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Case Report Open Access

Intra-abdominal Synovial Sarcoma Presenting as Hemoperitoneum: A Case Report and Review of the Literature

Elizabeth L McKinnon[#], Thomas J Cummings[#] and Xiaoyin Sara Jiang[*#]

Pathology Department, Duke University Medical Center, USA

[#]The three authors contributed to the authorship and meet author requirements.

[*]**Correspondence author:** Xiaoyin Sara Jiang, Pathology Department, Duke University Medical Center, DUMC 3712, Durham, NC, 27710, USA, Tel: 919-684-6453; Fax: 919-681-7634; E-mail: jiang009@mc.duke.edu

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Abstract

Synovial sarcoma is a soft tissue malignancy that generally arises adjacent to joint capsules. The development of this entity in the abdomen is an uncommon presentation. We present a case of a 38-year old male who presented to the emergency room with anemia and abdominal pain. The patient was found to have hemoperitoneum, and on imaging the patient was also noted to have nodular lesions of the abdominal wall and diaphragm. Histopathological analysis of these lesions revealed malignancy. An extensive immunohistochemical and genetic analysis was performed to classify the lesion, and it was diagnosed as primary intra-abdominal synovial sarcoma. We explore the intricacies of making this critical diagnosis and review the literature of primary intra-abdominal synovial sarcoma.

Introduction

Synovial sarcoma is an uncommon malignant mesenchymal tumor that primarily arises near tendon sheaths, and occurs adjacent to joint capsules [1]. The most common location for this tumor is in the lower limbs around the knee, particularly in middle aged patients. The name can be misleading, as synovial sarcoma can arise in areas with no associated synovial or periarticular tissues. More recently, the use of immunohistochemistry in histopathological analysis and the discovery of the t(X;18) chromosomal translocation has aided in diagnosing synovial sarcoma in almost all parts of the human body [2].

Primary intra-abdominal synovial sarcoma is an extremely unusual presentation of this uncommon tumor, with less than 50 published cases in the English medical literature to date [3]. We describe a case of primary intra-abdominal synovial sarcoma in a 38-year old male who presented with anemia and hemoperitoneum, and we review the literature on this rare entity.

Materials and Methods

Representative paraffin-embedded sections of the lesions were routinely processed and stained with hematoxylin and eosin stain. Immunoperoxidase stains (Table 1) for epithelial membrane antigen (EMA), cytokeratin 7 (CK7), cluster of differentiation 99 (CD99), transducer-like enhancer of split 1 (TLE-1), neural cell adhesion molecule (CD56), and hematopoietic progenitor cell antigen (CD34) were also applied to sections of formalin-fixed, paraffin-embedded tissue. Slides were stained using automated system Leica Bond III for TLE-1, EMA, and CK7 and Dako Autostainer Link 48 for CD34, CD56, and CD99.

Case Report

A 38-year old male with a history of hypertension and pulmonary embolism (for one year, on warfarin therapy) presented to the hospital with a three-day history of abdominal pain without nausea and vomiting and one episode of black stools. The patient denied any recent trauma. His primary care physician had him transferred to the hospital after noting an INR of 4.6, hemoglobin> 7, and a CT scan that revealed a 12 × 8 × 13 cm left-sided abdominal hematoma and hemoperitoneum. The CT also noted nodular areas in the left hemidiaphragm and left hemipelvis that were concerning for carcinomatosis. Endoscopy to further explore the cause of the black stools was not performed due to the acuity of the patient's situation and imaging findings of hematoma.

Antibody	Source	Dilution
EMA	Leica	Predilute
CK7	Dako	1:100
CD99	Dako	Predilute
TLE-1	ABCAM	1:300
CD56	Dako	1:100
CD34	Dako	Predilute
Leica Bond III is a product of Leica Biosystems-Buffalo Grove, IL (USA), Dako Autostainer Link 48 is a product of Dako-Carpinteria, CA (USA), TLE-1 immunostain is a product of Abcam-Cambridge, MA (USA).		

Table 1: Immunohistochemical Reagents and Level of Titration.

The patient was brought to the OR for laparoscopic washout. An abdominal wall implant was present in the right lower quadrant and sent for frozen section, demonstrating a malignant tumor.

