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CASE REPORT

Inflammatory pseudotumor-like follicular dendritic cell sarcoma: A brief report of two cases

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Abstract

BACKGROUND

Follicular dendritic cell (FDC) sarcoma/tumor is a rare malignant tumor of follicular dendritic cells, which is considered a low-grade sarcoma that can involve lymph nodes or extranodal sites. Conventional FDC sarcomas are negative for Epstein-Barr virus (EBV), whereas the inflammatory pseudotumor-like variant consistently shows EBV in the neoplastic cells.

CASE SUMMARY

We report two cases of inflammatory pseudotumor-like FDC sarcoma in the liver that received 3D laparoscopic right hepatectomy and open right hepatectomy separately.

CONCLUSION

EBV probe-based *in situ* hybridization and detection of immunohistochemical markers of FDC play an important role in the diagnosis and differential diagnosis of inflammatory pseudotumor-like FDC sarcoma. Complete surgical excision combined with regional lymphadenectomy may be effective in reducing the postoperative recurrence and metastasis and improving long-term survival rates.

Key words: Inflammatory pseudotumor-like follicular dendritic cell sarcoma; Epstein-Barr virus; Liver; Spleen; Case report

Core tip: There have been 48 previously reported cases of inflammatory pseudotumor-like follicular dendritic cell (FDC) sarcoma, which occurs almost exclusively in the liver and spleen. Here we report two cases of inflammatory pseudotumor-like FDC sarcoma in the liver that were treated by 3D laparoscopic right hepatectomy and open right hepatectomy separately.

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INTRODUCTION

Follicular dendritic cell (FDC) sarcoma/tumor is a rare malignant tumor of follicular dendritic cells, which are mesenchymal cells in the lymphoid follicles with antigen presenting ability. It is considered a low-grade sarcoma that can involve lymph nodes or extranodal sites[1-5]. In 1996, Shek *et al*[6] reported the first case of primary FDC sarcoma in the liver. The histology was similar to an inflammatory pseudotumor and it was related to Epstein-Barr virus (EBV)-related clonal proliferation[6]. Inflammatory pseudotumor-like FDC sarcoma was first described as a distinctive variant of FDC sarcoma and associated with EBV in 2001[7]. There have been 48 previously reported cases of inflammatory pseudotumor-like FDC sarcoma, which occurs almost exclusively in the liver and spleen (Table 1). Ancillary tests, including detection of immunohistochemical markers of FDC such as CD21, CD23, or CD35 and EBV probe-based *in situ* hybridization, are required for this diagnosis. Here we report two cases of inflammatory pseudotumor-like FDC sarcoma in the liver that were treated by 3D laparoscopic right hepatectomy and open right hepatectomy separately.

CASE PRESENTATION

Chief complaints

Case 1: A 31-year-old woman was admitted to hospital for evaluation of a four-week history of anorexia.

Case 2: A 48-year-old man stumbled across a liver mass through a routine ultrasound examination.

History of present illness

Unremarkable.

History of past illness

Case 1: Her past medical history was chronic hepatitis B for more than 10 years without antiviral treatment.

Case 2: Unremarkable.

Personal and family history

Unremarkable.

Physical examination upon admission

Case 1: Physical examination revealed mild tenderness to palpation in the right upper quadrant.

Case 2: Physical examination was unremarkable.

Laboratory examinations

Case 1: Laboratory tests showed seropositivity for HBsAg, HBeAb, and HBcAb. Furthermore, serum level of hepatitis B virus-DNA was lower than detection limit.

Case 2: Laboratory tests were unremarkable.

Imaging examinations

Case 1: Abdominal magnetic resonance imaging revealed two well-circumscribed masses in the right posterior lobe of the liver (Figure 1).

Case 2: An abdominal computed tomography examination revealed an ill-defined 10 cm mass in the right lobe of the liver accompanied with enlargement of hepatic portal lymph nodes (Figure 2).

