

Splenic Inflammatory Pseudotumor-Like Follicular Dendritic Cell Tumor

Konstantinos Vardas^a Dimitrios Manganas^a Georgios Papadimitriou^a
Vasileios Kalatzis^a Georgios Kyriakopoulos^a Maria Chantziara^b
Dimitrios Exarhos^c Spiros Drakopoulos^a

^aFirst Department of Surgery and Transplant Unit, and Departments of ^bPathology and ^cRadiology, Evangelismos General Hospital, Athens, Greece

Key Words

Inflammatory pseudotumor · Follicular dendritic cells · Follicular dendritic cell tumors

Abstract

Inflammatory pseudotumor of the spleen with expression of follicular dendritic cell markers is an extremely rare lesion with only a few cases reported previously. The present study reports on an inflammatory pseudotumor of the spleen 10 × 8 × 7 cm in size that was incidentally found in a 61-year-old man and increased gradually in size during a period of 3 months. Abdominal ultrasonography revealed a well-circumscribed splenic mass, and abdominal computed tomography confirmed the presence of a well-circumscribed isodense lesion in the splenic hilum with inhomogenous enhancement in the early-phase images and no enhancement on delayed-phase contrast-enhanced images. Magnetic resonance imaging of the abdomen showed a well-defined isodense tumor on T1-weighted images with mildly increased signal intensity on T2-weighted images, and this is only the second study that provides MRI findings of this entity. The patient underwent an uncomplicated open splenectomy for definitive histologic diagnosis. Under microscopic examination, the lesion was an admixture of lymphocytes, plasma cells and spindle cells. In situ hybridization analysis for Epstein-Barr virus (EBV) revealed that most of the spindle cells were positive for EBV, and immunochemistry showed the expression of the follicular dendritic cell markers CD21, CD35 and CD23 within the tumor. The diagnosis of inflammatory pseudotumor-like follicular dendritic cell tumor was established.

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Konstantinos Vardas, MD, MSc
General Surgeon
68 Chrisanthemon St.
GR-15772 Zografou, Athens (Greece)
E-Mail costas_vardas@yahoo.gr

Introduction

Inflammatory pseudotumors constitute a heterogeneous group of reactive lesions characterized by a mixture of inflammatory cells and a minor component of spindle cells [1]. This benign lesion needs to be distinguished from an inflammatory pseudotumor-like follicular dendritic cell (IPT-like FDC) tumor, a distinctive low-grade malignant neoplasm with consistent Epstein-Barr virus (EBV) association that has a similar morphology [2]. The IPT-like variant of FDC tumor is usually found in the spleen or liver and appears to be much more indolent compared to conventional FDC sarcoma [2]. Splenic IPT-like FDC tumors are extremely rare lesions, and only a few cases have been previously reported. Some of the cases referred to as IPT in the literature should be reclassified as IPT-like FDC tumors, especially when spindle cells are positive for EBV and there are no data for the expression of FDC markers within the lesion [3]. We present a case of a splenic IPT-like FDC tumor that was incidentally found in a 61-year-old man and increased gradually in size during a period of 3 months. Despite abdominal computed tomography (CT) and magnetic resonance imaging (MRI) findings, the definitive diagnosis was established only after immunohistochemical study of the resected spleen.

Case Presentation

A 61-year-old male was admitted to the Emergency Surgical Department of our hospital due to a car accident. He presented with mild abdominal pain without having any external signs of injury. Basic laboratory tests of peripheral blood on admission were within normal range, and physical examination was unremarkable.

Abdominal ultrasonography examination incidentally revealed a well-circumscribed splenic mass 4 cm in diameter. Abdominal CT confirmed the presence of a well-circumscribed isodense lesion 4.2 × 4 cm in size in the splenic hilum with subtle inhomogeneous enhancement in the early-phase images (fig. 1). MRI of the abdomen with contrast showed inhomogeneous enhancement on Gd-enhanced images (fig. 2) with areas of mildly increased signal intensity on T2-weighted images (fig. 3), measuring 5 × 5 cm. The differential diagnosis according to our radiology department included hamartoma and lymphoma. Carcinoembryonic antigen, cancer antigen 19-9 and α -fetoprotein were within normal range. A follow-up MRI scan of the abdomen 3 months later confirmed the above-mentioned findings regarding the same signal characteristics on T1- and T2-weighted images, but the tumor had increased in size and measured 7.5 × 6 × 6 cm. Two months later, the patient was referred to our surgical department for operative intervention and definite diagnosis. Preoperatively, he received vaccination against hemophilus, pneumococcus and meningococcus, and an uncomplicated open splenectomy was performed.

