Tumour-like lesions of the spleen

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Abstract

Tumour-like lesions of the spleen are very rare lesions but can cause diagnostic confusion due to their varying morphologic patterns. These lesions behave in a benign fashion. Included in this group are hamartomas, sclerosing angiomatoid nodular transformation (SANT), inflammatory pseudotumors, and possibly IgG4-related disease. Clinically, these lesions are often discovered incidentally on imaging or at autopsy. However radiological and morphological findings can be misleadingly worrisome. It is therefore important to be familiar with these lesions to distinguish them from malignant lesions.

Keywords IgG4-related disease; inflammatory myofibroblastic tumour; inflammatory pseudotumor; sclerosing angiomatoid nodular transformation; spleen; splenic hamartoma; tumour-like lesions

Introduction

The spleen functions as a key component of the mononuclear phagocyte system (reticuloendothelial system) and has an important role in immunology, haematopoiesis, and cell metabolism. The spleen consists of two essential functional structures: white pulp and red pulp. The red pulp contains sinusoids with fenestrated endothelium and macrophage containing cords to filter red blood cells and remove wastes and particulates from circulation. The white pulp supports the immune response with malpighian corpuscles that contain lymphoid follicles with B cells and periarteriolar lymphoid sheaths with T cells.[7]

The spleen can have both primary lesions and tumours (especially vascular tumours) and metastasis from other sites. Tumour-like lesions are exceptionally rare, and the pathophysiology is often unknown or only speculated. Often these lesions, especially SANT, inflammatory pseudotumors, or IgG4-related disease have an infiltrating inflammatory component, perhaps pointing to an immunologic aetiology; whereas a splenic hamartoma has been described as both a malformation or acquired proliferative neoplasm. Nevertheless, these lesions have caused a great deal of confusion among even the most experienced diagnosticians. Thus, it is important to recognize these lesions in the differential diagnosis of splenic lesions and to avoid misdiagnosis of these lesions as malignant.

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Hamartoma

Splenic hamartomas are benign lesions that were first reported in 1861. These lesions have also been called splenomas, splenadenomas, or nodular hyperplasia of the spleen. Since it was first described in 1861 more than 150 cases have been reported.[1,2] According to autopsy series, the incidence ranges from 0.024% to 0.13%.[3]

Clinical presentation

Patients are generally asymptomatic with only a minority of cases presenting with abdominal pain, hypersplenism or splenic rupture. There is an association with diseases that contain multiple hamartomas of other organs such as tuberous sclerosis and Wiskott–Alchrich syndromes.[4,5] On ultrasound imaging, the lesions are typically hyperechoic solid masses that may be associated with cystic changes, whereas on computed tomography (CT), the lesions are hypoattenuating solid masses and show heterogeneous contrast enhancement when compared to the background spleen (Figure 1). The lesions are well-circumscribed and bulging. They are mainly solitary masses, or rarely multinodular, and can be quite large (from <2 cm up to 20 cm).[4,6]

Histopathology

Hamartomas are a malformation of normal splenic red pulp elements. The lesions do not have a true capsule separating them from the normal parenchyma (Figure 2). Splenic hamartomas are characterized by architecturally disorganized vascular channels lined by endothelial cells and surrounded by fibrotic cords of predominant splenic red pulp, which can be seen better with a reticulin stain (Figure 3).[4,7] Organized lymphoid follicles (malpighian corpuscles) are usually not present.[3] Plasmacytosis, extramedullary haematopoiesis, and increased numbers of macrophages, eosinophils, and mast cells can be seen.[3]

Differential diagnosis

Pathologic differentiation of hamartoma from haemangioma can be difficult. The endothelial cells of splenic hamartoma are CD8 positive whereas those of haemangioma are not.[4] These endothelial cells are also positive for CD31, factor VIII-related antigen and vimentin. Finally, hamartomas contain sinus and pulp cordlike elements, whereas haemangiomas only encompass well-organized lymphoid tissue.

Sclerosing angiomatous nodular transformation (SANT)

SANT, also called cord capillary haemangiomas and multinodular haemangioma, are rare splenic tumours originally

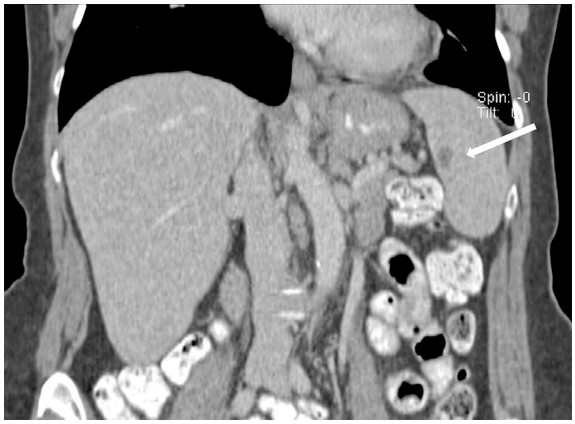

Figure 1 Splenic hamartoma. Coronal reformat contrast enhanced abdominal CT reveals a well circumscribed, hypoattenuating to splenic parenchyma mass in the posteromedial spleen.

