Synovial sarcoma of the popliteal fossa

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SUMMARY

Soft tissue sarcomas are heterogeneous group of neoplasms making up to 1% of all malignant tumors in the adult population. The tumor generally appears on the extremities near large joints of middle-aged patients, especially in the popliteal fossa. Our patient presented in February 2014 due to a slowly enlarging, darker-colored swelling in the left popliteal fossa. Upon physical examination, a somewhat nodular, immobile, tender subcutaneous mass was observed. There was no locoregional lymphadenopathy. Patohistological findings showed a high-grade primary malignant mesenchymal tumor, biphasic synovial sarcoma type. The patient underwent surgery with wide surgical excision, followed by radiotherapy treatment. Magnetic resonance imagining follow up after one year revealed tumor recurrence. Neurovascular bundle involvement was detected, but without adjacent bone and muscular invasion and above-the-knee partial amputation of the left leg was performed. The intervention resulted in a remission of the neoplastic process and the patient was scheduled for regular check-ups. Broad surgical resection of the tumor with negative margins was the primary treatment in this case. Mutilating operations are necessary when anatomical structures around the tumor do not allow complete reintervention.

KEY WORDS: *Synovial sarcoma, knee, neoplasms*

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INTRODUCTION

Soft tissue sarcomas (STSs) are a collection of rare malignancies (1). They represent a heterogeneous group of tumors arising from embryonic mesodermal cells (2). The majority of the soft tissue sarcomas (almost 75%) are bone sarcomas - osteosarcoma, chondrosarcoma, chordoma, angiosarcoma and leiomyosarcoma. followed by gastrointestinal stromal tumors (15%) and Ewing's sarcoma (10%) (3,4). Adult STSs have an incidence of 4-5/100,000 in Europe and they are considered as rare diseases (4). Soft tissue sarcomas include over 80 histological subtypes, making up to 1% of all solid tumors. The most common are malignant fibrous histiocytes (28%), liposarcoma (15%), leiomyosarcoma (12%), synovial sarcoma (SyS, 10%), and peripheral nerve sheath tumor (6%) (3,4). Sarcomas are classified according to the type of mesenchymal tissue from which they originate. They are divided into two genetic groups, those with a simple karyotype that carry specific genetic alterations and those with a complex karyotype (5). Most sarcomas fall under following histological subtypes: 1) well-differentiated associated with genomic 12q13-15 amplification; 2) dedifferentiated with 12q13-15 amplification and loss of 3p14-21, 11q23-24 and 19q13; 3) myxoid with FUS-DDIT3 genomic alteration; 4) round cell FUS-DDIT3 translocation and 5) pleomorphic with Rb/p53 loss (6).

Synovial sarcomas are the fourth most common type, preceded by fibrous histiocytoma, liposarcoma and rhabdomyosarcoma. They are localized on the extremities near the large joints, especially the knee and hamstring, and associated with the joint capsule, tendons, *bursa* and fascial structures. Head and neck region, including the pharynx, larynx, and orbit are rare and unexpected localizations (7). This type of tumor is the most common in the adult population aged 15-40, with an incidence of less than 2/100,000 (4). Median age for biphasic synovial sarcoma is 34 (1).

Herein we present the case, diagnosis and management of a 65-year-old woman with biphasic synovial sarcoma in popliteal *fossa* involving a neurovascular bundle and making the therapeutic procedure challenging. Clinical and radiological features with treatment approach were described.

CASE PRESENTATION

A 65-year-old woman presented with a slowly-enlarging, darker-colored swelling in the left popliteal *fossa*. Initial symptoms appeared in February 2014 as a nonspecific painless swelling, slowly growing and associated with tenderness, with no bleeding but with a functional and mechanical interference. Upon physical examination, a somewhat nodular, immobile, tender subcutaneous mass was noted. Tinel's sign was negative on percussion. There was no locoregional lymphadenopathy. Patient had no co-morbidities. Results of biochemical and hematological laboratory tests were normal. Radiological findings showed a well-defined, lobulated mass with fine, dystrophic calcifications. Magnetic resonance imaging (MRI) showed a circumscribed, vascularized, multicentric, relatively well rounded tumor mass, size 5x4x4 cm behind the metaphysis of the femur and *musculus vastus medialis* surrounded by local edema and without invasion of the surrounding structures (Figure 1). Fluid-sensitive sequences in the areas of cystic degeneration showed a very high signal, a relatively high signal in the soft tissue components and also areas of low signal intensity due to dystrophic calcifications and fibrotic bands. Computed tomography of the lung showed no metastases at the time of diagnosis.

