Hamartoma of the Spleen

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Hamartoma of the spleen is a rare, benign vascular proliferation that is often found incidentally while working up other complaints or at autopsy. Women more commonly present with symptoms related to mass effect than men. Histologic findings consist of unorganized vascular channels of varying width, with intervening red pulp–like disorganized stroma with or without lymphoid follicles. The endothelial cells are similar to those of normal splenic sinuses. Although rendering a diagnosis can be difficult, endothelial cells that are positive for CD8 are a key feature that differentiate hamartoma from other vascular lesions of the spleen. Clinical, radiologic, and histologic correlation is essential to ensure this benign lesion is not mistaken for malignancy.

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Vascular neoplasm is the most common primary neoplasm of the spleen.1 Of the various vascular tumors of the spleen, splenic hamartoma and littoral cell angioma occur only in the spleen.2 Since the first report in 1861 by Rokitansky,3 splenic hamartomas have also been called splenomas, spleen within a spleen, hemangiomas, post-traumatic scars, fibrotic nodules, tumorlike congenital malformations, and hyperplastic nodules.4,5 Splenic hamartomas are very rare with only 3 described in 200,000 splenectomies at a medical center during a 17-year period6 and an incidence of 0.024% to 0.13% in a review of autopsies.8 More than 150 cases of splenic hamartoma have been documented in the literature to date.9 Improvements in imaging techniques have led to increased detection of this entity and a secondary rise in incidence.5 Although hamartomas are benign and usually asymptomatic, it is important to distinguish this benign lesion from malignancy.

CLINICAL HISTORY

A 29-year-old woman, with no significant medical history, presented with persistent right-sided abdominal pain. No organomegaly was noted in the abdomen on physical examination. Ultrasound of the abdomen demonstrated a homogenous, hypoechoic, 3.9-cm mass of the spleen, without internal color Doppler flow. Computed tomography displayed a hypoenhancing and hypodense lesion (Figure 1, A). Magnetic resonance imaging revealed a mildly hypointense and hypovascular lesion on T1- and T2-weighted images (Figure 1, B). Subsequently, the lesion demonstrated heterogeneous enhancement, becoming mildly hyperintense to the spleen. Differential diagnoses included inflammatory pseudotumor, lymphoma, and atypical hemangioma. On further evaluation, the patient was found to have biliary dyskinesia and underwent a laparoscopic cholecystectomy and splenectomy for tissue diagnosis. The resected 200-g spleen contained a 3-cm, well-circumscribed solid mass (Figure 2). Histology of the mass showed partially solid and cystic areas, containing a mixture of unorganized vascular channels lined by plump endothelial cells (Figures 3 and 4). No areas of cytologic atypia, mitosis, or necrosis were identified (Figure 5). Immunostain for CD8 was positive for lining cells (Figure 6). CD68 was diffusely positive in macrophages and focally positive in lining cells, and CD34 was positive in lining cells; CD31 was diffusely positive, and CD21 was negative. The combined morphologic and immunohistochemical profile supported a diagnosis of splenic hamartoma.

CLINICAL FEATURES

Splenic hamartomas occur in any age group (11 months to 86 years),2 with equal occurrence in males and females, usually without symptoms.8,10 The average size of the lesion is reported1 to be larger in females, suggesting hormonal influence. Hence, clinical manifestations associated with larger lesions, such as splenomegaly, palpable mass, or spontaneous rupture, are more common in women.11 Some reported cases were associated with hypersplenism, such as thrombocytopenia, anemia, and pancytopenia, or hematologic conditions, including malignancy.4,6,12 Although even rarer in the pediatric population, the percentage of affected children who are symptomatic is higher than that of adult patients.4,5 Rare cases of splenic hamartoma associated with tuberous sclerosis have also been reported.4,13,14 Most splenic hamartomas are hyperechoic solid masses, with or without cystic changes in ultrasonogram, and are hypervascular in both color Doppler ultrasound and angiogram. On computed tomography, hamartomas appear as isodense or hypodense solid masses and demonstrate heterogeneous contrast enhancement relative to adjacent normal parenchyma.11 (Figure 1). Most of the lesions are isointense in T1-weighted magnetic resonance images and heterogeneously hyperintense in T2-weighted magnetic resonance images.11,15 Although splenic hamartoma may be suggested by radiologic findings, definitive diagnosis
Figure 1. Incidentally found splenic hamartoma in a 29-year-old woman. A, Contrast-enhanced computed tomography scan showing hypodense lesion (arrow) in the dome of the spleen. B, The lesion (arrow) is mildly hypointense on a T1-weighted image.