On gross examination, the spleen measured 13 × 11 × 7 cm and weighed 422 g. The cut surfaces of the tumor revealed a well-circumscribed solid tumor 10 × 8 × 7 cm, milky white with a central necrotic area measuring 5 cm. There were no lymph nodes in the splenic hilum. Under microscopic examination, the lesion was an admixture of lymphocytes, plasma cells and a smaller percentage of spindle cells (fig. 4). Mitotic figures were not observed in the spindle cells. All of the spindle cells were stained with CD35 and a smaller percentage with CD21 and CD23. In situ hybridization analysis for EBV-encoded small RNA revealed that most of the spindle cells in the lesion were positive for EBV. T-lymphocytes predominated within the lesion compared to B-lymphocytes. The plasma cell population was found to be polyclonal. IPT-like FDC sarcoma was diagnosed based on immunohistochemical study.

The patient had an uneventful postoperative course and was discharged 3 days later. The patient remains disease-free with no evidence of recurrence on the last follow-up 1 year postoperatively.

Discussion

FDCs are part of the accessory immune system and are found in the primary and secondary lymphoid follicles serving as antigen-presenting cells for B cells that stimulate B cell proliferation and differentiation [4]. FDC sarcoma is a neoplastic proliferation of spindle to ovoid cells showing morphologic and immunophenotypic features of FDCs [5]. It is usually observed as lymphadenopathy, but it can also be present in a variety of extranodal sites and intra-abdominal organs, including the spleen [2]. FDC sarcomas are rare neoplasms with less than 200 cases previously reported in the literature [3] and constitute a heterogeneous group of tumors with subtypes showing different histologic appearances and behavior.

The IPT-like variant of FDC sarcoma was first classified as a distinct variant of FDC sarcoma by Cheuk et al. [2]. It differs from conventional FDC sarcoma in the following basic aspects: it is characterized by consistent association with EBV, selective localization in intra-abdominal organs and female predominance. Most importantly, it exhibits less aggressive behavior compared to conventional FDC sarcoma [2]. The IPT-like variant of FDC tumors is composed of a polymorphic population of inflammatory cells including B-lymphocytes, T-lymphocytes, plasma cells and spindle cells in addition to the expression of FDC markers and EBV expression.

Clinicopathologic characteristics and radiologic findings of the previously published cases of IPT-like FDC tumors are summarized in table 1. There is a slight female predominance (female/male: 8/7), the median age of patients with IPT-like FDC tumors is 62 years, and the mean tumor diameter 7.2 cm. The maximum tumor diameter ranged from 3.2 to 22 cm [2, 3]. The most significant fact is that most of the patients are asymptomatic and without evidence of recurrence during a follow-up period that reaches 4 years or 6.5 years in some studies [3, 12].

The pathogenesis of IPT-like FDC tumors is not clear. Lewis et al. [6] proposed that these tumors may arise from a common mesenchymal cell that is capable of differentiating along different pathways. Under the stimuli of EBV, some of them would differentiate to a myofibroblastic phenotype with expression of vimentin and SMA, while others would acquire FDC characteristics with expression of FDC markers, such as CD21, CD23 or CD35. Similarly, Shia et al. [4] proposed that the mesenchymal cells in IPT-like conditions would undergo transformation in FDC tumors under certain oncologic stimuli, such as EBV infection, and eventually become neoplastic.

CT and MRI findings of IPT-like FDC tumors seem to be similar to the conventional IPT lesions due to their similar morphology and due to the presence of inflammatory cells and fibrotic stroma in both cases [7]. On CT scans, they are usually found as hypodense masses with occasional calcifications and heterogeneous slow enhancement [8]. MRI depicts a low to isointense mass on T1-weighted images and highly intense areas with surrounding low intensity on T2-weighted images [8]. Imaging findings of IPT-like FDC tumors of the spleen are described in only a few studies due to the rarity of the disease [7]. Of the 13 previously reported studies of IPT-like FDC tumors of the spleen, 5 describe imaging findings on CT. All of them are characterized by low-density lesions on plain or enhanced CT. MRI findings are available in only one case other than ours, and according to this, the lesion had areas of low

