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Case Report

Inflammatory myofibroblastic tumor of the spleen: a case report and review of the literature

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Abstract: Inflammatory myofibroblastic tumor of the spleen (IMTS) is an extremely rare, intermediate malignant tumor with unclear etiology, and is most frequently detected incidentally. IMTS presents with nonspecific symptoms that pose a diagnostic challenge to clinicians or presents with the similar appearances to splenetic malignant neoplasms that pose a misdiagnose prior to surgery. Histopathology of the resected specimen remains the gold standard for diagnosing these rare splenic tumors. But these tumors may be misdiagnosed if pathologists are not familiar with the histologic pattern of their variations. In this paper we report a rare case of IMTS in a 55-year-old female admitted to the Xingtai People's Hospital affiliated to Hebei Medical University, with a mass of the spleen. The mass was identified incidentally two months ago and was initially diagnosed as a splenic lymphoma. The patient underwent laparoscopic splenectomy and the histologic study of the specimen revealed findings consistent with IMTS. Histological examination of the nodular growth revealed spindle cells in a hyalinized stroma with inflammatory infiltration of predominantly plasma cells and lymphocytes, coupled with lymphoid follicle structures. Immunohistochemical staining was performed to confirm the diagnosis of IMTS. Splenectomy is both diagnostic and curative for IMTS, and prognosis is generally favorable following the procedure. Our case report of IMTS adds to pathologists' knowledge of diagnosis. Meanwhile, the description and the review of features of IMTS, based on published cases, should help to improve the understanding and diagnosis level of this rare disease.

Keywords: Inflammatory myofibroblastic tumor, spleen, diagnosis, misdiagnosis, antidiastole

Introduction

Inflammatory myofibroblastic tumor (IMT) is typically intermediate malignant tumor with a potential of local recurrence or a low risk of metastatic. IMT was originally detected in the lung by Brunn [1] and was initially denoted as inflammatory pseudotumor (IPT) until the World Health Organization (WHO) officially named it inflammatory myofibroblastic tumor (IMT). So far, the etiology and the pathogenesis of IMT remain ambiguous. There are many inflammatory myofibroblastic tumors (IMTs) that have been reported in a number of different organ systems, including digestive system, bladder, heart, soft tissues, lymph nodes, liver, mesothelial membranes, and spleen, of which lung and orbit are predilection sites [2-4]. IMTS is extremely rare and frequently misdiagnosed as malignant or other tumors prior to surgery [3, 5, 6]. At present, only about 115 cases have been reported in the medical literature since the first 2 cases were reported in 1984 by Contelingam and Jaffe. Moreover, these tumors may be misdiagnosed if pathologists are not familiar with the histologic pattern of their variations. To improve pathologists' clinical and pathological knowledge of these tumors, we report a case of IMTS and review clinicohistopathological findings, diagnosis, and antidiastole of some literatures in this paper.

Case report

A 55-year-old female presented to the Xingtai People's Hospital Affiliated to Hebei Medical University due to a hypodense lesion occupying the lower pole of the spleen that had been identified incidentally in a routine ultrasound scan on examination two months ago. This patient had no specific clinical symptoms for example abdominal pain, fever, loss of appetite, weight

