Olgu Sunumu / Case Report
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A Case Of High-Grade Myxofibrosarcoma With Rare Axillary Localization

Aksiller Lokalizasyonu Olan Nadir Yüksek Dereceli Miksofibrosarkom Olgusu

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ÖZET

Özet

Miksofibrosarkom nadir görülen yumuşak bir doku sarkomudur. Çoğunlukla ekstremitelerde lokalizedir. Kesin tanı histopatolojik inceleme ile yapılsa da, görüntüleme yöntemleri derecelendirme ve tedavi planlamasında önemli rol oynamaktadır. Aksiller bölge nadiren dahil olabilse de literatürde bildirilmiş bir vaka yoktur. Tümörün bol miktarda nörovasküler bir yapıya sahip olması göz önüne alındığında, tümörün geniş cerrahi sınırlarla eksize edilmesi zordur. Olgumuz literatürde aksiller lokalizasyonu olan ilk olgu olduğu için dikkat çekicidir. Geniş sınırlı cerrahi eksizyon tedavinin en önemli basamağıdır. R0 rezeksiyonu sağkalım üzerinde önemli bir etkiye sahiptir. Sonuç olarak, aksiller MFS'de kemoterapinin ardından geniş cerrahi eksizyonun lokal nüksü azaltmada olumlu bir katkısı olacağını düşünüyoruz.

Anahtar Kelimeler: miksofibrosarkom, aksilla, malign

ABSTRACT

Myxofibrosarcoma is a rare soft tissue sarcoma. It is mostly localized at extremities. Although definitive diagnosis is made by histopathological examination, imaging modalities play an important role in grading and treatment planning. Although axillary region can be involved rarely, there is no reported case in the literature. Given that tumor has an abundant neurovascular structure, it is challenging to excise tumor with wide surgical margins. Our case is striking as it is the first case with axillary localization in the literature. The surgical excision with wide margin is the most important step of the treatment. The R0 resection has an important impact on survival. In conclusion, in axillary MFS, wide surgical excision followed by chemotherapy will have positive contribution in reducing local recurrence.

Keywords: myxofibrosarcoma, axilla, malignant

INTRODUCTION

Myxofibrosarcoma (MFS), previously known as myxoid malignant fibrous histiocytoma, was first described as a variant of fibrosarcoma that exhibits variable myxoid stroma, pleomorphism and wide, tortuous vascular pattern in 1977 (1). It is generally seen in elderly individuals (sixth-to-eighth decades). It is mostly localized at extremities, dermis and profound skeletal muscle, as lower extremity being most common localization (2). Retroperitoneal area and abdomen are rare sites of involvement. In the literature, there is no case report describing axillary localization as in our case. The MFSs with profound localization are larger, less nodular and more infiltrative when compared to those with superficial localization. Time to symptom onset varies from 2 weeks to 15 years (3). The tumor has predominant myxoid structure (>50%) and low level of cellularity in histological manner. It harbors many nodular contours. Elongated, curvilinear and thin vascular structures are the characteristic of tumor. Tumor cells generally localized along with these vascular structures and are embedded into fusiform, stellate and myxoid matrix (4). Matrix mainly consists of hyaluronic acid (4). In immunohistochemical studies, tumor shows diffuse positive staining for vimentin and focal staining patterns with muscle-specific and smooth muscle actin. Tumor cells are negative for CD68, Mac-387, factor XIIIa and desmin. Tumor cells are positively stained for both epithelial growth factor and its receptor in most instances. Tumor cells have nuclei with intensive chromatin at periphery and occasional cleavage. Golgi apparatus is well-developed in the

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cytoplasm. In addition, numerous mitochondria and rough endoplasmic reticulum are present in the cytoplasm (2).

The MFSs are classified into 4 grades based on cellular structure, atypia, mitotic activity and myxoid content. The prognosis is better in low-grade MFS and those localized at subcutis while risk for metastasis is high in those with necrosis and those larger than >5 cm (5). Again, metastatic risk is higher in high-grade MFS and those with profound localization (6). The treatment options include wide local excision, chemotherapy and radiotherapy for MFSs (7). Recurrence rate has been reported as 16-54% after surgical resection. The recurrent tumors generally have higher grade than primary tumor and can be metastatic. The correlation between positive surgical margin and survival was attributed to infiltrative growth pattern, frequently seen in MFS, and high local recurrence rate. In previous studies, it was reported that R0 resection followed by radiotherapy decreased recurrence rate. The effects of adjuvant radiotherapy on survival are still controversial (8).

Myxoma, myxoid liposarcoma and fibromyxoid sarcoma should be considered in the differential diagnosis. The myxoma is hypo-vascular and has no curvilinear vessels. It is distinguished from MFS by less cellular atypia. Myxoidliposarcoma contains lipoblasts and has no perivascular tumoral cell condensation. Fibromyxoid sarcoma has more abundant cellular atypia and fibrous stroma with higher frequency of metastasis (9). When compared to other subtypes of sarcoma, myxofibrosarcoma has relatively better prognosis (9).

