Myxoid liposarcoma is a subtype of liposarcoma. This specific subtype can be identified based on its characteristic histological and cytogenetical features. The tumor has a fusion transcript of the CHOP and TLS genes, which is caused by t(12;16)(q13;p11). Most of the fusion transcripts that have been identified fall into three categories, specifically type I (exons 7-2), type II (exons 5-2), and type III (exons 8-2). A total of seven myxoid liposarcomas associated with the rare phenomenon of cartilaginous differentiation have been documented in the literature. Currently, only one of these cases has been cytogenetically analyzed, and the analysis indicated that it was a type II TLS-CHOP fusion transcript in both the typical myxoid liposarcoma and cartilaginous areas. This study presents a second report of myxoid liposarcoma with cartilaginous differentiation, and includes a cytogenetical analysis of both the myxoid and cartilaginous areas.

Key Words: Liposarcoma, myxoid; Cartilaginous differentiation; Cartilage; Heterologous component; TLS/CHOP fusion transcript

Case Report

A 45-year-old female visited the hospital with a palpable mass on the medial aspect of her thigh. The mass was observed by the patient 3 months previously and the size was perceived to be rapidly increasing. Computed tomography of the site showed an 11 cm-sized well-circumscribed mass with heterogeneous intensity, calcification and septation (Fig. 1). A diagnostic incisional biopsy was performed, and the tissue that was biopsied showed cartilage with atypical cytological features and focal necrosis. Analysis determined that myxoid stroma surrounded the cartilage, with the presence of some scattered lipoblasts within the myxoid stroma. Based on these findings, the biopsy was diagnosed as a malignant cartilage-forming tumor, and wide excision was performed on the entire mass. The specimen exhibited...
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Fig. 1. Computed tomography of the left distal thigh. A well-demarcated mass (arrowheads) within muscle with heterogeneous density and calcification.

Fig. 2. Gross picture of resected specimen. An 11 cm-sized, well-demarcated lobulated mass with hemorrhage and cystic change. Soft myxoid, gray firm fibrotic, and bluish resilient cartilaginous areas (arrowheads) are noted.

a well-demarcated ovoid mass with lobulation (Fig. 2), and each lobulated area was found to have different appearances that ranged from a solid gray fibrotic firm lobule, to a brown fibrotic soft lobule with a focal hemorrhage and cystic change, to a solid gray lobule with a focal glistening translucent myxoid appearance and a bluish firm resilient area with a focal calcification. Microscopic analysis revealed that the solid gray fibrotic area showed diffuse proliferation of bland fusiform cells with ovoid elongated nuclei and a moderate to abundant cytoplasm, and fine, delicate capillary vessel networks were noted within the fibrotic area (Fig. 3A). The brown fibrotic and hemorrhagic area contained coagulative necrosis of bland fusiform cells with hemorrhage, and a previous biopsy was proposed as the cause for the change in tissue. The myxoid area was characterized by a prominent basophilic myxoid matrix with scattered bland fusiform cells and lipoblasts (Fig. 3B). The lipoblasts had eccentrically located, small, elongated nuclei that were pushed to the periphery of the cell by clear, abundant intracytoplasmic vacuoles. The bluish resilient areas, which accounted for about 10% of the tumor volume, were characterized by cartilage with enchondral ossification, which showed mature bone without osteoid (Fig. 3C, D). The cartilage was moderately cellular and was composed of chondrocytes with atypical nuclei. Based on the immunohistochemistry, some of the fusiform cells and the lipoblasts were determined to be S-100 protein positive (1:300, Thermo Fisher Scientific, Waltham, MA, USA) (Fig. 4A), but were negative for smooth muscle actin (1:500, Dako, Glostrup, Denmark), desmin (1:1,000, Dako), and myogenin (1:100, Dako). Less than 5% of the cells were determined to be p53 positive (1:1,000, Dako) (Fig. 4B), and the Ki-67 (1:100, Dako) labeling index was also less than 5%. Based on these findings, a diagnosis of myxoid liposarcoma was considered. Molecular evaluation was performed on both the typical myxoid liposarcomatous and the cartilaginous areas, to confirm the proposed diagnosis. The final diagnosis was determined to be myxoid liposarcoma with cartilaginous differentiation, and the patient was scheduled for radiation therapy because the tumor was very close to the resection margin. Currently, after 6 months of follow-up, the patient has not presented with any evidence of metastasis or recurrence.

