Inflammatory pseudotumor of the liver : Case report and review of literature

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Inflammatory pseudotumor (IPT) is a benign tumorous lesion of unknown cause, which is composed of fibrous tissue with infiltration of plasma cells and lymphocytes.
A 57-year-old male with gastritis was indicated to have hepatic dysfunction during observation of the course of gastritis at a nearby hospital. He was referred to our facility to undergo detailed examinations. When he visited our hospital for the initial examination, he had no subjective symptoms. His past medical history was unremarkable. There were no distinct abnormalities on the medical examination. Blood tests revealed a white blood cell count of 10400 / L, CRP of 0.29mg/dl, AST of 31 IU/L, ALT of 46 IU/L, ALP of 583 IU/L and -GTP of 408 IU/L, showing a mild inflammatory reaction and elevated hepatobiliary enzymes. Abdominal ultrasonographic examination revealed a tumor mass approximately 4 cm in diameter in a Lateral hepatic Segment. The margin and center of the mass were hypoechoic and iso- to hyperechoic, respectively, and the inside of the mass was non-homogeneous. Needle biopsy revealed only inflammatory findings with no indications of malignancy. Since computed tomography (CT) of the abdomen, done 4 months after detection of the tumor mass, revealed the mass to have increased to approximately 6 cm in diameter, excision biopsy was considered. The CT taken 2 months later revealed the mass to have regressed to approximately 2 cm in diameter, but excision of the Lateral hepatic Segment was undertaken at the patient's request. As a result, the diagnosis of IPT of the liver was confirmed.
Imaging findings of hepatic IPT are variable and specific findings are lacking. Since the rate of correct diagnosis with needle biopsy is also low, IPT of the liver is often very difficult to differentiate from malignant tumors. On the other hand, since it may show spontaneous regression, indications for surgery must be assessed very carefully.

Key words: Inflammatory pseudotumor (IPT) of the liver

INTRODUCTION

Inflammatory pseudotumor (IPT) is a benign tumorous lesion of unknown cause, which is composed of fibrous tissue with infiltration of plasma cells and lymphocytes. This tumor mass commonly develops in the lung, and can reportedly appear in many organs, such as the orbit, oral cavity, parotid gland, pleura, liver, stomach, ovaries and retroperitoneum. IPT of the liver, reported by Pack et al. for the first time in 1953, is a rare disease, and differentiation of which from malignant tumors often becomes an issue. We experienced a patient with IPT of the liver. Herein, our patient is discussed along with references from the literature.

CASE REPORT

Patient: A 57-year-old male.
Chief complaint: No subjective symptoms. Hepatic dysfunction was indicated on the examination.
Past history: Non-contributory.
Present illness: The patient had gastritis and was under observation of the course on an outpatient basis at a nearby hospital. Hepatic dysfunction was indicated in November 2004. He was referred to our hospital for detailed examinations in December 2004.
Condition on admission: His consciousness was clear; pulse, 76/min; blood pressure, 112/74 mmHg; body temperature, 37.1°C; no findings of anemia or jaundice; abdomen was flat and soft; no palpable tumor.
Laboratory test findings (data) on admission (Table 1): White blood cell (WBC) count, 10400/ul, CRP, 0.29 mg/dl; AST, 31 IU/L (normal value <30 IU/L); ALT, 46 IU/L (normal value <30 IU/L); ALP, 583 IU/L; and γ -GTP, 408 IU/L. These data showed slightly elevated hepatobiliary enzymes. There were no other abnormal findings.
Ultrasonic examination of the abdomen on admission (Fig. 1): A tumor mass was revealed in the Lateral hepatic Segment. The margin and center were hypoechoic and iso- to hyperechoic, respectively, and the inside was non-homogeneous. Color Doppler examination revealed low blood flow in the tumor.
Computed tomographic (CT) findings of the abdomen on admission (Figs. 2a and b): A Lateral hepatic Segment hypodense tumor mass lesion was recognized.

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Table 1 Laboratory data on admission

WBC	10.400 /μl	Na	138 mEq/l
RBC	432×10⁶/μl	K	3.9 mEq/l
Hb	13.4 g/dl	Cl	102 mEq/L
Plt	23.4×104/μl	BUN	13 U/l
		Cr	0.7 mEq/l
TP	9.2 g/dl	CRP	3.72 mg/dl
Alb	3.7 g/dl	APTT	28.2 sec
AST	20 U/l	PT	12.2 sec
ALT	16 U/l		
LDH	224 U/l	HBsAg	(-)
ALP	200 U/l	HCV	(-)
γ-GTP	17 U/l	CEA	0.9ng/ml
T-bil	0.6 mg/dl	CA19-9	6U/ml
		AFP	3.3ng/ml
		IL2R	1680ng/ml