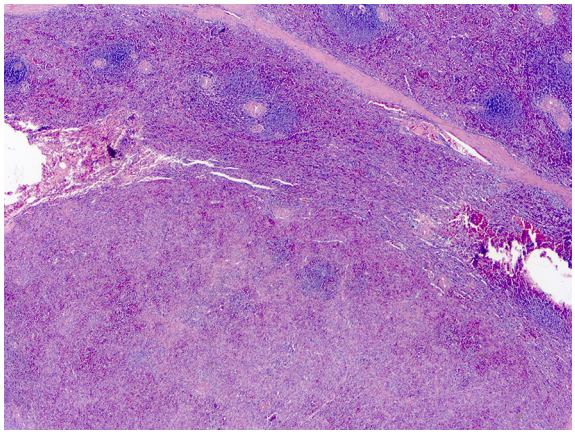

Figure 2 Splenic hamartoma. H&E stain. Well-circumscribed lesions comprised of splenic red pulp without a true capsule in comparison to the uninvolved splenic parenchyma. Magnification: 25×.

described in 2004 by Martel et al.[8] A literature review reveals that less than 100 cases have been reported.[9] The aetiology is unknown but hypothesized to be immune related.

Clinical presentation

SANT lesions are more common in women and most cases are in the 30–60 age range.[9] Most patients are asymptomatic and the tumours are found incidentally on imaging but, for symptomatic patients, abdominal pain is the most common sign.[10] On ultrasound imaging, the lesions are hypoechoic. Unenhanced CT shows lesions with lobulated or smooth margins that are heterogeneous and mildly hypoattenuating (Figure 4).[11]

Histopathology

SANT is a well circumscribed and unencapsulated firm mass with multiple red-brown nodules with diameters ranging from 3 to 17 cm separated by fibrotic stroma (Figure 5).[12] Microscopic examination reveals a multinodular lesion composed of slit-like round or irregular vascular spaces separated by concentric dense collagen fibres (Figure 6).[10] The vascular spaces are lined by plump endothelial cells while the intervening stroma contains myxoid to dense fibrous tissue with scattered myofibroblasts and inflammatory cells including plasma cells. Atypia, mitotic figures and necrosis are usually absent. Immunohistochemical staining can be used to highlight the three distinct types of vessels found in SANT: well-formed cord capillaries (CD34+/CD31+/CD8−), splenic sinusoids (CD34−/CD31+/CD8+), and small veins arranged in a very intricate mesh-like pattern (CD34−/CD31+/CD8−).[10]

Differential diagnosis

The differential diagnoses include haemangioma, hemangioendothelioma, littoral cell angioma, hemangioendothelioma, angiosarcoma, and IgG4-related disease (see below for further discussion).[7,10] Splenic haemangiomas are much more common vascular lesions with endothelial cell lined vascular spaces that are positive for CD31 and CD34, but will not have the three distinct vessel pattern as seen in SANT. Littoral cell angiomas are also vascular lesions, but arises from the littoral cells of splenic sinuses and thus have a characteristic immunophenotype: CD34−, CD68+, CD21+ and CD8−.[7,10] Hemangioendothelioma have varying histology with mild to moderate cytologic atypia and CD34 and cytokeratin positivity on immunohistochemistry not seen in SANT lesions. Angiosarcoma, malignant vascular tumour, has a diffuse, invasive growth with cytologic atypia and mitoses.[10] These features are not present in SANT.

Inflammatory myofibroblastic tumours (inflammatory pseudotumors)

Inflammatory myofibroblastic tumour (IMT), also known as inflammatory pseudotumor (IPT), is a rare lesion that was first described by Brunn in 1930s and the first splenic lesions were noted by Cotelingam and Jaffe.[13,14] The lesions can occur in a variety of anatomical sites with approximately two thirds of cases being extrapulmonary and one third intrapulmonary.[15] Previously thought to be a benign process, studies in the last two decades have shown possible evidence of chromosomal anomalies, association with the Epstein–Barr virus, immunologic derangement, and rare aggressive behaviour in IMTs.[13]

Clinical presentation

The lesions in the spleen most commonly occur in children or younger adults (<50 years old), and are more common in women. Patients often present with nonspecific symptoms including weight loss, unexplained fever, abdominal pain, anaemia, lymphadenopathy, and splenomegaly.[16,17] Unenhanced CT typically shows a low-attenuated, well-circumscribed lesion that may have calcifications. Central satellite area with radiating lines indicating the fibrous plaque and hypoattenuation on early contrast enhancement CT is characteristic features of IMT (Figure 7). The lesions are also well-circumscribed and hypoechoic on sonography.[18]

Histopathology

Splenic IMTs are typically solitary lesions ranging in size from 0.5 cm to >10 cm. Multiple lesions are rare and smaller in size. Histologically, the lesions contains fibrous bands that partially delineate from the uninvolved parenchyma and spindled cells with bland nuclei in a background of mixed inflammatory cells,