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Case Report

Pediatric splenic angiosarcoma

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Abstract: Angiosarcomas are malignant vascular neoplasms that usually occur in deep soft tissue. Patients diagnosed with angiosarcoma are usually elderly and are given poor prognoses. Pediatric splenic angiosarcoma is extremely rare, and its pathogenesis is not as well understood as that of older patients. We describe a case of 4-year-old male who had undergone splenectomy for splenic mass. Histopathological examination revealed primary splenic angiosarcoma. We then reviewed published literatures to characterize its clinical characteristics.

Keywords: Angiosarcoma, spleen, pediatric, distant metastasis, prognosis, clinicopathological features

Introduction

Angiosarcomas are malignant tumors of the inner lining of blood vessels that recapitulate the histological features of normal vasculature and endothelium. Most tumors are in the deep muscles of the lower extremities or the abdominal cavity. Patients with angiosarcoma are usually in their 60 s. The prognosis for this cancer is poor.

Primary splenic angiosarcoma arises from the vascular endothelium of the spleen. The mean age at presentation is between 50 and 60 years of age [1, 2]. This malignancy is extremely rare, and pediatric primary splenic angiosarcoma is rarer still: Only approximately 200 cases of primary splenic angiosarcoma have been reported worldwide, and a very small portion of these were in patients aged 18 years or younger.

In this study, we present a case of primary splenic angiosarcoma of a 4-year-old male who had undergone a total splenectomy. We then summarize the information on pediatric splenic angiosarcoma that is available in the literature in the English language to date, and place the new information gained from this case in the context of what is known.

Materials and methods

Case

Pediatric splenic angiosarcoma was diagnosed at Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea. Representative sections were excised, stained with hematoxylin and eosin (H&E), and reviewed by three pathologists (S. K. Kim, T. Chung, and C. K. Park).

Immunohistochemistry

Tumors were fixed in formalin and embedded in paraffin. Briefly, 5-μm thick sections were cut using a microtome, transferred onto adhesive slides, and dried at 62°C for 30 min. Immunohistochemistry with antibodies against CD31, CD34, Ki67 (Catalog#s M0823, M7165, and M7240, respectively; DAKO, Glostrup, Denmark), Fli-1 (Catalog# 254M-15, Cell Marque, Rocklin, CA, USA) was performed with an automated immunohistochemical staining instrument (Ventana Discovery® XT, Ventana Medical System, Inc., Oro Valley, AZ, USA).

Results

Case

A 4-year-old male patient was referred to our hospital after an incidental detection of a splenic mass. His medical history was unremarkable, except that he had been born during the 35th week of gestation with a birth weight of 1.9 kg. On radiological examination, abdominal computed tomography revealed splenomegaly with heterogeneity of the splenic parenchyma, with hypervascularity and necrosis (**Figure 1A**). Multiple enhancing lesions were noted in the liver (**Figure 1B**). There was no specific atypical

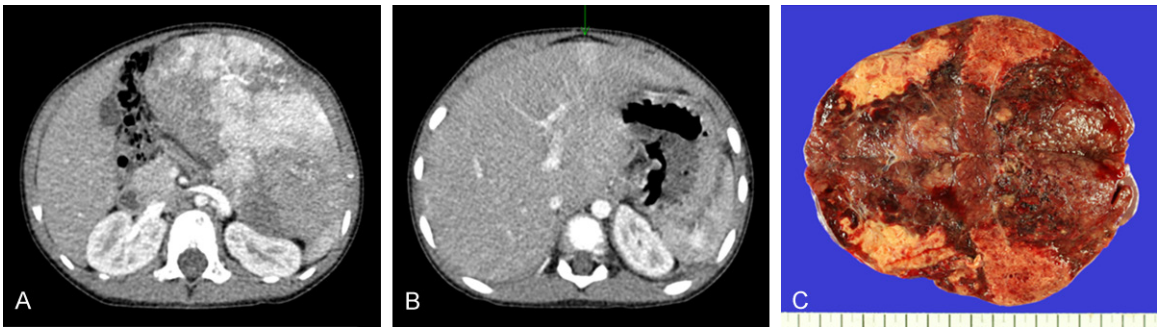

Figure 1. Results from radiological and gross examination. A and B. Computed tomography of abdomen. Note splenomegaly with heterogeneous hypervascular and necrotic portions within the spleen and the multiple enhancing lesions within the liver, indicated by the arrow. C. Gross image of the specimen. Note heterogeneous cut surface with multiple ill-defined grayish soft solid areas, dark red hemorrhagic or sponge-like areas, and yellowish necrotic areas.

