Case Report

A case report of 2 distinct primary sarcomas arising in an extremity in rapid succession✩

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ABSTRACT

A 59-year-old male presented with a primary synovial sarcoma around his knee. Two months after resection, he presented with a new, rapidly-growing mass in the ipsilateral proximal thigh. A biopsy of the new mass demonstrated a pleomorphic liposarcoma, distinct from the prior synovial sarcoma. He underwent neoadjuvant radiation, followed by wide resection. He is now undergoing surveillance for recurrence. While 2 distinct primary sarcomas developing in rapid succession is rare, this case emphasizes the need for a complete work-up, including obtaining a tissue diagnosis for suspected recurrent lesions as this may alter treatment and follow-up recommendations.

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Introduction

Soft tissue sarcomas (STS) are rare malignant tumors of mesenchymal origin that account for approximately 1% of all adult malignancies [1]. These tumors can appear at any age, with more than 100 histologic subtypes identified [2]. In 2021, an estimated 13,460 people were diagnosed with a new STS in the United States [1].

The development of multiple, histologically distinct STS is quite rare. When this occurs it often follows prior radiation treatment or is associated with mutations in tumor suppressor or proto-oncogenes that predispose patients toward the development of cancer [3,4]. The development of multiple primary STS in the absence of these genetic mutations is uncommon. We present an extremely rare case of 2 primary sarcomas with no histologic resemblance arising in the same anatomic region in rapid succession.

Case report

A 59-year-old man presented for a follow-up appointment approximately 6 months after a right total knee arthroplasty. During this visit he complained of a new mass along the in-
side aspect of his contralateral (left) knee, which had previously undergone a knee replacement one year prior. On physical examination, there was a soft, mobile mass located at the anteromedial aspect of the knee, measuring approximately 4 cm × 4 cm. The mass was nontender and it did not limit his range of motion at the knee.

Initial radiographic evaluation showed soft tissue swelling corresponding to the location of the palpable mass (Fig. 1). Magnetic resonance imaging (MRI) demonstrated a multilobulated irregular mass located just deep to the medial patellofemoral retinaculum and inferior to the vastus medialis muscle. The mass demonstrated slight hyperintense T1 signal relative to muscle and heterogeneous, predominantly hyperintense T2 signal with enhancement on the post-contrast sequences (Fig. 2). Given its indeterminate appearance on imaging, a biopsy was indicated.

Histopathologic analysis of the core needle specimens demonstrated a proliferation of monotonous spindle cells with overlapping nuclei and scattered wavy collagen bundles (Fig. 3). The tumor cells were positive for pan-cytokeratin (AE1/AE3) and S100, but were negative for SOX10, actin, CD34, and desmin. Molecular testing was positive for the SS18 rearrangement. The radiologic and pathologic findings were consistent with a diagnosis of synovial sarcoma (SS).

Initial staging was performed with chest computed tomography (CT) and whole-body positron emission tomography (PET)-CT, which were interpreted as negative for metastatic disease (Fig. 4). The patient underwent neoadjuvant radiation (50Gy) followed by wide resection with negative surgical margins. Final pathology confirmed SS.

Approximately 2 months after resection of the synovial sarcoma, the patient reported a new onset of rapid swelling in the medial thigh of the ipsilateral lower extremity. Axial and coronal CT imaging of the left thigh demonstrated a large, irregular soft tissue mass within the adductor compartment. The mass demonstrated mixed density with areas of internal low

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**Fig. 1** – AP radiograph shows a mass at the medial aspect of the left knee with soft tissue density similar to muscle (arrowheads).

**Fig. 2** – On axial MRI, the mass demonstrated slight T1 hyperintense signal relative to muscle (A), heterogeneous but primarily hyperintense T2 signal (B), and heterogeneous enhancement on T1 post-contrast subtraction imaging (C).

**Fig. 3** – Histopathology of the first biopsy specimen (hematoxylin and eosin, 400 x magnification) demonstrates a lesion composed of compact fascicles of monotonous spindle cells with overlapping nuclei and scattered wavy collagen bundles. These features are characteristics of a monophasic synovial sarcoma.
Fig. 4 – Initial staging PET-CT MIP image (A) demonstrates abnormal hypermetabolism at the medial aspect of the left knee (arrowhead), which corresponds to the location of the biopsy-proven synovial sarcoma. There is a tiny focus of low-level hypermetabolism within the medial soft tissues of the proximal left thigh (arrow), which is in the same region as the subsequent biopsy-proven pleomorphic liposarcoma and therefore likely represents a very early synchronous manifestation of a second distinct primary soft tissue tumor. Subsequent staging PET-CT MIP image following clinical discovery of the left thigh mass (B), shows marked hypermetabolism of the large mass in the thigh (arrow) and low level hypermetabolism in the surgical resection bed at the medial aspect of the knee (arrowheads).