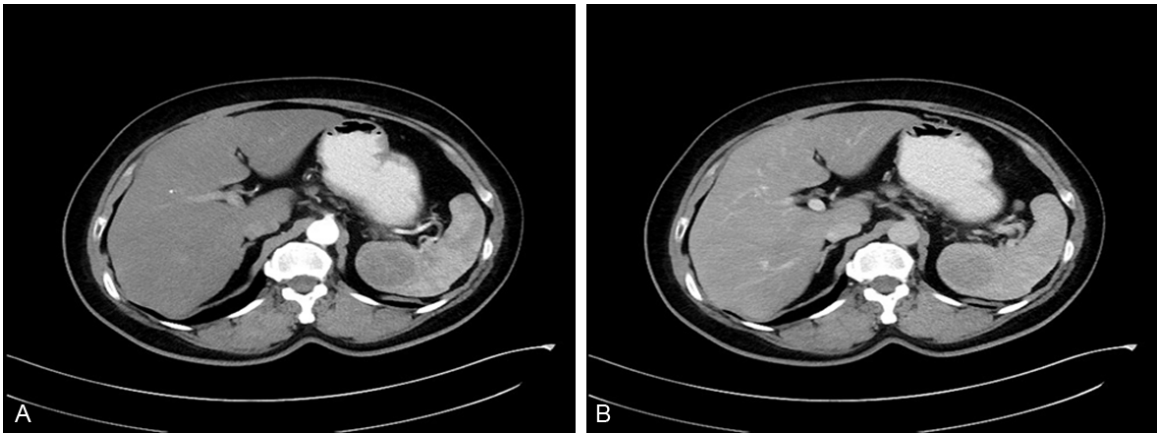

Figure 1. Contrast-enhanced computed tomography (CT) of the abdomen revealed a splenic mass lesion. A. A low-density mass in the arterial phase of CT scan. B. A low-density mass in the venous phase of CT scan.

loss and so on. A complete blood count was within normal range. Contrast-enhanced computed tomography (CT) of the abdomen revealed a low-density mass lesion of the spleen measured 4.1 × 3.2 cm (**Figure 1**). The initial diagnosis was splenic lymphoma based on the radiological findings. Therefore, the patient underwent laparoscopic splenectomy. A mild splenomegaly with a tumor occupied the lower pole was visible during the operation, and the resected specimen was sent for histopathologic examination.

On gross examination, a well-circumscribed and non-encapsulated nodular growth producing a bulge in the splenic contour was seen on the lower pole of the spleen. The mass was measured 4 × 3 × 2 cm in diameter and appeared tan-white on cut section (**Figure 2A**). Microscopic examination of the nodular growth revealed spindle cells and admixture of inflammatory cells (**Figure 2B** and **2C**). Spindle cells in a hyalinized stroma (**Figure 2D**), inflammatory infiltration of predominantly plasma cells and lymphocytes (**Figure 2E**), along with lymph follicles (**Figure 2F**); some histiocytes were also seen along with djacent splenic tissue with blood stasis.

On immunohistochemical staining, the spindle cells of the tumor were positive for Vimentin (**Figure 3A**), Desmin and smooth muscle actin (SMA) (**Figure 3B**). The background lymphocytes were composed of cells which were positive for CD3 or CD20. Moreover, there were a number of cells expressing CD68 (**Figure 3C**). Immunohistochemistry showed negative staining for anaplastic lymphoma kinase (ALK), S100, CD21 (**Figure 3D**), CD35, CD15 and CD30. The final pathological diagnosis was IMTS. The patient has been followed-up regularly and has remained asymptomatic for two years subsequent to surgery.

Discussion

Inflammatory myofibroblastic tumor (IMT) was known as benign neoplasm earlier and initially denoted as inflammatory pseudotumor, plasma cell granulomas, inflammatory myofibroblastic proliferation, plasma cell pseudotumor, and inflammatory fibrosarcoma [7, 8]. The WHO classification of soft tissue tumors considered this entity as intermediate malignant tumor with a risk of metastatic spread below 5% and officially named it IMT in 2002 [7]. The local recurrence rate of IMT was reportedly about 25% by the literature [9]. IMTs occur in a variety of organs and locations, of which lung and orbit are predilection sites. However, IMTS is extremely rare lesion that is usually located incidentally. To the best of our knowledge, since Cotelingam and Jaffe first reported 2 cases of IMTS in 1984, only about 115 cases have been reported in the medical literature [10].

The pathogenesis of IMT is under debate. There are different theories about its etiology: trauma, surgery, bleeding or rupture of hemangioma, bacterial or viral infections, immunological derangements and neoplastic process [3, 6, 8, 10]. Viruses which were hypothesized to affect the development of IMT include HIV, HHV-8 and EBV [11-14]. However, the real pathogenesis remains unknown.