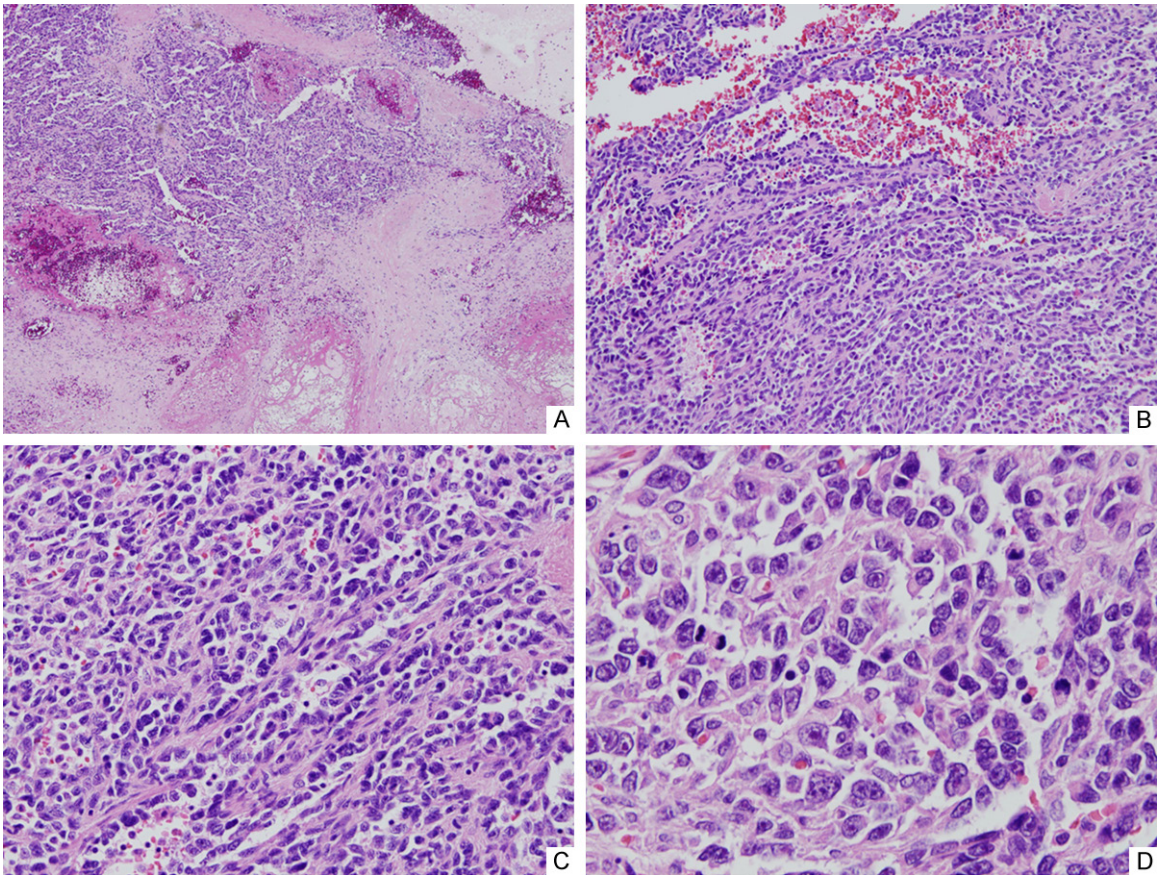

Figure 2. Images from histological examination after H&E staining of specimens of the spleen at different magnification. A. 40× magnification; note hypercellular area with slit-like spaces, necrosis, and hemorrhage. B. 100× magnification; note that the slit-like spaces containing red blood cells anastomose with each other. C. Magnification 200×; note that the lining cells are highly pleomorphic with prominent nucleoli. D. Magnification 400×; note frequent mitoses.

finding in laboratory tests, although the patient's hemoglobin level was 9.1 g dL^{-1} on admission, which was slightly low.