A large quantity (623 gm, 25 × 15 × 5.5 cm) of blood clot with admixed tissue was removed from the patient's abdomen. Tumor tissue within the blood clot was adherent to the omentum and body wall and was grossly tan-white and firm.

Histopathological examination of the tumor revealed a predominantly epithelioid proliferation with glandular appearance (Figure 1) and an infiltrative pattern invading into adjacent tissues. Admixed with the epithelioid proliferation, there were also areas of a spindled stromal proliferation with rare mitotic figures (Figure 2).

Immunohistochemistry was performed to characterize the high-grade tumor. Tumor cells were positive for EMA, CK7, CD99, and TLE-1 (Figure 3).

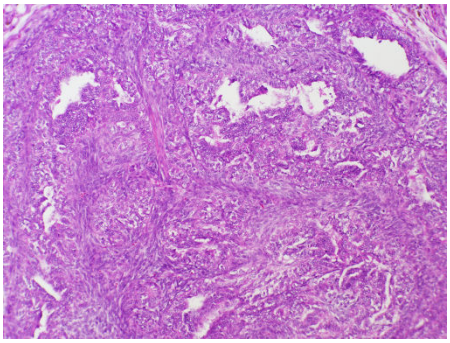

Figure 1: (H&E, 10x)-The tumor revealed a predominantly epithelioid proliferation with glandular appearance.

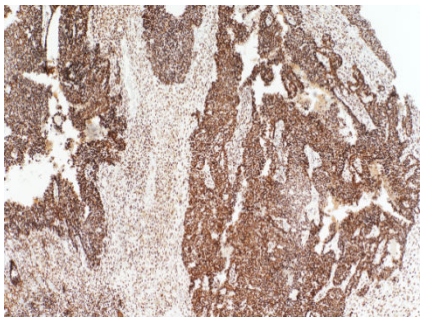

Figure 2: (10X) Immunohistochemistry shows positive nuclear staining for TLE-1.

The tumor cells were weakly positive for CD56. Tumor cells were negative for CD34. Synovial sarcoma was strongly considered as the diagnosis. Additional stains were performed to exclude germ cell, renal, urothelial, mesothelial, lung, thyroid, and gastrointestinal differentiation of the tumor. Given the lack of definitive staining for these epithelial malignancies, and the spindled stromal component, a portion of tissue was sent for a FISH study to confirm synovial sarcoma. The study revealed that 84% of observed tumor cells exhibited rearrangement of the SS18 gene, consistent with a positive result (Figures 4 and 5). The tumor was diagnosed as consistent with primary intra-abdominal synovial sarcoma.

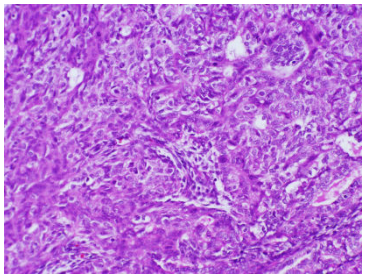

Figure 3: (H&E, 20X)-Admixed with the epithelioid proliferation of the tumor, there were also areas of a spindled stromal proliferation with rare mitotic figures.

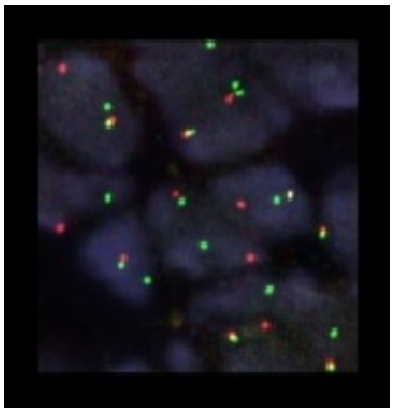

Figure 4: Red and green signals show independent SYT and SSX1 or SSX2 genes, indicating a cell with abnormal break-apart and positive for rearrangement of the SS18 gene locus. Yellow signals indicate normal genes with no evidence of break-apart signals.