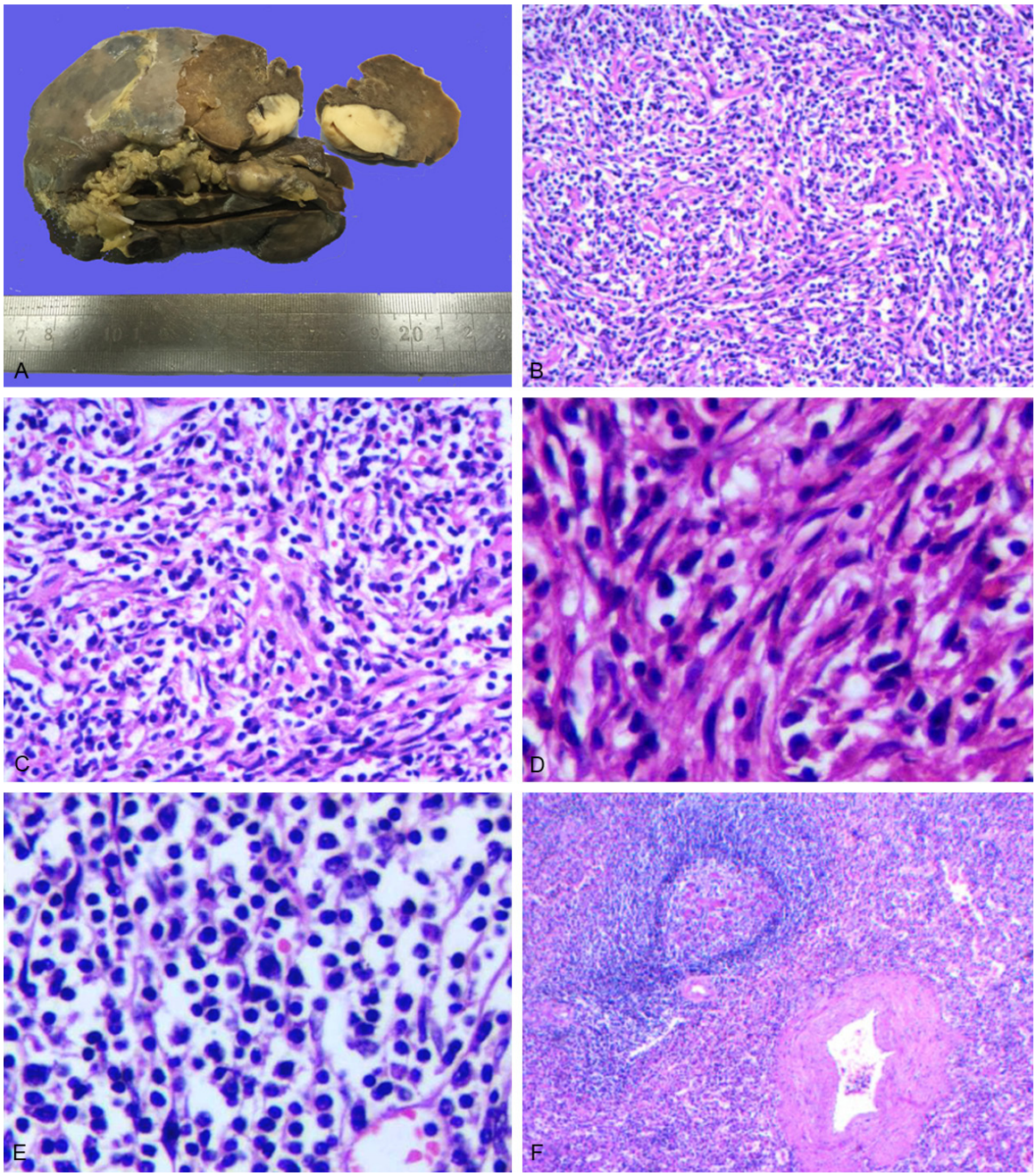

Figure 2. (A) Gross examination. A nodular growth of the spleen was seen, cut section of the nodule showing a well-circumscribed and non-encapsulated growth with tan-white areas. (B-F) Hematoxylin and eosin staining. (B, C) Microscopic examination of the nodular growth revealed spindle cells and admixture of inflammatory cells (magnification B: × 100, C: × 200). (D) Proliferation of spindle cells in a hyalinized stroma was visible (magnification × 400). (E) Polymorphous inflammatory cells, mainly plasma cells and lymphocytes, besides, some histiocytes were also found (magnification × 400). (F) Microscopic examination of the nodular growth revealed lymph follicles (magnification × 100).