Table 1 Review of inflammatory pseudotumor-like follicular dendritic cell tumor/sarcoma

Ref.	Sex/age	Location	Maximum diameter (cm)	Symptom	Treatment	Follow-up (mo)	Outcome
Li *et al*[13]	F/64	Spleen	7.2	Upper abdominal pain	Laparoscopic splenectomy	8	NED
	M/61	Spleen	6.2	Asymptomatic	Laparoscopic splenectomy	16	NED
	F/42	Spleen	4	Left-sided flank pain	Laparoscopic splenectomy	9	NED
	F/57	Spleen	13.3	Upper abdominal pain	Laparoscopic splenectomy	4	LWD, pulmonary metastasis
	M/52	Spleen	2 masses: 3.7, 2.9	Back pain	Laparoscopic splenectomy	5	LWD, bone metastasis
Hang *et al*[14]	M/57	Spleen	2.7	Asymptomatic	Laparoscopic partial splenectomy	9	NED
Ge *et al*[15]	F/54	Spleen	3.5	Left-sided flank pain	Splenectomy	10	NED
	M/79	Spleen	6	Asymptomatic	Splenectomy	18	NED
Pan *et al*[16]	F/78	Colon	3.9	Abdominal discomfort, bloody stool	Polypectomy	5	NED
Choe *et al*[17]	F/64	Spleen	5.5	Asymptomatic	Splenectomy	78	NED
	F/72	Spleen	7.2	Asymptomatic	Splenectomy	18	NED
	F/53	Spleen	3.2	Asymptomatic	Splenectomy	13	NED
	M/76	Spleen	3.2	Asymptomatic	Splenectomy	8	NED
	M/72	Spleen	6	Asymptomatic	Splenectomy	18	NED
	M/75	Spleen	3.5	Abdominal pain	Splenectomy	30	NED
Granados *et al*[18]	F/57	Liver	13	Abdominal pain, vomiting	Partial hepatectomy	24	NED
Cheuk *et al*[7]	F/19	Liver	12	Right upper quadrant pain, abdominal mass, weight loss	Partial hepatectomy	40	NED
	F/56	Liver	15	Abdominal discomfort	Partial hepatectomy	56	LWD, recurrence in liver
	F/40	Liver	12.5	Upper abdominal pain, weight loss	Partial hepatectomy	108	LWD, intraabdominal recurrence
	F/49	Liver	4.2	Asymptomatic	Partial hepatectomy	9	NED
	M/37	Liver	15	Abdominal mass, weight loss	Partial hepatectomy	42	NED
	F/35	Liver	20	Abdominal discomfort, fever, weight loss	Partial hepatectomy	95	DOD, disseminated in liver and peritoneum
	F/31	Liver	15	Abdominal distension, weight loss	Partial hepatectomy	60	NED
	F/58	Spleen	22	Abdominal mass	Splenectomy	4	NED
	F/39	Spleen	7.5	Weight loss, fever	Splenectomy	2	LWD, persistent fever
	F/61	Spleen	3.5	Asymptomatic	Splenectomy	NA	NA
	F/49	Peri-pancreas	15	Abdominal distension	Whipple's operation	NA	NA
Li *et al*[19]	F/49	Spleen	4.7	Asymptomatic	Splenectomy	NA	NA
	F/56	Spleen	8	Abdominal pain	Splenectomy	17	NED
	M/38	Liver	8.5	Anorexia	Partial hepatectomy	11	NED
	F/42	Liver	2 masses: 2, 1.7	Abdominal pain	Partial hepatectomy	36	NED