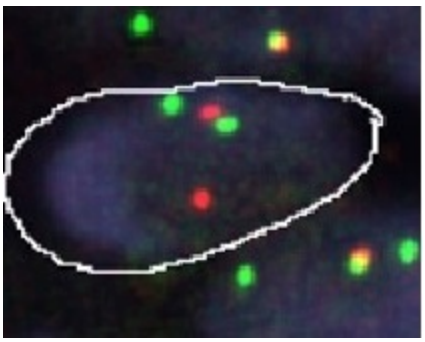

Figure 5: (Encircled in white) Red and green signals show independent SYT and SSX1 or SSX2 genes within the encircled cell, which is positive for the break-apart probe and thus positive for gene rearrangement. Yellow signals surrounding in other cells indicate normal, intact genetic material.

Discussion

Synovial sarcoma is the fourth most common type of soft tissue sarcoma [3]. It follows malignant fibrous histiocytoma, liposarcoma, and rhabdomyosarcoma in terms of incidence [3]. The pathogenesis of synovial sarcoma is unknown, but it is hypothesized to be derived from primitive mesenchymal cells [4]. Synovial sarcomas most commonly occur in patients between the ages of 15 and 40 years, with an incidence of 2.5 per 100,000 patients [4]. Of all soft tissue tumors, synovial sarcoma ranges from 5.6 to 10% in terms of frequency [5-6]. The most common location for synovial sarcoma to arise is close to large joints, particularly the knee in the popliteal fossa [3]. It has an intimate association with joint capsules, tendon sheaths, and fascia, but can occur less commonly in the head and neck regions [3,7]. Case reports of synovial sarcoma in the retroperitoneum, mediastinum, bones, and visceral organs have been published [3,8]. Synovial sarcoma represents 1% of retroperitoneal tumors, but this may be lower than the actual incidence since some cases formerly diagnosed as hemangiopericytoma, fibrosarcoma, or other types if soft tissue tumors can be reclassified as monophasic synovial sarcomas [1].

Primary intra-abdominal synovial sarcoma is very rare, with 47 published cases in the English literature [3]. Primary synovial sarcoma of the abdominal wall was reported in 1950 by Pack and Ariel [9].

In primary intra-abdominal synovial sarcoma, there is a female predominance (up to 3.5:1 in one study); however synovial sarcomas of the extremities, head, and neck occur more frequently in male patients at a ratio of 3:2 [10]. Most cases are specified as being retroperitoneal, although some cases are too large to properly assess their true anatomic location [1].

Intra-abdominal bleeding is an uncommon presentation of synovial sarcoma, but in patients on warfarin therapy, spontaneous bleeding in the abdomen has been known to occur. Because synovial sarcomas are rich in hemangiopercytomatous vessels, we can postulate that this combined with the patient's use of warfarin could have led to hemoperitoneum [11].

Tumors usually present as slow-growing, palpable, painful or painless nodules associated with vague abdominal symptoms [3] Imaging findings of synovial sarcoma include eccentric or peripheral speckled calcifications, found in up to 30% of cases [3].

The most common CT appearance of synovial sarcoma is mixed soft tissue with attenuation equal to or slightly less than that of muscle. The heterogeneous areas may represent necrosis or hemorrhage of the tumor. MRI images appear isointense to slightly hyperintense on T1-weighted images, and hyperintense to muscles on T2-weighted images. Marked heterogeneity and enhancement are highly suggestive of synovial sarcoma on both CT and MRI [3].

Morphologically, the subtypes of synovial sarcoma include biphasic, poorly-differentiated, and monophasic. The classic biphasic synovial sarcoma is more readily recognized and has both epithelial and spindle cell components [1]. In poorly-differentiated synovial sarcoma, tumor cells have more hyperchromatic nuclei, but there is sparse cytoplasm and little pleomorphism [1]. Monophasic tumors demonstrate predominantly spindle cell morphology resembling fibrosarcoma [3].

The most specific chromosome aberrations in synovial sarcoma are t(X;18) (p11.2:q11.2), found on 90% of synovial sarcomas, and fusion of the SYT gene on chromosome 18 with either SSX1 or SSX2 on the X chromosome [12]. All biphasic subtypes of synovial sarcoma predominantly express SYT-SSX1 fusion transcription whereas monophasic subtypes predominantly express SYT-SSX2 [13].

Immunohistochemical staining for synovial sarcoma shows positivity for EMA, cytokeratin (AE1/AE3) and E-cadherin. A combination with a negative CD34 is important to complete the diagnosis [13]. In our patient, we also found that CK7, CD99, and TLE-1 were positive. CK7 was positive in the epithelial component.