We aimed to present a case with high-grade myxofibrosarcoma and atypical localization of axillary region and our treatment approach.

CASE

A 44-years old man presented with an enlarging, painless mass at left axillary region. In the physical examination, a palpable mass (4 x 4 cm in size) was detected (Figure 1). On the magnetic resonance imaging of left axillary region, a mass lesion with dense contrast enhancement (50 x 33 x 48 mm in size) was observed with surrounding edema and inflammation (Figure 2). Based on radiological findings, the lesion was preferentially considered as conglomerated lymphadenopathy and soft tissue tumor. On positron emission tomography (PET) CT scan, there was a hyper-metabolic lesion (44 mm in size) occupying level 2 and 3 at left axillary region.

Figure 1. *Palpable mass in the axillary region (4 x 4 cm in size)*

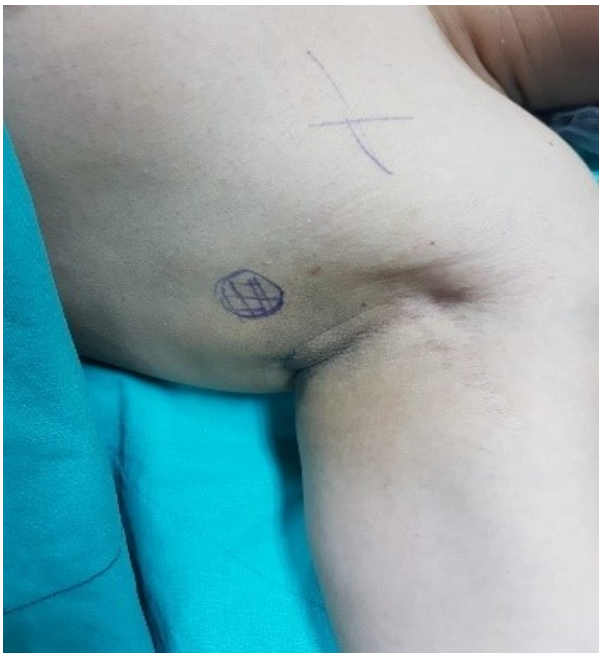
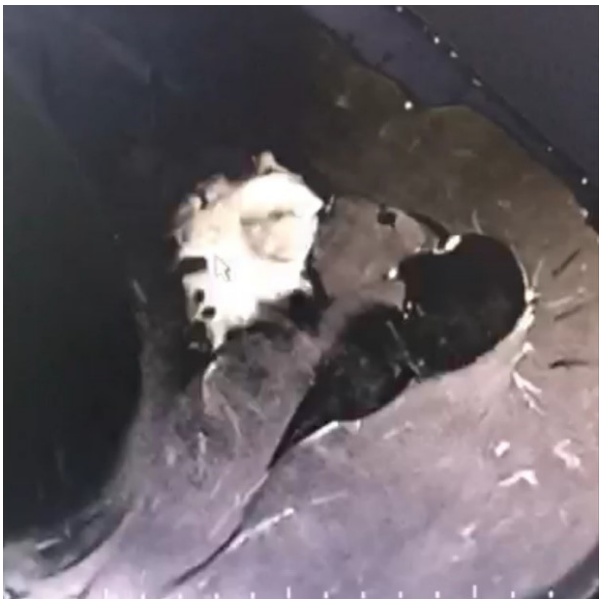


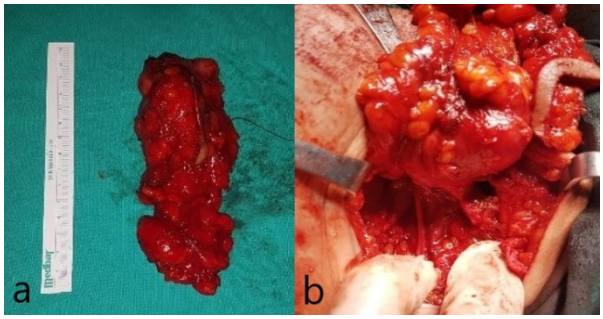
Figure 2. *On the magnetic resonance imaging of left axillary region, a mass lesion with dense contrast enhancement (50 x 33 x 48 mm in size)*



There was no finding suggestive of distant metastasis. A Tru-cut biopsy was performed. On microscopic examination, it was seen that it was a spindle-like cell malignant mesenchymal tumor rich for myxoid stroma. In immunohistochemical examination, it was found that tumor cells were stained positive with vimentin, smooth muscle actin while negative with desmin, S100, oscar-

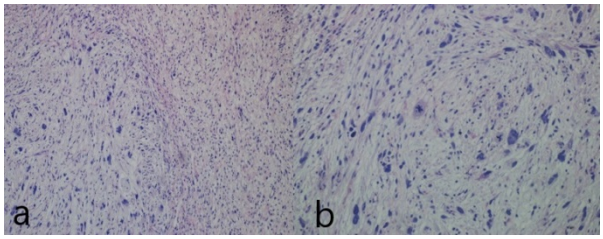
cytokeratin, MDM-2 and CD31. The lesion was classified as high-grade myxofibrosarcoma based on immunohistochemical study and undifferentiated histological pattern. The mass was excised surgically. Since the mass lesion was adhered to axillary vein, it was dissected over vein and axillary dissection specimen (12.5x6x5 cm) was removed. During dissection, attention was given to preserve thoracicus longus and thoracodorsal nerves (Figure 3a-b).