	M/50	Spleen and liver	Spleen: 10 Liver: 3	Abdominal bloating	Splenectomy and partial hepatectomy	17	NED
	F/39	Liver	9	Asymptomatic	Partial hepatectomy	84	NED
Chen *et al*[20]	F/28	Liver	6	Abdominal pain, fatigue, anorexia	Partial hepatectomy	48	LWD, recurrence in liver
	M/39	Spleen	7.4	Asymptomatic	Splenectomy	40	NED
	M/48	Liver	23.3	Abdominal pain, fever, fatigue	Partial hepatectomy	23	NED
	M/65	Spleen and liver	Spleen: 22.3 Liver: 5.8 (multi masses)	Abdominal pain, fever, fatigue, anorexia, weight loss	Splenectomy	2	DOD
	M/51	Spleen	8.5	Weight loss	Splenectomy	19	NED
	M/68	Spleen	2.3	Asymptomatic	Splenectomy	6	NED
	F/51	Spleen	5.3	Abdominal discomfort	Splenectomy	5	NED
	M/67	Spleen	7.5	Asymptomatic	Splenectomy	5	NED
	M/60	Liver	3	Asymptomatic	Partial hepatectomy	3	NED
	F/52	Spleen	0.9	Asymptomatic	Splenectomy	12	NED
Kitamura *et al*[21]	F/74	Spleen	3.6	Asymptomatic	Splenectomy	24	NED
Bui *et al*[22]	F/50	Spleen	6	Abdominal pain	Splenectomy	NA	NA
Vardas *et al*[23]	M/61	Spleen	10	Abdominal pain	Splenectomy	12	NED
Kim *et al*[24]	M/76	Spleen	3.2	Asymptomatic	Splenectomy	NA	NA
Horiguchi *et al*[25]	F/77	Spleen	8.5	Abdominal pain	Splenectomy	36	NED
Present case	F/31	Liver	2 masses: 3.5, 2.5	Anorexia	3D laparoscopic right hepatectomy	10	NED
	M/48	Liver and hepatoduodenal ligament lymph node	Liver: 10 Lymph node: 3.5	Asymptomatic	Open right hepatectomy, lymph node excision	2	NED

M: Male; F: Female; NED: No evidence of disease; DOD: Dead of disease; LWD: Live with disease; NA: Not available.

FINAL DIAGNOSIS

Case 1

EBV-positive inflammatory pseudotumor-like FDC sarcoma in the liver (Figure 3).

Case 2

EBV-positive inflammatory pseudotumor-like FDC sarcoma in the liver with hepatoduodenal ligament lymph node involvement (Figure 4).

TREATMENT

Case 1

3D laparoscopic right hepatectomy.

Case 2

Open right hepatectomy combined with regional lymphadenectomy.

OUTCOME AND FOLLOW-UP

Case 1

Follow-up for 10 mo showed no recurrence or metastasis.

Case 2

Follow-up for 2 mo showed no recurrence or metastasis.

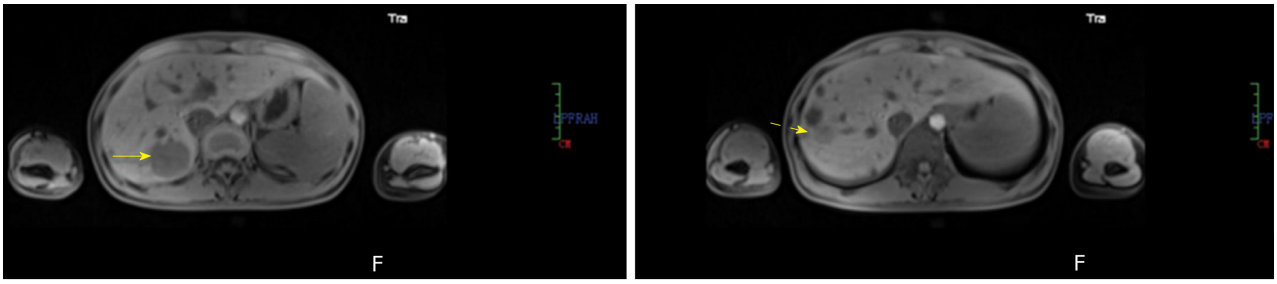

Figure 1 Magnetic resonance imaging. Two well-circumscribed lesions with long T1 and long or equal T2 signal (arrows). The multiple lesions with long T1 and long T2 signal are hepatic cysts verified by pathological examination later.

