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Case report

Inflammatory pseudotumor-like follicular dendritic cell tumor of the spleen: a case report and approach to differential diagnosis ☆,☆☆

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ABSTRACT

We present a case of an inflammatory pseudotumor-like follicular dendritic cell tumor of the spleen. The patient is a 44-year-old woman, without significant underlying history, who presented with nonspecific abdominal pain for a few months. Both a contrast enhanced computed tomography and magnetic resonance imaging revealed a new 2.5 cm enhancing splenic lesion, which demonstrated hypermetabolic activity on subsequent positron emission tomography and computed tomography scan. Since the lesion was new compared to more remote imaging and hypermetabolic, a splenectomy was performed. Pathology confirmed the diagnosis and demonstrated positivity for Epstein-Barr Virus .

Introduction

Often dubbed the "forgotten organ," the spleen and many of its normal physiological roles are still poorly understood and often overlooked. Though incidentally encountered splenic lesions can be a challenge, the majority of these lesions are benign. A wide spectrum of splenic lesions exists ranging from post-traumatic findings to vascular neoplasms such as hamartomas, lymphangiomas, and SANTS (sclerosing angiomatoid nodular transformation). Imaging features suggestive of malignancy have been identified including absence of splenomegaly, ill-defined margins, solid nature, lack of calcification, and the presence of underlying malignancy [1].

One extremely rare neoplasm of the spleen is the follicular dendritic cell tumor. Often present in cervical and axillary

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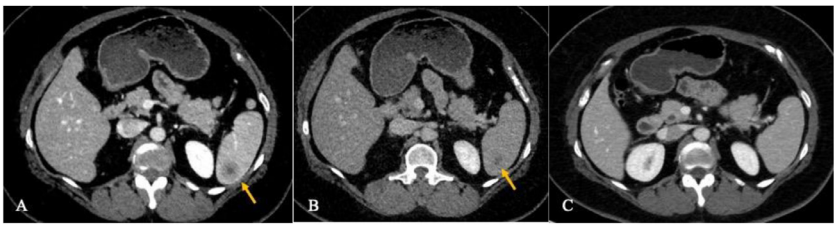

Fig. 1 – Contrast-enhanced CT of the abdomen and pelvis was performed. (A) Axial CT of the abdomen in portal venous phase. There is a new 2.5 cm splenic lesion (yellow arrow) with hypoenhancing thick rind of soft tissue and central fluid density which may represent necrosis. (B) Axial CT of the abdomen in delayed phase. The splenic lesion (yellow arrow) has similar enhancement compared to the splenic parenchyma. There is persistent central low density which may represent necrosis. (C) Axial CT of the abdomen in portal venous phase from one year prior. The current splenic lesion described in A and B was not present 1 year ago.

nodes, follicular dendritic tumors can occur in extra-nodal sites such as the tonsils, lungs, gastrointestinal tract, orbits, and, as we report here, within the spleen [2].

Case report (clinical and radiologic findings)

A 44-year-old woman presented with 4 months of pulsatile left upper quadrant abdominal pain and pressure which radiated to her back with associated nausea. She has a history of hepatitis C virus, which was treated with Harvoni.

Portal venous phase contrast-enhanced computed tomography (CT) of the abdomen revealed a new 2.5 cm splenic lesion (Fig. 1). The lesion appeared hypoenhancing with a thick rind of soft tissue and central fluid density, suggestive of necrosis. On the delayed phase, the splenic lesion had similar enhancement to the splenic parenchyma, except for the central area of low density which persisted. The lesion was not present on a CT scan from one year earlier.

Further imaging with magnetic resonance (MR) imaging was recommended (Fig. 2). T2- and T1-weighted sequences, multiphase contrast-enhanced sequences, and diffusion-weighted imaging were performed. The T2-weighted sequence demonstrated that the splenic lesion had an intermediate to hyperintense signal in the periphery surrounding a hyperintense central region that has signal intensity similar to fluid. The diffusion-weighted imaging, with a b-value of 800 s/mm^2, showed restricted diffusion within the lesion, which was confirmed by an apparent diffusion coefficient image. On T1-weighted sequence, the lesion was mostly isointense on precontrast phase, with delayed homogeneous enhancement peripherally. A differential diagnosis included hemangioma and hamartoma. A splenic hemangioma commonly has similar imaging characteristics as a liver hemangioma, with nodular peripheral enhancement that progresses in a centripetal fashion. A splenic hamartoma is a rare tumor that can avidly enhance but can be heterogenous with a central hypovascular region. In this case, as the lesion had newly developed within the past year, a positron emission tomography and computed tomography scan (PET-CT) was recommended. The PET-CT showed that the splenic mass was intensely hypermetabolic, which was concerning for malignancy (Fig. 3).

