liposarcoma based on the presence of *TLS-CHOP* and *EWS-CHOP* translocations [14].

The head and neck is a rare location for liposarcoma, however, myxoid liposarcoma is the most common type of liposarcoma reported in the head and neck region [15-17]. And while most types of liposarcoma metastasize most commonly to the

lungs, myxoid liposarcoma frequently metastasizes to unusual locations [1-2]. Primary myxoid liposarcoma has been described in the thyroid, supraclavicular fossa, supraglottic larynx, retropharyngeal space, sinonasal tract, and mediastinum (with secondary involvement of the anterior neck) [3-10]. Diagnostic *CHOP* FISH was not utilized in these prior reported cases.

In summary, we report the first case of a primary myxoid liposarcoma of the central compartment of the neck confirmed by *CHOP* FISH. This case also highlights the broad differential that must be considered when dealing with a myxoid neoplasm, especially in a small core biopsy, or in an unusual location. While our case showed relatively classic morphology, given the unusual location, the pertinent lymphoma history, and the limitations of making a diagnosis on a small core biopsy, confirmatory FISH testing for the *CHOP* translocation was indispensable for making a correct diagnosis. In challenging cases that show unusual morphology, or overlapping histologic features, confirmatory *CHOP* FISH testing may have even greater utility.

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