DISCUSSION

FDC sarcoma is a neoplastic proliferation of spindled to ovoid cells exhibiting morphological and immunophenotypic features of FDCs. Histologically, FDC sarcomas are classified into two types: (A) Conventional FDC sarcoma consisting of spindled to ovoid cells forming fascicles, storiform arrays, whorls, diffuse sheets, or vague nodules with an array of small lymphocytes; and (B) Inflammatory pseudotumor-like FDC sarcoma composed of neoplastic spindled cells that are dispersed within a prominent lymphoplasmacytic infiltrate[3]. To date, 48 cases of inflammatory pseudotumor-like FDC sarcoma have been reported in the English-language literature, located in the liver (16/48), spleen (32/48), colon (1/48), and peri-pancreas (1/48), respectively. These cases included 19 males and 29 females (male/female ratio of 1: 1.5), with a mean age of 55 years (range, 19-79 years). Clinical manifestations include abdominal pain, abdominal bloating, abdominal mass, weight loss, fever, fatigue, and anorexia, but most cases are asymptomatic (Table 1).

The origin of FDC sarcoma remains controversial. Phenotypic marker studies and *in vitro* experiments with fibroblast-like cell lines have developed FDCs from fibroblast-like cells[8]. The neoplastic cells are often positive for FDC markers, such as CD21, CD23, and CD35, with the staining ranging from extensive to very local. FDCs appear to be closely related to bone marrow stromal progenitors, with several myofibroblast features[9]. Two studies examining the transcriptional profile of FDC sarcoma have revealed: (A) A peculiar immunological microenvironment enriched in follicular helper T cells and Treg populations, with special relevance to the inhibitory immune receptor programmed cell death protein 1 and its ligands, programmed cell death-Ligand 1 and programmed cell death-Ligand 2; and (B) The highly specific expression of the genes encoding for FDC secreted peptide and serglycin[10-11].

Conventional FDC sarcomas are negative for EBV, whereas the inflammatory pseudotumor-like variant consistently shows EBV in the neoplastic cells[7]. EBV-encoded small RNA was detected in both of the present cases by *in situ* hybridization. EBV-encoded latent membrane protein 1, which has been found to have an oncogenic role, has been identified in 74% (26/35) cases of inflammatory pseudotumor-like FDC sarcomas by immunohistochemical staining[7,17,19-21,25]. Recently, Takeuchi *et al*[12] reported increased numbers of EBV-infected cells in IgG4-related lymphadenopathy, compared with other reactive lymphadenopathy or extranodal IgG4-related disease, which suggests that there may be a relationship between IgG4-related disease and EBV[12]. Interestingly, Choe *et al*[17] reported that significant numbers of IgG4-positive plasma cells were found in six cases of EBV-positive inflammatory pseudotumor-like FDC sarcoma of the spleen, suggesting that EBV plays a critical role in inflammatory pseudotumor-like FDC sarcoma and IgG4-related sclerosing disease[17]. Generally, the pathogenic mechanism of EBV in inflammatory pseudotumor-like FDC sarcoma remains unclear and further investigation is required.

FDC sarcoma is usually treated by complete surgical excision, with or without adjuvant radiotherapy or chemotherapy. A pooled analysis of the literature revealed local recurrence and distant metastasis rates of 28% and 27%, respectively. Large tumor size (≥ 6 cm), coagulative necrosis, high mitotic count (≥ 5 mitoses per 10 high-power fields), and significant cytological atypia are associated with a worse prognosis[2,5]. Regarding the prognosis of patients with inflammatory pseudotumor-like FDC sarcoma, based on the literature reports of inflammatory pseudotumor-like FDC sarcoma with a median follow-up period of 17 mo, 35 patients had no evidence of disease. Five patients exhibited distant metastasis and two had local recurrence, with traits similar to large tumors and multiple masses. One of the current cases presented with liver and hepatoduodenal ligament lymph node involvement,