The differential diagnosis for intra-abdominal synovial sarcoma includes other biphasic neoplasms, spindle cell sarcomas, and small round blue cell tumors. Biphasic synovial sarcomas need to be morphologically distinguished from mesothelioma, Wilms' tumor, and malignant nerve sheath tumors with epithelial elements [1]. Biphasic mesothelioma is associated with long-term exposure to asbestos and will present in older age groups and have bigger, more pleomorphic nuclei [14]. Extra-renal Wilms' tumor and malignant nerve sheath tumors with epithelial elements should both be considered in the differential, and such markers as CD99 and CD56 will be helpful in ruling out both [8,15]. Synovial sarcoma will be positive for CD99 and CD56, while Wilms' will be CD99 positive and CD56 negative, and malignant nerve sheath tumors will be CD99 negative and CD56 positive [16].

Mullerian adenosarcoma and carcinosarcoma arise in the abdomen of older patients, but these will be more pleomorphic than synovial sarcoma and will have more diffuse cytokeratin positivity [1]. Additionally, gastrointestinal stromal tumors (GIST), hepatocellular carcinoma, and splenic hemangiopericytomas have been reported to cause spontaneous intra-abdominal bleeding, including occurrences in patients on anti-coagulant therapies [17-19]. GISTs showed specific staining patterns for discovered on GIST-1 (DOG1) and negative for CD117 and CD3 [17]. Our patient did not have diseases of the liver and imaging of the liver was negative for intrahepatic neoplasms. Hemangiopericytomas typically are large in size and demonstrate moderate to high cellularity, thick-walled, "stag-horn" vessels surrounded by a connective tissue sheath, and a monotonous appearance in microscopy [19]. As previously mentioned, hemangiopericytoma may demonstrate similar morphology for monophasic synovial sarcoma, but would negative for the chromosome aberration t(X;18) (p11.2:q11.2). Since this was positive in our patient's tumor, this confirmed synovial sarcoma.

Poorly-differentiated synovial sarcoma can resemble other small round cell sarcomas. Immunohistochemistry and genetic testing is required to rule this out [2]. Cytokeratins can be used to differentiate synovial sarcoma from other poorly-differentiated site-specific carcinomas [20].

Monophasic synovial sarcomas can resemble many other neoplasms, including solitary fibrous tumor [21], malignant peripheral nerve sheath tumor, leiomyosarcoma, and the aforementioned GIST tumor [22]. These entities can be ruled out with the use of immunohistochemistry [2].

If there is a possibility of metastatic synovial sarcoma to the abdomen, this should be ruled out based on clinical history and findings on imaging [3].

Lastly, it is important to consider the possibility of metastatic lesions to the abdomen, especially in tumors with a predominant epithelioid component, such as in our case. Metastatic malignancies of a wide range of epithelial origins may be in the differential, and therefore

careful history and immunohistochemistry should be evaluated for an accurate diagnosis.

Wide surgical excision is the treatment of choice with adjuvant radiation therapy, chemotherapy, or both [3,23]. Survival rate and prognosis are largely related to tumor size, histological subtype, mitotic rate, tumor necrosis, and vascular invasion [3]. Up to 50% of all synovial sarcomas recur locally within 2 years of excision, but some may recur many years later [14]. Synovial sarcomas typically metastasize to the lungs, and less commonly to the bones and lymph nodes [13].

In one study of intra-abdominal tumors, patients with retroperitoneal synovial sarcoma died within 2 years with local recurrence, but no metastatic lesions beyond the abdomen were found [1]. For all synovial sarcoma, tumors with poorly-differentiated morphology tend to have the worst prognosis [16,20].

Primary intra-abdominal synovial sarcoma is very rare, but should be considered in cases in which there is a primary intra-abdominal malignancy. The varied appearances of this tumor may pose a diagnostic challenge with an extremely wide range of possibilities in the differential diagnosis depending on morphology. Proper history, imaging, histopathology, immunohistochemistry, and genetic analysis are helpful in making the appropriate diagnosis. Specifically, assessments for alterations in the SYT gene are critical to making the diagnosis in uncommon presentations of this entity.

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