IMTS usually affects middle- and advanced-aged adults, the patients ranged in age from 6 to 81 years, with a median age of 47.2 years. There is controversy over the association between IMTS and gender. Currently, the majority of studies have suggested that women are more frequently affected [15, 16]. More than one third of the patients with IMTS were found in physical examination. In addition, a few cases with clinical presentations have been de-

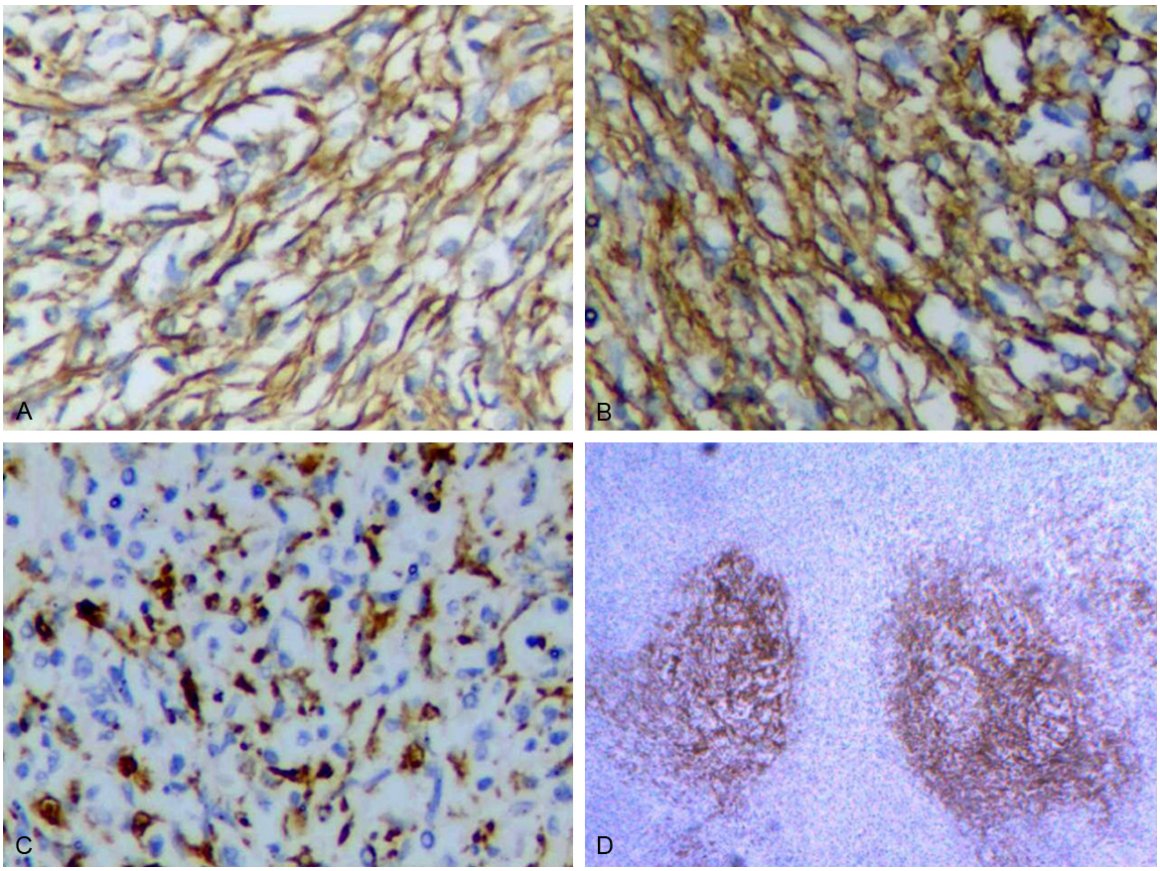

Figure 3. Immunohistochemistry. A. Immunohistochemical staining showing spindle cells positive for vimentin (magnification × 400). B. Immunohistochemical staining showing spindle cells positive for smooth muscle actin (magnification × 400). C. Immunohistochemical staining showing histiocytes positive for CD68 (magnification × 400). D. Immunohistochemical staining showing only follicular dendritic cells (FDC) positive for CD21, spindle cells negative for it (magnification × 100).

scribed for this disease, including nonspecific left upper quadrant abdominal pain, fever and splenomegaly, anemia, weight loss, or a discrete splenic mass. However, these symptoms are not unique to IMTS.