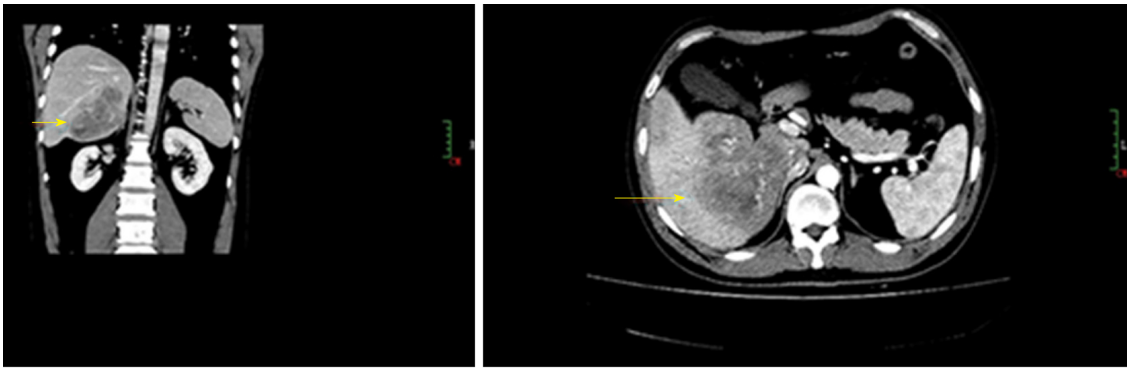

Figure 2 Abdominal computed tomography examination. The images show an ill-defined and low-density 10 cm mass (arrows) in the right lobe of the liver, accompanied with enlargement of hepatic portal lymph nodes.

suggesting that inflammatory pseudotumor-like FDC sarcoma presents an increased risk of lymph node metastasis. Complete surgical excision combined with regional lymphadenectomy may be effective in reducing the postoperative recurrence and metastasis and improving the long-term survival rates.

CONCLUSION

In conclusion, there is little specificity in the clinical manifestations of inflammatory pseudotumor-like FDC sarcoma. EBV probe-based *in situ* hybridization and detection of immunohistochemical markers of FDC play important roles in the diagnosis and differential diagnosis of inflammatory pseudotumor-like FDC sarcoma. Radical surgical resection is the main therapeutic intervention for inflammatory pseudotumor-like FDC sarcoma, especially for cases with lymph node involvement, and patients require long-term post-surgical follow-up.