Figure 2. Photograph of the cut surface of the resected spleen illustrating well-circumscribed solid mass (arrow) (10% buffered formalin-fixed).

Figure 3. Scanning view of the mass without malpighian corpuscles (left field), in contrast to the adjacent normal splenic parenchyma with white pulp (right field) (hematoxylin-eosin, original magnification ×40).

requires tissue examination. Tissue examination can also exclude malignancy and, in some cases, relieve symptoms. Fine-needle aspiration of hamartomas has been performed in a limited number of cases. Splenectomy is curative for rare symptomatic hamartomas, but a partial splenectomy may be sufficient in some cases.

PATHOLOGIC FEATURES

Hamartomas are solitary or multiple, round, well-circumscribed, unencapsulated bulging nodules compressing the adjacent normal splenic parenchyma (Figure 2). Focal fibrosis and cystic areas can be seen. The color is usually dark red to grayish white. The size ranges from a few millimeters to centimeters, with a median size of 5 cm, but lesions as large as 20 cm have been reported. Histologic findings reveal disorganized vascular channels lined by slightly plump endothelial cells without atypia, mixed with intervening splenic red pulp–like stroma with or without white pulp (Figures 3 through 5). Organized lymphoid follicles (malpighian corpuscles) are not present. Four cases of splenic hamartoma with large, atypical stromal cells have been described recently. The bizarre stromal cells expressed desmin and keratin, suggestive of immunophenotype similar to that of accessory reticulin cells. Laskin et al interpreted this immunophenotypic modulation as a response to pathologic stimuli and emphasized that the presence of bizarre stromal cells should not be misinterpreted as malignancy. Additionally,
plasmacytosis, extramedullary hematopoiesis, and increased numbers of macrophages, eosinophils, and mast cells can be seen.7,10

A key immunohistochemical feature is CD8 positivity of the lining cells of the vascular channels21 (Figure 6). The cells are also positive for CD31, factor VIII–related antigen, and vimentin.2,0,12,18,22 Immunostaining results for the lining cells with CD34 have been inconsistent,2,9,12,18,20,22 and the endothelial cells are negative for CD21. CD68 is positive in scattered stromal macrophages but negative in the lining cells of the vascular channels. The endothelial nature of the lining cells with Weibel-Palade bodies has been confirmed by ultrastructural studies.2,8

PATHOGENESIS

The pathogenesis of hamartoma is controversial. Some consider hamartomas congenital malformation of the splenic red pulp, a neoplasm, excessive and disorganized growth of abnormally formed red pulp, or a reactive lesion to prior trauma.2,7 With documented cases associated with hematologic malignancy, others believe hamartoma is an acquired proliferative process.11

DIFFERENTIAL DIAGNOSIS

Splenic hamartomas must be differentiated from other vascular tumors of the spleen, including hemangioma, littoral cell angioma, lymphangioma, hemangioendothelioma, sclerosing angiomatoid nodular transformation of the spleen and angiosarcoma (Table). Solid mass–forming lesions of the spleen, such as inflammatory myofibroblastic tumor, lymphoma, metastatic disease, disseminated fungal or mycobacterial infections, and sarcoidosis are also included in the radiologic differential diagnosis.23

Splenic hemangiomas are the most common benign neoplasm arising from sinusoidal epithelial cells. Usually, hemangiomas are asymptomatic, measuring less than 2 cm in diameter. However, there is a risk of a spontaneous rupture with a large lesion.15 The cavernous type is more common than the capillary type, and diffuse angiomatosis replacing the whole spleen has been documented. Histologically, hemangiom a is composed of proliferating vascular channels, which are lined by flat endothelial cells and separated by thin fibrous septa or red pulps.11 The vascular channels are filled with red blood cells. Larger lesions may show thrombosis, infarction, fibrosis, and pseudocystic degeneration.15 The flat endothelial cells are positive for endothelial markers including CD31 and CD34 and are negative for CD8, CD21, and CD68.