Reverse transcription polymerase chain reaction investigation of mRNA expression

Typical myxoid liposarcomatous and cartilaginous areas were marked on a paraffin block after the hematoxylin and eosin slides were reviewed. Five 10 µm sections of each area were cut from the resection specimen blocks and placed into Eppendorf tubes. The total RNA was extracted from the formalin-fixed, paraffin embedded samples using an RNeasy mini kit (Qiagen, Valencia, CA, USA) following the manufacturer’s instructions. After preparation, 1 µg of each of the total RNA samples were reverse transcribed using a RevertAid First Strand cDNA Synthesis kit (Thermo Fisher Scientific), and a nested polymerase chain reaction (PCR) was performed using outer and inner primer sets that were based on a previous report.

The outer primer set was TLS-CHOP outer forward (5'-AGCAAAAGCTATAATCCCCCAG-3') and TLS-CHOP outer reverse (5'-GAAGGAGAAAAAGGCAATG-ACTCA-3'), and inner primer set consisted of TLS-CHOP inner forward (5'-GACAGCAGAACCAGTACAAGCAG-3') and TLS-CHOP inner reverse (5'-GCTTTCAGGTGTGGTGATGTAGAAG-3'). The expected size of the nested
Fig. 3. (A) Fusiform cells and capillary networks are observed in the fibrotic area. (B) Lipoblasts are seen in the myxoid area. (C, D) Cartilage with moderate cellularity, cytological atypia, and enchondral ossification are found in the bluish resilient area.

Fig. 4. Immunohistochemical staining reveals that some of the fusiform cells and round lipoblasts are positive for S-100 protein (A). A few cells (less than 5%) are determined to be positive for p53 (B).

PCR products for the three common types of fusion transcripts were 379 bp, 103 bp, and 412 bp for type I (exons 7-2), type II (exons 5-2), and type III (exons 8-2), respectively. The results of the nested PCR for this study exhibited type II fusion transcripts in both the typical myxoid liposarcomatous and cartilaginous areas (Fig. 5).
cases presented with cytological atypia, while the other two cases did not. This report did not discuss these specific details about the cartilaginous area, however, the image of the area indicated that there was cytological atypia of the chondrocytes. As Siebert et al. discussed, the appearance of the cartilaginous area can cause confusion with other benign or malignant soft tissue tumors. In this case, the situation could potentially be more problematic based on the biopsied material because a differential diagnosis of the myxoid chondrosarcoma from this tumor could be difficult to categorize accurately. But myxoid chondrosarcomas rarely show areas of mature cartilage. And even if the mature cartilage is noted, cyorgenetical analysis of the spindle cell area and the cartilaginous area can be used to support an accurate diagnosis of the tumor.

Follow-up studies of the t(12;16) in myxoid liposarcoma have indicated that the translocation is a distinct characteristic feature of the tumor. The specific translocation results in the fusion of CHOP (also known as GADD153 and DDIT3) on chromosome 12 and TLS (also referred to as FUS) on chromosome 16. To date, twelve different kinds of TLS-CHOP fusion transcripts have been detected. The portions of the genes that fuse can range from almost the entire CHOP gene to varying lengths of the TLS gene, which differs according to the type of fusion transcripts. The differences are caused by varied break points within each gene, but generally, three types of transcripts are commonly observed and the remaining transcripts are rare. Previous studies have not identified any specific correlation between the types of fusion transcript and a prognosis. However, this study demonstrated a correlation between the type II fusion transcript and p53 overexpression, and although the TLS-CHOP fusion is found in a high percentage of the myxoid liposarcomas, there are reports of other cytogenetic aberrations. For example, a small number of myxoid liposarcoma cases with an EWS-CHOP fusion have been reported. In addition, one study detected an aberration of the p53 gene in about 30% of the myxoid liposarcomas.

Previous studies have determined several prognostic factors of myxoid liposarcoma, which include the percentage of round cell components, tumor necrosis, and p53 overexpression. The prognostic importance of round cell components was first identified by Enzinger and Winslow and has been confirmed in follow-up studies. In addition, the overexpression of p53, determined by a 5% cut off value, was reported to be signifi-
The abrupt transition between the two areas and the absence of osteoid formation by the tumor cells, enchondral ossification was considered as the pathophysiologic bone formation mechanism instead of osteosarcomatous differentiation. Authors of previous case reports have speculated that the heterologous component could be derived from common progenitor cells. However, additional follow-up studies are needed to investigate whether the cartilaginous component is created by proliferating mesenchymal cells or by metaplasia.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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