Biopsy of the thigh mass revealed bizarre cells with large, hyperchromatic nuclei and pleomorphic lipoblasts. There was no histologic resemblance to the previous SS at the knee (Fig. 6). The tumor tissue was negative for keratin, S-100, and actin. FISH study was negative for SS18 rearrangement. These findings were consistent with a pleomorphic liposarcoma (PLS). Repeat staging chest CT and PET-CT demonstrated no evidence of metastatic disease. Based on recommendations following multidisciplinary review, the patient received 50Gy neoadjuvant radiotherapy to the thigh and subsequent wide surgical resection.

The patient recovered from surgery uneventfully and was referred to our clinical genomics department for evaluation of germline mutations that might lead to sarcoma predisposition. No mutations were found. The patient is undergoing routine surveillance per our institutional protocol.

Discussion

STS are a group of heterogeneous malignant tumors with more than 100 unique subtypes. Differentiation of the vari-
ous subtypes is based on histopathology, immunohistochemistry, and molecular analysis [5]. Although the vast majority of sarcomas arise sporadically, approximately 3% of STS have been linked to cancer-predisposing syndromes such as Li-Fraumeni, retinoblastoma, and neurofibromatosis type 1(NF-

1) [6]. These syndromes are characterized by mutations in genes such as TP53, Rb gene mutation, phosphatidylinositol-4, 5-bisphosphate 3-kinases gene mutation, and isocitrate dehydrogenase gene mutation. Li-Fraumeni syndrome, for example, has been associated with an increase in the lifetime cancer risk for sarcomas, leukemia, and carcinomas such as adrenal cortical carcinoma [7]. Our patient was evaluated by our genetics team and was not found to have an associated genetic syndrome.

In contrast to those associated with genetic syndromes, most soft tissue sarcomas are associated with somatic abnormalities (including gene fusions, mutations, or amplifications) in the tumor tissue [4,8,9]. In these instances it has been reported that these patients will be at an increased risk of a secondary malignancy, most commonly carcinoma of the breast or kidney [4,10]. It is extremely rare for patients to develop a second STS. It has been estimated that this will occur in 1 in 1225 (0.0082%) to 1 in 2500 (0.004%) cases [11]. The appearance of a second sarcoma in the same extremity, as in our case, has only been reported once before [12].

Our initial presumption for the new mass was the development of a regional metastasis of the SS. Recurrence of SS is relatively frequent, occurring in up to 50% of patients. The median lag of recurrence is 2.5 years from the initial diagnosis [13]. In our patient, although the presumptive initial diagnosis of the second mass in the ipsilateral thigh was regional metastasis, the histologic appearance and lack of SS18-SSX translocation in the tumor did not support this presumption.

Fig. 5 – Initial axial fused PET-CT image (A) of the left thigh shows a tiny focus of low-level signal (arrow) along the surface of the adductor compartment musculature. There is a very subtle lesion with lower density compared to muscle (arrow) on the corresponding axial CT image (B). Subsequent axial and coronal CT imaging (C and D) show a large irregular mass centered within the adductor muscle compartment at the posteromedial aspect of the left thigh with areas of internal low density consistent with necrosis.

Fig. 6 – Histopathology of the second mass (hematoxylin and eosin, 400x magnification) is composed of bizarre cells with large, hyperchromatic nuclei including pleomorphic lipoblasts showing nuclear indentation by clear vacuoles. These findings were consistent with a pleomorphic liposarcoma.
Retrospective identification of a hypermetabolic focus at the site of the pleomorphic liposarcoma excludes the possibility of a short-latency radiation-induced pleomorphic sarcoma. While 2 distinct primary sarcomas developing in rapid succession is extremely rare, this case emphasizes the need for a complete work-up, including obtaining a tissue diagnosis for suspected recurrent lesions as this may alter treatment and follow-up recommendations.

**Patient consent**

The authors have obtained consent from the patient for publication of their case report in “Radiology Case Reports”.

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