For imaging examination, CT scan, ultrasound, MRI and PET scan are all commonly employed. CT imaging commonly reveals a low-density mass in both enhanced and nonenhanced modes. Ultrasonography may show a partially calcified, well-defined echogenic mass or hypoechoic discrete lesion, while MRI demonstrates low to isointensity on T1-weighted imaging, and high intensity with surrounding low intensity on T2-weighted images. PET/CT scan usually shows variable uptake, with occasional intense uptake [3, 5, 6, 10]. But to date they do not demonstrate many defining diagnostic characteristics allowing differentiation from other lesions. So that is why clinical diagnosis is difficult and misdiagnosis is common [17, 18]. Histopathology of the resected specimen remains the gold standard for diagnosing splenic masses [10].

The typical macroscopic appearance of an IMT nodular growth is that of a well-circumscribed and non-encapsulated mass with the color of tan-white. The microscopic findings are composed mainly in varying proportions of plump spindle cells in a hyalinized stroma along with polymorphous inflammatory cell infiltrate consisting mainly of plasma cells, mature lymphocytes and histiocytes [3, 19]. Besides, rarely neutrophils and eosinophils are seen in a fibroblastic stroma in certain cases, and coagulative necrosis is also located centrally in some patients. The majority of the lymphocytes are T cells, with fewer numbers of B cells. Based on

the microscopic proportions of major component, some researchers subdivided the IMT into 3 histopathological subtypes: xanthogranuloma type, plasma cell granuloma type, and sclerosing pseudotumor. On immunohistochemical staining, the majority of the cases show positivity for SMA, desmin and vimentin. The positive rate range of ALK is 30%-65% [20]. The background lymphocytes were composed of CD3 and CD20 positive cells. There were also a number of histiocytes expressing CD68. Additionally, immunocytochemistry revealed negative results for myogenin, myoglobin, S100, CD21 and CD35. Based on the CD21, CD35, CD15 and CD30 negativity together with the diffusely positive SMA and desmin, we are confident in our diagnosis of IMTS in this case.

IMTS often share similarities to splenic neoplasms and other inflammatory diseases, so it needs to be differentiated histologically with the addition of immunohistochemistry. Foremost, it is vital to distinguish IMTS from malignant lymphoma. When a lesion occurs as a primary splenic tumor, lymphoma is usually clinically suspected. Imaging examinations have been unable to provide conclusive results, only pathological and immunohistochemical studies following splenectomy have enabled definitive diagnoses. Next, there is a need to distinguish IMTS from plasmacytoma. Plasmacytoma is consisted of immature plasma cells that have mitotic figures without Russell bodies. However, the plasma cells of IMT are mature ones with Russell bodies. Thirdly, there seems to be a certain difficulty in distinguishing IMTS from malignant fibrous histiocytoma (MFH) because the similar histologic appearance. The differential points are striking nuclear atypia and mitotic figures of MFH cells. Immunohistochemistry also provided helps for distinction. Fourthly, inflammatory pseudotumor-like follicular dendritic cell sarcoma (IPT-like FDC sarcoma), which is an extremely rare lesion, has a similar histologic appearance to IMTS, and can be more aggressive [21]. IPT-like FDC sarcoma is classically CD21, CD23 and CD35 positive on immunostaining, and EBV is almost always clonally expanded in the tumor cells [21, 22]. The other major mesenchymal lesions in the spleen that should be excluded include splenetic harmatoma, hemangiomas, sclerosing angiomatoid nodular transformation (SANT), and age-related EBV-associated lymphoproliferative disease; in these cases, the application of various FDC markers is also essential.

To date, the predominant therapy for the treatment of IMTS remains complete resection of the tumor. If the lesion is not too large, a splenectomy is unnecessary, and a partial splenic resection using laparoscopic or open surgery is a relatively suitable surgical approach [10]. According to the published cases, the prognosis is good after splenectomy, and the clinical long-term follow-up is necessary since a few IMTS cases with local recurrence or distant metastasis after surgery have been reported [23, 24].

Disclosure of conflict of interest

None.

Abbreviations

ALK, anaplastic lymphoma kinase; CT, computed tomography; EBV, Epstein-Barr virus; FDC, follicular dendritic cell; HHV-8, human herpes virus type 8; HIV, human immunodeficiency virus; IMT, inflammatory myofibroblastic tumor; IMTS, inflammatory myofibroblastic tumor of the spleen; IPT, inflammatory pseudotumor; MRI, magnetic resonance imaging; MSH, malignant fibrous histiocytoma; PET, positron emission tomography; WHO, world health organization; SANT, sclerosing angiomatoid nodular transformation; SMA, desmin and smooth muscle actin.

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