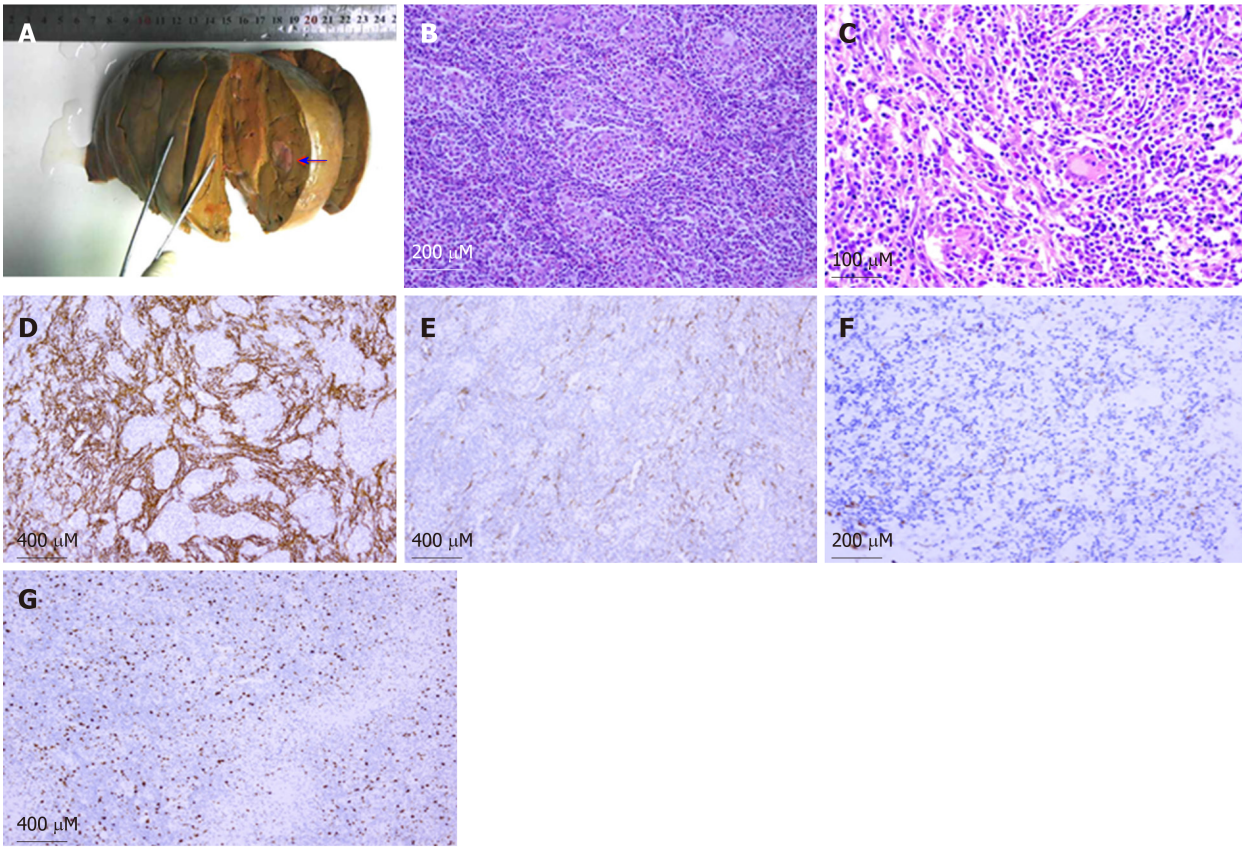

Figure 3 Epstein-Barr virus-positive inflammatory pseudotumor-like follicular dendritic cell sarcoma in the liver. A: Gross picture of an inflammatory pseudotumor-like follicular dendritic cell sarcoma of the liver. A well-circumscribed solid nodule was found in the liver. Note the grayish-white colored and soft cut surface with focal hemorrhage (arrow); B: Haematoxylin and eosin stained image showing that the tumor tissue had a meshwork-like architecture (× 200); C: On high-power field, the tumor was composed of oval to spindle cells with vesicular chromatin and distinct nucleoli. There was less degree of atypia. The background showed abundant lymphocytes and plasma cells (× 400); D: CD21 was detected on the membrane of almost all of tumor cells by immunohistochemistry (× 100); E: Smooth muscle actin was detected in the cytoplasm of a part of tumor cells by immunohistochemistry (× 100); F: Epstein-Barr virus-encoded small RNA-based *in situ* hybridization demonstrated positive nuclei of the neoplastic dendritic cells (× 200); G: Ki-67 was detected in the nuclei of almost all of tumor cells by immunohistochemistry (30%; × 100).