The patient underwent an extensive surgical resection of tumor with *ex-tempore* biopsy. Macroscopically, the mass measuring 5×5.5×4 cm was firm, relatively well-circumscribed, and lobulated with a gray-white cut surface. Pathohistological findings showed high-grade primary malignant mesenchymal tumor of the biphasic synovial sarcoma type, cystic subtype that was positive for CK AE1/AE3 focally, CK7 diffuse, CK19 focally, EMA focally-diffuse-1, Vimentin diffuse, Bcl-2 diffuse, CD99 diffuse, Ki-67 positive in > 70% of resection margin and TTF-1, CD34, and CK20 negative. The pathological findings were with viable cells on the margins, so the wide excision was followed by radiotherapy treatment with a total dose of 50 Gray in 25 fractions locally over five weeks.

The tumor recurred locally within one year - a follow-up MRI scan after 9 months showed a dominant tumor of 7x7x6.5 cm and one smaller tumor in the distal femoral epiphysis. Tumors had smooth, well defined

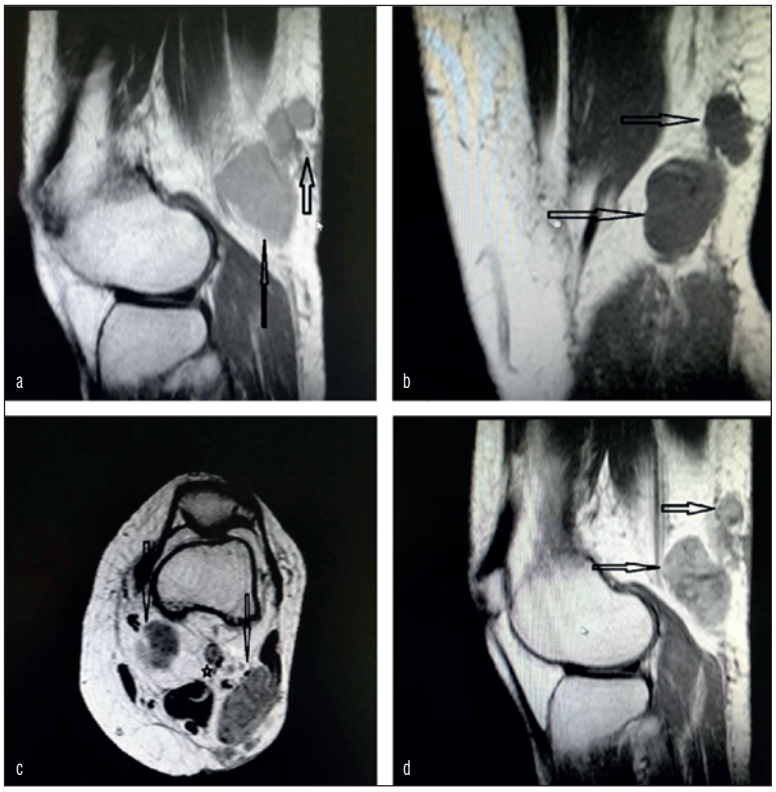

Figure 1. Magnetic resonance imaging of knee and popliteal fossa. Synovial sarcoma in the popliteal region behind the metaphysis of the femur and musculus vastus medialis: a) Proton density weighted sagittal view expressing hypointense, well rounded soft tissue mass, b) T1W coronal view showing multicentric, relatively well rounded T1 hypointense soft tissue masses, c) T1W axial CE view expressing the heterogeneous contrast enhancement of both masses without local invasion on vascular and other structures and d) T1W CE sagittal view showing multicentric, relatively well rounded T1 hypointense soft tissue masses

contours, homogeneous signal characteristics, with severe perifocal edema behind the distal femoral epiphysis (Figure 2). Neurovascular bundle involvement was detected, but without adjacent bone and muscular invasion.