signal intensity on T2-weighted images and was isointense on T1-weighted images [7]. Nevertheless, the degree and distribution of inflammatory cells and proliferating capillaries in IPT and IPT-like FDC lesions influence the staining patterns observed in CT/MRI examination, and there is not a single imaging modality that can distinguish IPT from other splenic tumors [7, 9]. Similar CT/MRI findings are observed in primary splenic lymphoma and hamartoma, metastasis and angiosarcoma [8]. Therefore, it is difficult to discriminate safely benign lesions as IPT and malignant tumors as lymphoma.

The IPT-like variants of FDC tumors found in the spleen are low-grade malignant neoplasms, and their prognosis seems to be excellent. From the previously published data for localized disease, total splenectomy is the mainstay of treatment without need of adjuvant therapy [14]. Nevertheless, due to the rarity of the disease, the short follow-up and the incompleteness of the published data, it is difficult to assess the need and benefit of adjuvant treatment. This is the first study that demonstrates a significant increase in size during a short period preoperatively and provides both CT and MRI imaging findings.

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Table 1. Cases of IPT-like FDC tumors reviewed

Author/ year	Sex/ age	Presentation	Maximum diameter, cm	FDC markers	CT	MRI	Follow-up
Arber et al., 1995 [10]	M/70	Asymptomatic	5.5	(+)	No data	No data	No data
Cheuk et al., 2001 [2]	F/58	Abdominal fullness and easy bruising	22	CD21 CD35(+)	No data	No data	Alive and well at 4 months
	F/39	Malaise, weight loss and fever for several months	7.5	CD21 CD35(++)	No data	No data	Alive at 2 months with persistent fever
	F/61	Asymptomatic	3.5	CD21 CD35(+)	No data	No data	No data
Horiguchi et al., 2004 [11]	F/77	Two-week epigastralgia	8.5	CD35(+) focal	Low-density, well-defined mass. On enhanced CT its central area not enhanced	No data	3 years no recurrence or metastasis
Brittig et al., 2004 [12]	M/54	Asymptomatic	12	CD21(+) CD23(+)	Hypodense lesion	No data	4 years asymptomatic
Kiryu et al., 2009 [7]	F/56	Asymptomatic	4	CD21(+)	Low-density mass	Isointense on T1, low intensity on T2-weighted images	Alive and well at 2 years
Choe et al., 2013 [3]	F/64	Asymptomatic	5.5	CD21(+) CD23(+)	No data	No data	Alive and well at 78 months
	F/72	Asymptomatic	7.2	CD21(+) CD23(+) CD35(+)	No data	No data	Alive and well at 18 months
	F/53	Asymptomatic	3.2	CD23(+) CD35(+)	No data	No data	Alive and well at 13 months
	M/76	Asymptomatic	3.2	CD21(+) CD35(+)	No data	No data	Alive and well at 8 months
	M/72	Asymptomatic	6	CD23(+) CD35(+)	No data	No data	Alive and well at 18 months
	M/75	Abdominal pain	3.5	CD23(+) CD35(+)	No data	No data	Alive and well at 30 months
Rao et al., 2014 [13]	M/39	Asymptomatic	7.2	CD21(+) CD23(+) CD35(+)	Inhomogenous hypodense mass including patchy calcification with obvious heterogenous enhancement	No data	No data
Vardas et al., 2014	M/61	Asymptomatic	10	CD21(+) CD23(+) CD35(+)	Isodense lesion with no enhancement	Isodense tumor on T1	Alive and well at 12 months



Fig. 1. Axial post-contrast CT image depicts inhomogenous uptake. **a** Non-contrast. **b** Contrast enhanced.



Fig. 2. **a–c** Sequential MRI axial images post-contrast. The lesion depicts an inhomogenous enhancement.