The patient underwent a laparoscopic splenectomy. Histologic sections demonstrated a well-circumscribed 2.5 cm splenic nodule containing a proliferation of neoplastic spindled-to-ovoid cells set amidst a dense lymphoplasmacytic infiltrate (Fig. 4). Immunohistochemical stains confirmed that the neoplastic cells were of follicular dendritic cell origin, and in situ hybridization demonstrated strong positivity for Epstein-Barr virus (EBV). The morphological and immunophenotypic findings are consistent with a diagnosis of an inflammatory pseudotumor-like follicular dendritic cell tumor.

Discussion

The inflammatory pseudotumor-like follicular dendritic cell tumor is an extremely rare variant of the follicular dendritic cell tumor. While there are currently less than 200 cases of follicular dendritic cell tumors reported in the literature [3], the specific subvariant of inflammatory pseudotumor-like follicular dendritic cell tumor has less than 40 documented cases. Of these cases, less than 20 have been reported to occur within the spleen [4]. Almost all cases are related to clonal Epstein-Barr virus proliferation. Additional clinical associations include prior surgery, ventriculoperitoneal shunt, trauma, radiation therapy, and steroid usage [5]. To our knowledge, our patient had none of these risk factors.

Due to the paucity of reports in the literature and their vague presentation, these rare lesions may go undetected and underdiagnosed. There is a predilection for the female gender with a reported 2.2:1 female to male ratio. The median age of patients with the tumor is reported to be 56.5 [6]. Furthermore, almost all cases occur in either the liver or the spleen. Although patients may be asymptomatic, reported symptoms include abdominal discomfort, pain or fever [4].

Although there is no well researched imaging pattern for this tumor, some reports have shown both similarities and differences in both splenic and hepatic locations [7]. On CT, the lesion can be hypodense and homogenous, likely due to slow tumor growth. On MRI, the lesion can be heterogenous on T2-weighted sequence, with peripheral hypointensity that appears to represent a pseudocapsule, which is best appreciated on postcontrast T1-weighted sequence. The commonly

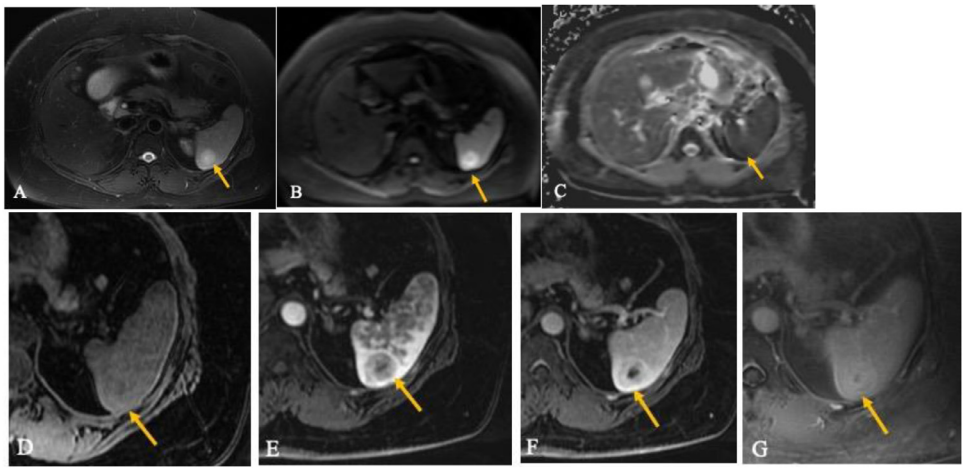

Fig. 2 – Further evaluation with contrast-enhanced MRI of the abdomen was performed. T1W, T2W, DWI/ADC, and multiphase contrast-enhanced sequences were obtained. (A) Axial T2W sequence with fat saturation. The splenic lesion (yellow arrow) is T2-intermediate to hyperintense. The central T2-hyperintense signal is similar to fluid signal intensity. (B). Axial DWI (B-value 800). (C). Axial ADC map. The lesion shows hyperintensity on DWI with corresponding mild hypointensity on ADC map which confirms restricted diffusion. (D) Axial T1W sequence with fat saturation precontrast. (E) Axial T1W sequence postcontrast arterial phase. (F) Axial T1W sequence postcontrast venous phase. (G) Axial T1W postcontrast delayed phase. The T1-isointense splenic lesion (yellow arrow) demonstrates gradual enhancement peripherally, with nonenhancing central cystic and/or necrotic area. The lesion is hypoenhancing on arterial phase compared to the splenic parenchyma (E) and becomes isoenhancing on delayed phase (G).

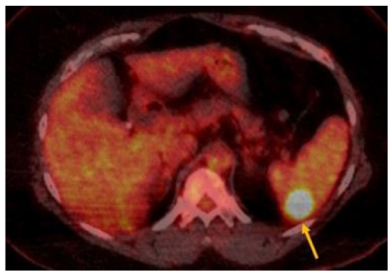

Fig. 3 – PET-CT was performed. Axial fused PET-CT image demonstrates intensely high metabolic activity in the splenic lesion.