The patient underwent a total splenectomy and a wedge-resection of one of the hepatic nodules. The spleen measured 16 cm along the

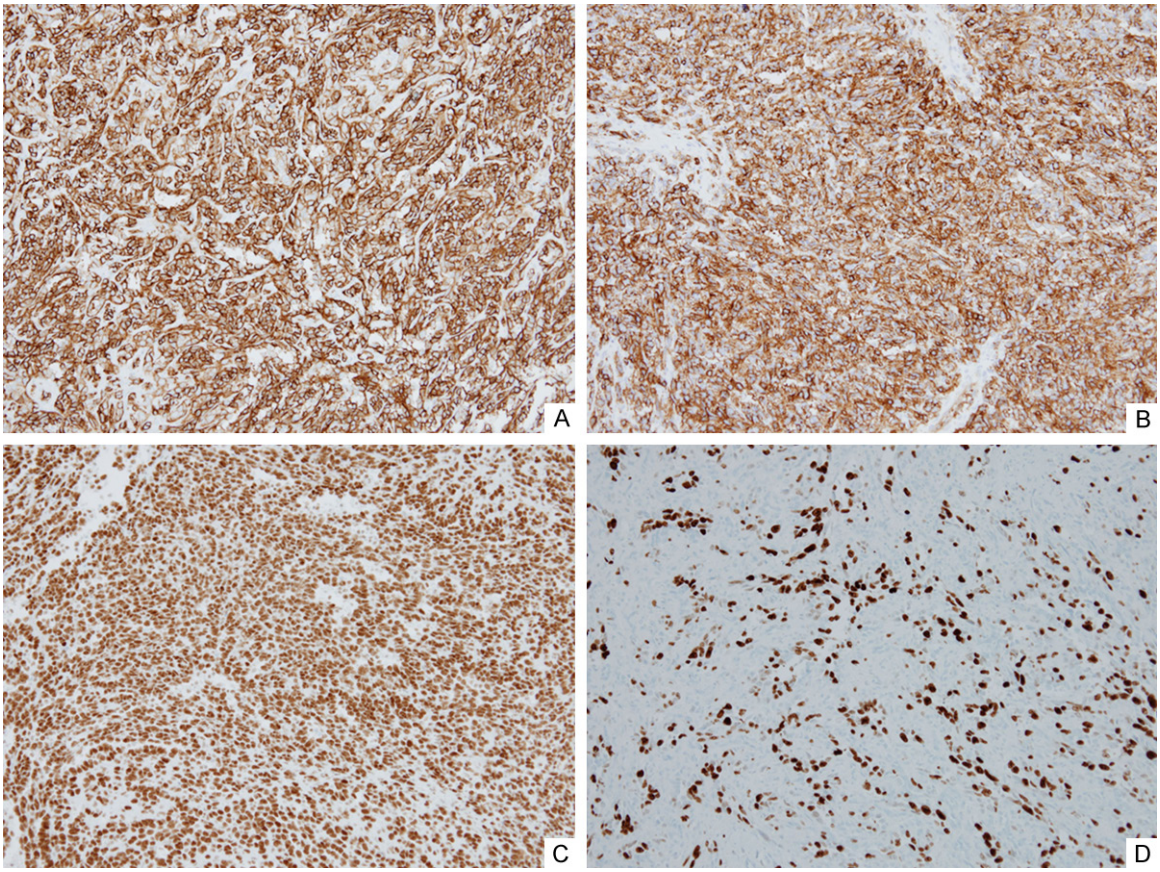

Figure 3. Results from immunohistochemical staining of specimens for the proteins: A. CD31; B. CD34; C. Fli-1; D. Ki-67.

long axis and weighed 466 g. Bisection revealed that the cut surface was variegated, with congestions, hemorrhages, multifocal necrosis, and ill-defined solid lesions (**Figure 1C**). Tissue sections were collected from various parts of the spleen and stained with H&E for histological examination under a light microscope.

Microscopic examination revealed hypercellular lesions with slit-like spaces, and confirmed the presence of necrosis and hemorrhage (**Figure 2A**). Under high magnification (**Figure 2B**), it was apparent that the slit-like spaces were irregularly anastomosed with one another and filled with red blood cells. These complex anastomosing channels were lined with atypical cells with short-spindle or epithelioid cytological features, eosinophilic cytoplasm, irregular nuclear shapes, and prominent nucleoli (**Figure 2C**, **2D**). Mitotic cells were common: there was an average of approximately 50 mitotic cells in 10 high-power fields.

Immunohistochemical staining revealed that vascular markers CD31, CD34, and Fli-1 had a strong positive signal in the tumor cells (**Figure 3A-C**). Staining for Ki-67 was positive in approximately 30% of tumor cells, revealing increased proliferative activity of tumor cells (**Figure 3D**). The wedge-shaped resected hepatic lesion had similar histological findings and immunohistochemical profiles as did the tumor cells.

These results allowed us to make a diagnosis of primary splenic angiosarcoma with multiple hepatic metastases. The patient was underwent a paclitaxel-based chemotherapy, and was scheduled for a 2-month follow-up radiological examination. This exam revealed that the disease status was stable. The patient died 12 months after the surgery.