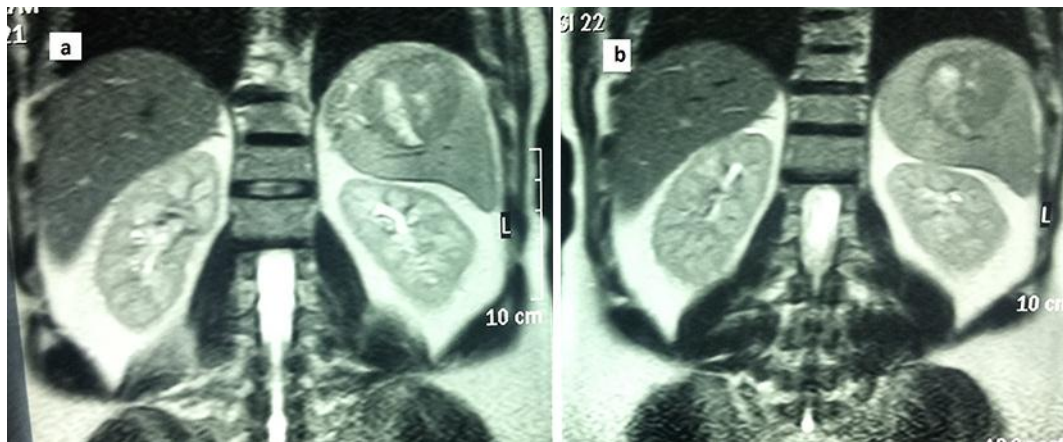


Fig. 3. a, b Coronal T2-weighted MRI sequential images depict areas of high signal intensity within the tumor which constitute necrosis or cystic components.

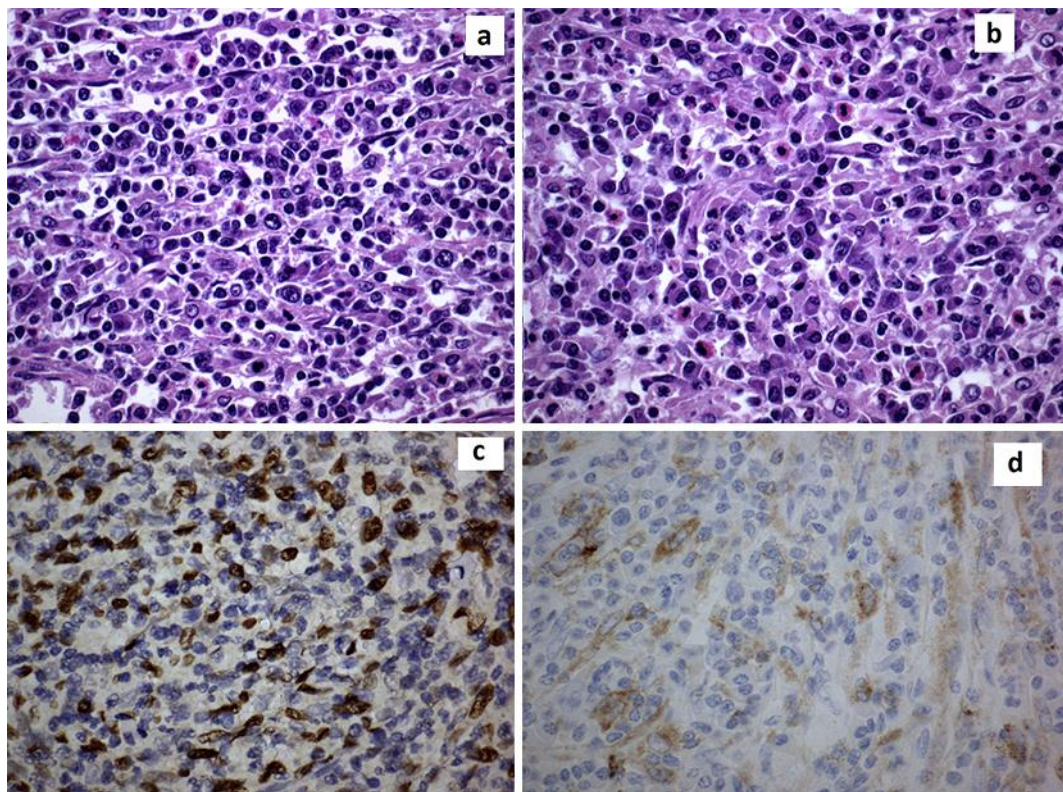


Fig. 4. a, b The neoplasm consists of spindle cells within a prominent lymphoplasmacytic infiltrate. c In situ hybridization for EBV-encoded RNA (EBER) highlights the nuclei of neoplastic spindle cells. d The neoplastic cells were expressing the follicular dendritic cell marker CD35 focally.