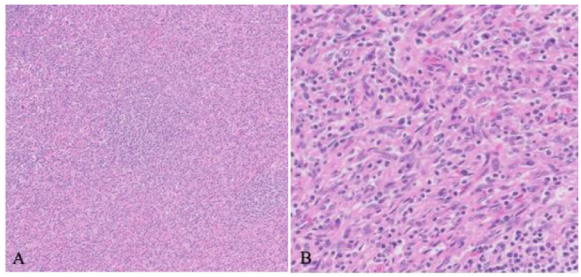

Fig. 4 – Hematoxylin and Eosin (H&E) stains of resected splenic lesion, 5x power (A) and 20x power (B). Histology demonstrated a proliferation of neoplastic follicular dendritic cells (spindled to ovoid cells) set amidst a dense lymphoplasmacytic infiltrate. The atypical follicular dendritic cells are characterized by large size, indistinct cell borders, elongated to oval nuclei, vascular chromatin, prominent nucleoli, and in some cases, pleomorphic nuclei with atypical mitotic figures.

reported imaging features of an inflammatory pseudotumor-like follicular dendritic cell (IPT-like FDC) in the spleen, as seen in our case, include peripheral hypodense/hypointense (T1 or T2) fibrotic component that gradually enhance and a central liquefactive necrotic region that is hypodense on CT or T2-hyperintense on MRI [7]. On diffusion-weighted imaging, IPT-like FDCs are hyperintense, likely a result of increased cell density. FDG-PET findings demonstrate hypermetabolic activity in these lesions [8].

The clinical significance derives from its similarity to other neoplastic processes. While other splenic masses can present similarly, it is important to identify distinguishing features in order to differentiate IPT-like FDCs from other common benign splenic lesions [9]. On the delayed contrast enhanced phase, the enhancement of an IPT-like FDC is similar to that of the splenic parenchyma. Therefore, a benign hemangioma can be a differential diagnosis. However, the classic feature of peripheral nodular enhancement that progresses in a centripetal fashion seen in a hemangioma is not seen in our case of IPT-like FDC. A splenic hamartoma can also be considered because the central hypodensity (or T2-hyperintensity) is also a feature that can be observed with a hamartoma. However, a hamartoma tends to be avidly hyperenhancing and heterogeneous, but our case of IPT-like FDC is homogeneously isoenhancing except for a central hypodense (or T2-hyperintense)

region. When a splenic lesion is not classically benign appearing, it is worthwhile to obtain additional imaging and to also consider a malignant process.

Immunohistochemically, follicular dendritic cell markers are useful for diagnosis, which include positive staining of CD21, CD35, and clusterin [2]. Positive EBV in situ hybridization further supports the diagnosis. Although the pathogenesis is currently unclear, it has been hypothesized that the carcinogenic properties of EBV directly stimulate the neoplastic transformation of mesenchymal cells within follicular dendritic cell tumors [10]. In our case, the stains revealed a proliferation of neoplastic follicular dendritic cells set amidst a dense lymphoplasmacytic infiltrate. The atypical follicular dendritic cells are characterized by their large size, indistinct cell borders, elongated to oval nuclei, vesicular chromatin, prominent nucleoli, and in some cases, pleomorphic nuclei with atypical mitotic figures.

Conclusion

Though exceedingly rare, splenic IPT-like FDCs pose a significant diagnostic conundrum. Due to its high vascularity, the spleen is very difficult to safely biopsy and thus it can be challenging to obtain a definitive diagnosis. IPT-like FDCs may mimic a wide range of clinical and imaging features as well as other neoplasms and inflammatory entities. In conjunction with splenectomy, histology and immunohistochemistry remain key for diagnosis.

In the case presented here, the patient's short interval development (within 1 year) of a new splenic lesion with hypermetabolic activity on PET-CT led the patient to a splenectomy, which was the appropriate treatment. In previous literature, IPT-like FDC recurrence rate post splenectomy has varied. Some studies have shown no evidence of recurrence during a follow-up period between 4 and 6.5 years [6], while others document rare instances of recurrence [11]. Overall, IPT-like FDCs exhibit less aggressive behavior than other malignant tumors [6].With low recurrence rate and non-aggressive behavior, it is appropriate to undergo radiological and clinical surveillance after splenectomy. However, more research needs to be done for these rare splenic masses to better characterize their imaging features and understand their clinical behavior.

Patient consent statement

Patient consent was obtained in person with the standard form provided by our institution. Patient was contacted and provided verbal consent at the beginning of July. Then a form was sent to the patient, who signed and provided paper consent on July 15, 2021. The form is available to submit if asked.

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