Clinical features of pediatric splenic angiosarcoma

The cases of pediatric splenic angiosarcoma that we collected from a literature search are presented in **Table 1**. If the single case discussed here is included, there have been 11 reported cases of this condition. Patients

Table 1. Cases of pediatric splenic angiosarcoma

Case No.	Age (yr)	Sex	Tumor size (cm)	Adjuvant therapy	Metastasis	Survival (follow-up period)	Reference
1	15	F	NA	NA	Liver	NA	Ferrara [3]
2	12	F	NA	Radiotherapy	Liver, bone	Died (1 month)	Sordillo [3]
3	1	M	NA	NA	Liver, lung	Died (3 months)	Alt [3]
4	13	M	5	NA	Liver, bone, serosal surfaces, skin	Died (10 months)	Wick [3]
5	15	M	17	Chemotherapy	Liver	Died (1 month)	Kren [3]
6	2	F	NA	Chemotherapy	Liver	Alive (2 years)	den Hoed [3]
7	7	M	13	None	None	Alive (16 years)	Hsu [3]
8	17	F	19	None	None	Alive (16 months)	Manouras [4]
9	13	F	5	None	None	Alive (7 months)	Mejri [5]
10	3	F	17	Chemotherapy	Liver	Died (8 months)	Serrano [3]
11	4	M	16	Chemotherapy	Liver, bone	Died (12 months)	Present case

NA, not applicable.

ranged from 1 to 17 years old, with a mean age of 9.27 years. Pediatric splenic angiosarcoma affected males and females equally. The lesions ranged from 5 to 19 cm in diameter, with a mean of 13.14 cm. Most tumors metastasized to the liver and then to bone. The overall survival rate was 40% (4 out of 10 patients survived; the follow-up period was 27.4 ± 58.27 months).

Discussion

Angiosarcomas are malignant neoplasms that arise in the endothelial cells of vascular tissue; primary splenic angiosarcomas occur in the spleen. In general, angiosarcomas have poor prognoses, but this is particularly true of primary splenic angiosarcoma because of its highly aggressive behavior and frequent metastases. The 6-month overall survival after diagnosis is less than 25% [3]. The rarity of this disease makes planning for treatment difficult. Splenectomy can be curative in early stages of the disease, and adjuvant chemotherapy with taxanes such as paclitaxel is also prescribed [3].

Primary splenic angiosarcomais extremely rare in pediatric patients, with only ten cases reported worldwide (**Table 1**) [3-5]. Among these cases, the most common clinical presentation was splenomegaly, and most patients had left upper abdominal pain. Anemia was a common laboratory finding in these patients [6]. Pediatric angiosarcoma of organs other than the spleen appears to occur slightly more often in males than in females [7, 8].

The pathogenesis of primary splenic angiosarcoma is not well characterized. Proposed causal factors include exposure to ionizing radiation, previous chemotherapy, or chemical agents such as arsenic [9]. A case report suggests that benign infantile hemangioma can be transformed into angiosarcoma by the mutation of KRAS gene [10].

Our microscopic examination and immunohistochemical study supports the diagnosis of primary splenic angiosarcoma. Microscopic examination revealed variably pleomorphic endothelial tumor cells lining irregularly anastomosing vascular spaces, well-known and typical histological features of angiosarcoma. Frequent mitoses, multifocal necroses, and hemorrhage were also identified in the tissue. Other diagnoses that should be considered include hemangioma, littoral cell angioma, angiosarcoma, lymphangioma, or lymphangiosarcoma [6]. Hemangioma is a benign vascular neoplasm with well-formed vascular structures that has no atypical cells, necrosis, or infiltrations. The case under consideration had high-grade nuclear atypia, frequent mitoses, and multifocal necrosis, which are presumed to be malignant. Littoral cell angioma and angiosarcoma are composed of splenic littoral cells, which have positive immunohistochemical staining for CD68 and CD163. Lymphangioma or lymph angiosarcoma are composed of lymphatic vessels and the endothelial cells of this tumor have variable immunohistochemical staining patterns with CD31 and CD34, but strongly positive staining with D2-40. We performed immunohistochemical staining for CD68 and D2-40 on the tumor cells in the case presented here, with negative results (data not shown). Thus, we are confident in our diagnosis.

Angiosarcoma of the spleen is extremely uncommon in adults and even less common in children. It is an aggressive cancer, characterized by fast growth, frequent metastasis, and a poor prognosis. We have described a case of primary splenic angiosarcoma in a young child. This case report presents a pediatric splenic angiosarcoma which has the characteristic histological and immunohistochemical features of this cancer.

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Disclosure of conflict of interest

None.

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