Littoral cell angioma is a vascular tumor arising from littoral cells originating from splenic sinuses. Littoral cells are characterized by their expression of both endothelial and histiocytic markers. This rare entity was first described in 199124 and 2 cases with malignant histology have been reported.25,26 One-third of previously reported littoral cell angioma cases were associated with visceral tumors.23 Littoral cell angiomas are frequently associated with splenomegaly and appear as low attenuating lesions in contrast-enhanced computed tomography.11 Histologic examination demonstrates anastomosing vascular channels lined by tall columnar cells, which often show hemophagocytosis.2 The lining cells are positive for both endothelial and histiocytic markers, CD31 and CD68, and are negative for CD8, CD21, and CD68. Unlike

CD8 immunostain is positive in the lining cells (arrow) and scattered lymphocytes (original magnification ×200).

Figure 4. The lesion containing a mixture of unorganized vascular channels (arrow) and fibrotic cords of splenic red pulp–like area (hematoxylin-eosin, original magnification ×200).

Figure 5. Higher magnification of the lesion reveals no cytologic atypia, mitosis, or necrosis (hematoxylin-eosin, original magnification ×600).

Figure 6. CD8 immunostain is positive in the lining cells (arrow) and scattered lymphocytes (original magnification ×200).
Epithelioid, spindle, and a combination of the 2 histology between benign hemangioma and angiosarcoma of the spleen. It is considered a lesion of intermediate proliferation. Microscopically, the lesion is composed of multiple confluent vascular nodules surrounded by concentric fibrous rims. The lining cells of the vascular channels show mild to moderate atypia with similar immunohistochemical staining patterns to littoral cell angioma, with positive immunostaining for endothelial and histiocytic markers. The lining cells are usually positive for CD31, factor VIII–related antigen, and CD34, variably positive for CD34 and cytokeratin. Sclerosing angiomatoid nodular transformation of the spleen, also known as multinodular hemangioma, is altered red pulp entrapped by nonneoplastic stromal proliferation. Microscopically, the lesion is composed of multiple confluent vascular nodules surrounded by concentric collagen fibers or fibrinoid rims. The central portion of the nodules consists of vascular channels of varying caliber lined by plump endothelial cells interspersed with ovid or spindle cells. There are numerous red blood cells, and intervening stroma is fibroelastic or myxoid with scattered myofibroblasts, siderophages, and inflammatory cell infiltrates. Immunostaining of the vascular area reveals 3 types of blood vessels: CD34+CD31−CD8− sinusoids, CD34+CD31+CD8+ capillaries, and CD34+CD31−CD8− small veins. Scattered macrophages are positive for CD68, and CD21 immunostaining is negative in the lining endothelial cells. Despite its similarity with splenic hamartoma in composition, sclerosing angiomatoid nodular transformation is a mixture of 3 types of blood vessels, whereas hamartoma consists of only sinusoid-type vessels.

Angiosarcoma is the most common nonlymphoid malignant primary tumor of the spleen. Although CD8 positivity of the lining cells in angiosarcoma of the spleen has been reported, the presence of irregular, anastomosing vascular channels associated with marked cellular atypia, frequent mitoses, and invasion of surrounding organs can aid in making a diagnosis. The lining cells are positive for endothelial cell markers, including CD31, CD34, factor VIII–related antigen, and the histiocytic marker CD68. Angiosarcoma is highly aggressive with a poor prognosis.

**CONCLUSION**

With the rapid advancement of imaging modalities, smaller asymptomatic lesions of the spleen are being identified. Splenic hamartoma is a benign vascular proliferation characterized by CD8 immunophenotype of the lining endothelial cells. We should be aware of this rare, benign entity and interpret histologic features in the context of clinical and radiologic findings to render a diagnosis and differentiate it from malignancy.

**References**


