**Case Report**

**Epstein-Barr Virus-Associated Inflammatory Pseudotumor-Like Follicular Dendritic Cell Tumor of the Spleen without Recurrence for 3 Years after Splenectomy**

Michiyo O. Asano,1 Yoshikazu Ito,1 Toshitaka Nagao,2 Jun Matsubayashi,2 Hiroshi Kusama,2 Yoshiaki Suzuki,3 Akihiko Tsuchida,3 Soichi Akata,4 Koichi Tokuuye,4 and Kazuma Ohyashiki1

1First Department of Internal Medicine, Tokyo Medical University, 6-7-1 Nishishinjuku, Shinjuku-ku, Tokyo 160-0023, Japan
2Department of Pathology, Tokyo Medical University, 6-7-1 Nishishinjuku, Shinjuku-ku, Tokyo 160-0023, Japan
3Third Department of Surgery, Tokyo Medical University, 6-7-1 Nishishinjuku, Shinjuku-ku, Tokyo 160-0023, Japan
4Department of Radiology, Tokyo Medical University, 6-7-1 Nishishinjuku, Shinjuku-ku, Tokyo 160-0023, Japan

Address correspondence to Yoshikazu Ito, yito@tokyo-med.ac.jp

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**Abstract** Inflammatory pseudotumor (IPT)-like follicular dendritic cell (FDC) tumor is a rare disease with distinct clinicopathological features. We report a case of so-called Epstein-Barr virus (EBV)-associated IPT-like FDC tumor of the spleen. We found a splenic mass lesion during his annual checkup. After recognizing the growing mass, splenectomy was performed. Histopathological and immunohistological studies revealed extensive proliferation of spindle cells positive for FDC markers. EBV was exclusively detected on these spindle cells by in situ hybridization analysis. Based on these findings, a diagnosis of EBV-associated IPT-like FDC tumor was made. Of note, neither recurrence nor metastasis occurred within 3 years postsplenectomy.

**Keywords** inflammatory pseudotumor; follicular dendritic cell tumor; Epstein-Barr virus; spleen

1. Introduction

Epstein-Barr virus (EBV)-associated inflammatory pseudotumor-like follicular dendritic cell (FDC) [EBV-associated IPT-like FDC] tumor is a distinct disease entity established in 2001. In 1989, Weiss et al. first reported the possible association of EBV with the development of an inflammatory pseudotumor (IPT) in the spleen [20]. The association of EBV with the formation of an IPT in the liver and spleen was confirmed in 1995 [2]. FDC markers (e.g., CNA.42) were also positively detected in the same tumor in the liver and spleen [9,15,17]. Cheuk et al. established a disease entity and reported 11 cases that were different from the common FDC tumors or other IPTs [7]. However, the clinical features of EBV-associated IPT-like FDC tumor have not been completely clarified. We present a case of a patient with EBV-associated IPT-like FDC tumor of the spleen which showed no recurrence or metastasis following splenectomy.

2. Case report

A patient visited our hospital and underwent a careful and precise examination of a splenic mass lesion which was found during an annual medical checkup. Although the patient was asymptomatic, abdominal ultrasound revealed a large splenic mass (Figure 1(a)). The medical history of the patient was uneventful except for a previous ureterocele and a colon polyp. There was no lymphadenopathy on either the surface or the depth. The manipulation of the abdomen demonstrated no abnormal findings. The liver and spleen were not palpable. No abnormal values were noted on initial laboratory studies except an elevated serum IL-2 receptor level of 704 U/mL. Abdominal computed tomography confirmed a low-density, well-defined, round mass of 3 cm diameter in the spleen (Figure 1(b)). Magnetic resonance imaging (MRI) showed a hyperintense mass on T1-weighted imaging and a hypointense mass on T2-weighted imaging (Figure 1(c)). On dynamic MRI, the lesion was enhanced with time (Figure 1(d)).