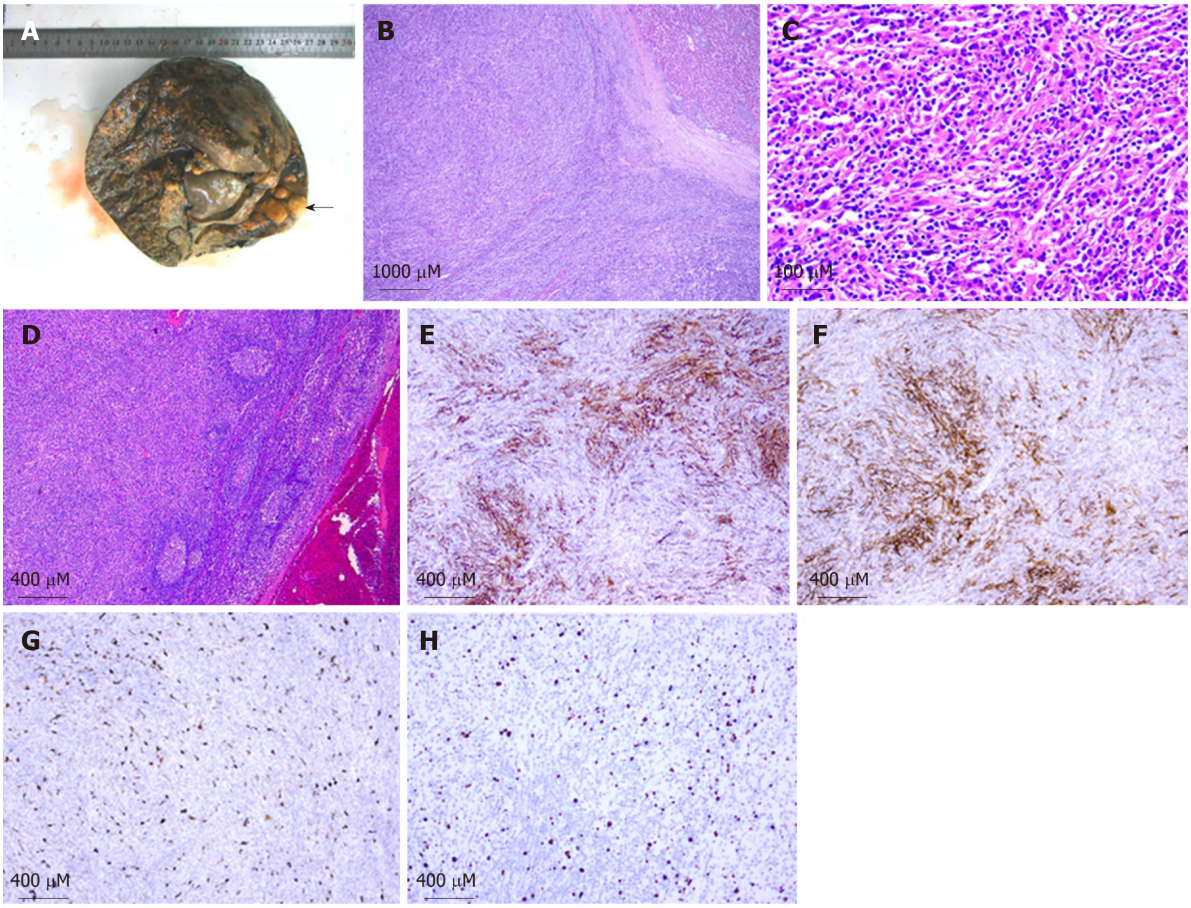

Figure 4 Epstein-Barr virus positive inflammatory pseudotumor-like follicular dendritic cell sarcoma in the liver with hepatoduodenal ligament lymph node involvement. A: Gross picture of an inflammatory pseudotumor-like follicular dendritic cell sarcoma of the liver. A large and multinodular confluent tumor was found in the liver (arrow); B: Histologic sections of follicular dendritic cell sarcoma showing an unencapsulated tumor (left) with a sharp margin from the adjacent liver parenchyma (right). The tumor tissue was arranged in whorls (× 40); C: On high-power field, the tumor was composed of oval to spindle cells with vesicular chromatin and distinct nucleoli. There was less degree of atypia. The background showed abundant lymphocytes and plasma cells (× 400); D: In the hepatoduodenal ligament lymph node, lymphoid follicles were pushed aside by tumor tissue (× 100); E: CD21 was detected on the membrane of almost all of tumor cells by immunohistochemistry (× 100); F: S100 was detected in the membrance and cytoplasm of almost all of tumor cells by immunohistochemistry (× 100); G: Epstein-Barr virus-encoded small RNA *in situ* hybridization demonstrated positive nuclei of the neoplastic dendritic cells (× 100); H: Ki-67 was detected in the nuclei of almost all of tumor cells (20%; × 100).

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