In November 2014., after previous limb salvage, the patient experienced local recurrence and progression of the disease with indication for further surgery. Surgical treatment was necessary due to the neurovascular recurrent mass, size of the tumor, pathohistologicaly positive surgical margins, high-grade of the tumor and scarring and fibrosis induced by previous treatments. Partial above-the-knee amputation of the left leg was performed. Recovery passed without complications and after the recovery period the patient got prosthesis. Long-term follow-ups were scheduled at recommended intervals (laboratory examinations, radiological examination of the lungs and magnetic resonance imaging). The patient occasionally felt dull and burning pains on the operated limb, which were intensified by weather changes and emotional stress and she was prescribed amitriptyline and carbamazepine.

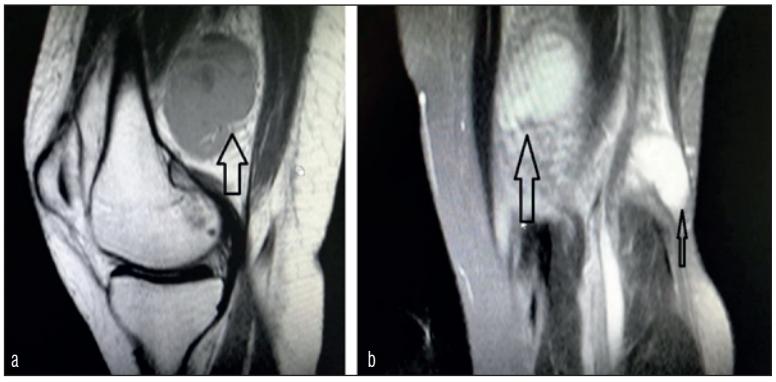

Figure 2. Magnetic resonance imaging of knee and popliteal fossa tumor recurrence: a) T1W sagittal view of the knee showing T1 hypointense, well rounded, recurrent mass behind the distal femoral epiphysis and b) T2W SPIR coronal view of the knee showing two soft tissue recurrent masses with severe perifocal edema behind the distal femoral epyphysis

DISCUSSION

The popliteal *fossa* is bordered proximally with the semimembranous and semitendinosus muscles represented by the medial and lateral boundary of *biceps femoris* muscle. The two heads of the *gastrocnemius* muscle border the region distally. The floor of the *fossa* consists of the posterior aspect of the distal femur, the posterior joint capsule and the popliteus muscle overlying the posterior proximal aspect of the tibia (8).

Synovial sarcomas most commonly affect joints and tendons of lower extremities. Biphasic SyS occurs in the lower limbs in 51.6% of cases (1). The name is incorrect because the tumor does not originate from synovial tissue but resembles *synovium* under a light microscope (9,10). However, due to the lack of anatomical structures representing circular boundaries around the popliteal *fossa*, tumors arising in this region need to be considered extra-compartmental. Additionally, the immediate vicinity of popliteal tumors to neurovascular structures passing through this region often limit the extent of the resection or require extensive reconstructions (8).

In SyS tumor size, tumor depth, tumor localization and the ability to achieve a complete resection are all factors affecting prognosis (1,11). Risk factors for sarcoma include hereditary disorders such as: retinoblastoma, neurofibromatosis, tuberous sclerosis, familial adenomatous polyposis, Li-Fraumen syndrome, Werner syndrome and basal cell nevus syndrome. Other factors associated with the development of sarcomas are radiation, lymphedema and exposure to chemicals (12). We did not find any of these factors n presented Case Report.

Any change suspected for soft tissue sarcoma should be referred to specialized Health Centers where it will be evaluated through a multidisciplinary approach. This means that any unexplained deep soft tissue mass as well as a superficial change >5 cm should raise suspicion of this type of tumor (4). Our patient waited a long time before referring to general practitioner.