As tumor enlargement was observed after 6 months, laparoscopic-assisted splenectomy was performed. The size of the spleen was 13.5 × 10.5 × 5.5 cm. The cut surface was well circumscribed and exhibited a solid, yellowish white to light tan tumor measuring 4 cm in diameter (Figure 2). Necrotic or hemorrhagic lesions were not evident. Histopathologically, the lesion showed a solid tumor with epithelioid granuloma formation surrounded by spindle cells (Figure 3(a)), predominantly lymphocytes and plasma cells (Figure 3(b)). Immunohistochemical analysis revealed that the tumor cells were positive for CD21 (Figure 3(c)), CD23 (Figure 3(d)), and CNA.42...
3. Discussion

IPTs are usually localized benign lesions characterized by spindle cell proliferation with abundant inflammatory cells, mainly lymphocytes and plasma cells [16,21], and these tumors occur in any organ [1,3,8,18]. EBV-associated IPT-like FDC tumor is a distinct disease entity different from the common IPT. This disease entity was definitively established by Cheuk et al. in 2001 [7]. Although the common IPT is basically a benign disease, this disease entity may be included under non-benign tumors.

FDCs are known as antigen-presenting cells found exclusively in the germinal center, which can be detected in B-cell lymphomas as reactive bystander cells [11,19]. FDC tumors are a rare disease derived from FDCs, and these tumors most commonly occur in lymph nodes but they may also develop in different extranodal sites. Among FDC tumors in the liver or spleen, those that have an IPT-like morphology and are infected with EBV may be considered to be different from other FDC tumors without EBV infection.

In the late 1980s, Weiss et al. discovered a method to detect EBV using in situ hybridization [20]. During the detection process, they confirmed the involvement of EBV in the development of a splenic IPT. Arber et al. examined the presence of EBV in various parts of an IPT and detected EBV genomes in 4 cases of splenic lesion and 1 case of
Figure 3: Histopathological and immunohistochemical findings. (a) Histopathological examination showing morphological features indicative of an inflammatory pseudotumor (IPT) demarcated from the normal splenic tissue with fibrous septa (hematoxylin and eosin, ×12.5). (b) Histopathological examination showing the presence of spindle and inflammatory cells (plasmacytes and lymphocytes) (hematoxylin and eosin, ×400). (c) Immunohistochemistry showing CD21 positivity in spindle cells (×200). (d) Immunohistochemistry showing CD23 positivity in spindle cells (×200). (e) Immunohistochemistry showing CNA.42 positivity in spindle cells (×200). (f) In situ hybridization for EBV-encoded RNAs: identification of EBV RNA in IPT (×200).

hepatic lesion [2]. In 1996, Delsol et al. [9] reported the first case of splenic IPT that was positive for both EBV and FDC markers [9,15,17]. In 2001, Cheuk et al. reported 11 cases of splenic IPT-like tumor positive for both EBV and FDC markers [7], which is considered to be a different disease entity from “follicular dendritic cell sarcoma” in the World Health Organization Classification (version 4).

The clinical features of EBV-associated IPT-like FDC tumor, which is different from the common EBV-negative FDC tumors, have been reported [4,5,10,12,13,14] as follows. The tumor has a marked female predominance and is generally observed to occur in the spleen or liver, although some cases occur in the peripancreatic region. There has been no report of extra-abdominal cases. The lesion is usually solitary, fleshy, and tan in color, and has central hemorrhage and necrosis. The clinical presentation of the tumor is nonspecific (i.e., weight loss and fever), and some patients are symptomatic. In many cases, the clinical course remains indolent. Although most patients are completely cured by surgical resection, some cases may have recurrence or metastasis. Unlike EBV-associated IPT-like FDC tumor, common FDC tumors occur in various anatomical sites without inducing any systemic symptoms. Recurrence may be observed in most cases within 1 year, and death occurs in many cases in 2 years. In the present case, some features were not typical. The patient did not complain of any symptoms pre- and postsplenectomy. All the histopathological features were compatible with this disease entity, although the apparent granuloma formation was not a typical feature. Interestingly, some cases of EBV-associated IPT-like FDC tumor of the liver easily recur [6].

In conclusion, when a solitary lesion in the spleen is encountered, it is important to consider the possibility of an IPT-like FDC tumor. The differential diagnosis from the common IPT is occasionally difficult. Although the possible role of EBV in the pathogenesis of this IPT-like FDC tumor remains uncertain, either EBV clonality or positivity of FDC markers is necessary to discriminate indolent IPT-like FDC tumor from aggressive FDC tumor.

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