Figure 3. *Axillary dissection and specimen*



Frozen section procedure was performed on the specimen and examined under gross inspection. The pathologist observed a positive superior surgical margin; thus, re-excision was performed. On gross examination of the re-excision specimen, two nodular tumoral masses next to each other (as largest being 4.5 cm and smallest being 3.5 cm) were observed in the axillary adipose tissue. On microscopic examination, tumor was myxoid and spindle cell morphology, highly cellular with pleomorphic cells (Figure 4a). Curvilinear vessels were observed along with tumor cells. There were numerous typical and atypical mitoses (Figure 4b).

Figure 4. *a) Spindle and pleomorphic tumor cells over myxoid base (HEx100) b) Atypical mitotic figures in tumor (HEx200)*



Based on FNCLCC grading, histological differentiation was rated as 3 while mitotic count as 3 (25/10 in high power field), necrosis presence as 1 (<50%, focal), estimating grade 3 tumor.

In immunohistochemical study, tumor cells showed focal positivity with CD163 and Cd34 while they were negative for smooth muscle actin, desmin, caldesmon, oscar-cytokeratin and s100. Together with these findings, the case was considered as high-grade myxofibrosarcoma-grade 3. Although superior surgical margin was benign, tumor was observed to be adjacent to surgical margins in samples from non-adipose areas of outer aspect of the tumor

DISCUSSION

The myxofibrosarcoma is one of the rare soft tissue sarcomas, which is generally seen in elderly men. It accounts for 5% of all soft tissue sarcomas. It is mainly seen at sixth or seventh decades of life. It has been reported that tumor is commonly found at subcutaneous or deeper tissues of extremities (77%), trunk (12%), retroperitoneal area or mediastinum (8%) and in other regions in rare cases (2).

In our case, a palpable mass lesion was present at left axillary region of a 44-years old man. The mass was adhered to axillary vein and excised over vein with meticulous dissection. The neurovascular structures were preserved during excision.

In MFS, the diagnosis is made by histopathological examination and tumors are classified as low-, intermediate- and high-grade (2). Low-grade tumors are characterized by cells with hyper-chromatic and pleomorphic nuclei and underlying large myxoid areas. The intermediate tumors are more cellular with nuclear atypia. Finally, high-grade tumors have abundant mitotic figures, areas of hemorrhage and necrosis and hyper-cellular regions. In previous studies, no relationship was found between tumor grade and local or distant metastasis; however, it has been proposed that tumor grade is an important predictor of recurrence (2). In a study by Sanfiippo et al., it was suggested that tumor size, tumor grade and surgical margin status were significant predictors of survival although no relationship was found between tumor grade and clinical course.

In myxoid, spindle cell tumors; the differential diagnosis includes many benign and malignant mesenchymal tumors. Our case was distinguished from benign lesion by cellularity, hyper-chromatic/pleomorphic tumor cells and atypical mitotic figures. Myxoid liposarcoma has less

atypical cells and lipoblasts, thin plexiform vascularity and tumor cells are not condensed at perivascular area (10). In addition, our patient had no MDM2 gene amplification. Low-grade fibrosarcoma consists of uniform fibroblastic cells with less frequent atypia and has swirl-like growth pattern with occasional collagen rosette but there is no curvilinear vascularity (11). After surgery, the mass excised was considered as high-grade myxofibrosarcoma-grade 3 according to FNCLCC classification. The tumor included 2 nodules (4.5 and 3.5 cm in size) and occasional necrotic areas. Mitotic count was 25>10 HPF. In microscopic examination, it was seen that tumor was adjacent to surgical margins despite benign superior surgical margin.

Although there are no guidelines describing optimal surgical margins in MFS, it seems reasonable to aim 1-to-2 cm negative margin whenever possible in anatomic manner. Positive surgical margin is defined as presence of tumor at stained aspect or 1 mm inner of stained margin as described by Lin et al (9, 12). Thus, it is important to adopt aggressive surgical approach to achieve local control and improve survival by ensuring wide negative margins in MFS (2). There is a significant difference in recurrence rate between R0 resection and positive surgical margin (18% vs. 71%), emphasizing to achieve widest resection whenever possible.

We excised tumor totally despite axillary localization which is challenging for resection. In histopathological examination, tumor was considered to be adjacent to surgical margin. Adjuvant chemoradiotherapy was planned in the MFS case due to negative surgical margin less than 1 mm in microscopic examination.

CONCLUSION

The MFSs, comprising minority of soft tissue sarcomas, are generally localized at extremities. Although axillary localization can be seen in rare instances, there is no reported case with axillary involvement in the literature. The presence of abundant neurovascular structures makes resection challenging in MFS. In conclusion, in axillary MFS, wide surgical excision followed by chemotherapy will have positive contribution in reducing local recurrence.

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