Diagnosis of synovial sarcoma begins with echo-sonographic examination, but the main visualization method is a magnetic resonance imaging. Multiple core biopsy follows if the tumor is <3 cm. *Ex tempore* biopsy and tumor excision are also recommended (4). A definitive diagnosis is made by histopathological and immunohistochemical analyzes (4). In some cases, absence of biphasic differentiation can occur. Therefore, immunohistochemical studies must be completed by assessing immunoreactivity of neoplastic cells to CK, EMA, Vimentin, Bcl-2, CD99 with the presence of focal immunoreactivity to S-100 protein, as well as the absence of CD34 and Desmin (13).

Cytogenetic analysis can reveal different patterns of chromosomal aberrations within the lesion (14,15). A commonly believed etiological cause for SyS is a chromosome abnormality known as T (x; 18) (P11.2;

q11.2), that results in the formation of SS18-SSX fusion oncogenes (1,16). The chromosomal translocation leading to the production of the SS18-SSX oncogene is first defined, and represents the archetype of sarcoma associated with translocation. STS has various morphological patterns, the main one being of biphasic type, glandular or solid epithelial structure with a monomorphic spindle cell and monophasic with spindle cell folds. There is significant morphological heterogeneity and overlap with other neoplasms which may present a diagnostic challenge, as SS18-SSX has not been detected in all STSs and may occur in other tumor types (17).

Extensive surgical resection of tumors with negative margins is the basic method of treatment (4). Consideration of the minimum margin in fixed tissues is a decision of an experienced operator and depends on present anatomical barriers such as muscle *fascia*, periosteal tissue and critical neurovascular structures. The percentage of complete resections varies from 41.8 - 76% (18,19).

If the pathologist finds viable cells on the margins of the resection, reoperation should be considered and when the surrounding tissue does not allow reintervention, a decision on radiotherapy is made. Our patient received preoperative radiotherapy. In some cases, mutilating/amputation surgery is the only option, such as herein, where it was not possible to perform a complete excision of the relapsed tumors due to the surrounding anatomical structures of the occluded popliteal *fossa* and the neurovascular bundle of recurrent mass. The disease progressed and the multidisciplinary team decided on further treatment. Chemotherapy plays a minor role (20). The rationale for radiation therapy in the continuation of surgical treatments comes from randomized studies showing the improvement of local disease control (4,21,22). Postoperative radiation therapy is performed at each high grade, >5 cm tumors while in other cases a conciliatory decision is made, taking into account the anatomical localization and histological subtype (4).

Local relapse of the disease is common despite complete excision of the tumor and the therapeutic procedure is the same as for the primary tumor. Metastases of biphasic synovial sarcoma can be regional and distant. Lymph gland metastases are rare and require a more aggressive therapeutic procedure, including radiation and chemotherapy.

Occurrences of metastases are hematogenous, with deposits in the lungs and the bones, liver and soft tissues. They cause circular shadows in the lungs, which can take on large dimensions i.e. cannonball (23). In the case of isolated metastases in the lungs, when computed tomography of the abdomen rules out extrapulmonary disease, they can be surgically resolved. If the disease has given extrapulmonary metastases, doxorubicin chemotherapy remains (23). A study has been published on significantly better results of the overall survival of patients treated with doxorubicin in combination with olaratumab, a monoclonal antibody available in some European countries (24). In the study of Aytekin et al, with 3228 patients SyS, biphasic type 5-year survival rate was 68.5% (1).

The highest frequency of disease relapse is in the first two to three years, after which the risk decreases. Relapses most often affect the surrounding structures and lungs. It is important to detect local recurrence and metastases in the initial stages, while they can be surgically treated. The role of an experienced general practitioner is important in order to perform a thorough clinical examination of the operated region, provide regular laboratory examinations and radiological examination of the lungs, which are all standards in monitoring patients, for the first two years quarterly, then semi-annualy for up to five years after surgery and once a year after that period (25).

Declaration of Interests

Authors declare no conflicts of interest.

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