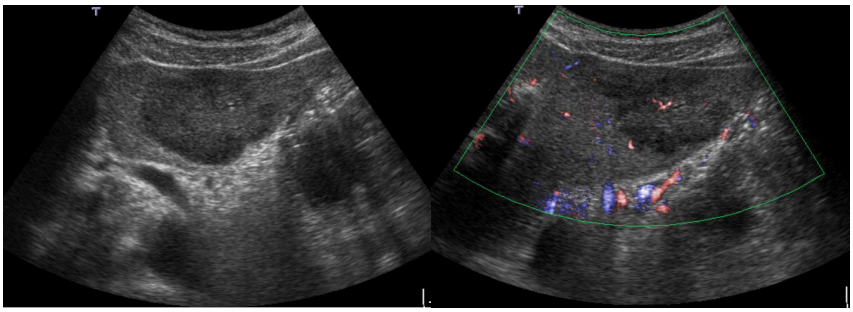

Fig. 1. Abdominal ultrasonography on admission: A tumor mass was recognized in a Lateral hepatic Segment; the margin was approximately 4 cm in diameter and hypoechoic, the center was iso- to hyperechoic and the internal portion was non-homogeneous. Color Doppler examination revealed low blood flow in the tumor mass.

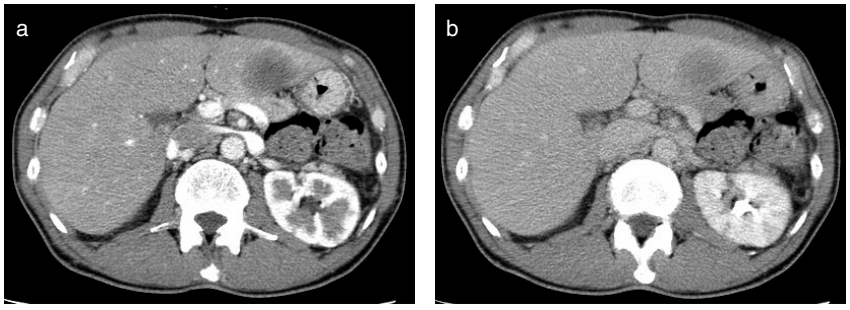

Fig. 2. Abdominal CT on admission:
a: early phase: The tumor mass is hypoechoic and the margin is soft, with deep staining.
b: late phase: The center of the tumor mass shows poor enhancement, the periphery a soft, deeply stained image.

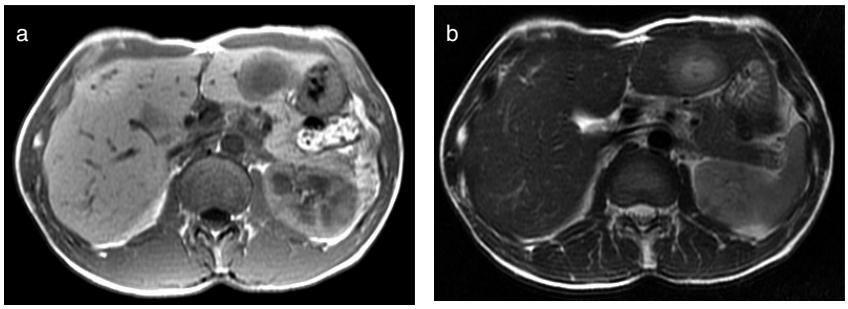

Fig. 3. Abdominal MRI on admission .
a: T1-weighted image: The periphery of the tumor mass is slightly hypointense.
b: T2-weighted image: The inside of the tumor mass shows a soft high-intensity signal, and the periphery is slightly hypointense.

Contrast-enhanced CT revealed a soft, deeply stained image of the margin of the mass in the early phase. In the late phase, enhancement of the center of the mass was poor, and there was a soft, deeply stained image around the center.

Magnetic resonance imaging (MRI) of the abdomen on admission (Figs. 3a and b): A tumor mass lesion approximately 4 cm in diameter was recognized in the left lobe of the liver. A T1-weighted image revealed the inside of the tumor mass to be hypo- to isointense and the peripheral region to be hyperintense. On T2-weighted imaging, the inside was hyperintense and the peripheral region was slightly hypointense.

Abdominal angiographic and Magnetic resonance cholangiopancreatography (MRCP) examinations: There were no distinct abnormalities.

Course after admission: For systemic screening, upper and lower gastrointestinal endoscopic examina-

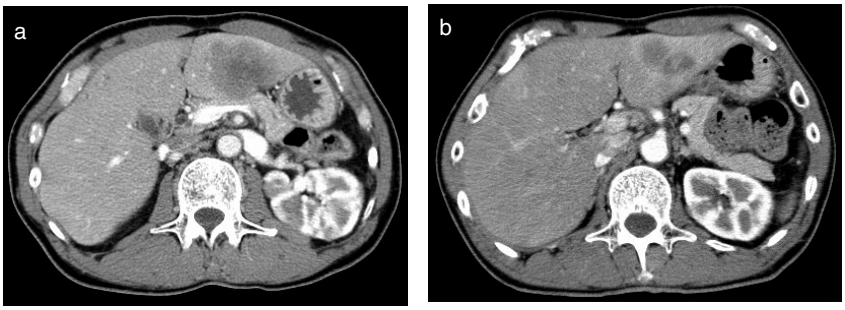

Fig. 4. Abdominal CT .
a: 4 months after IPT detection: The tumor mass has increased to approximately 6 cm in diameter.
b: CT obtained immediately before the operation: The tumor mass shows regression to approximately 2 cm in size on CT obtained 6 months after IPT detection (before the operation).

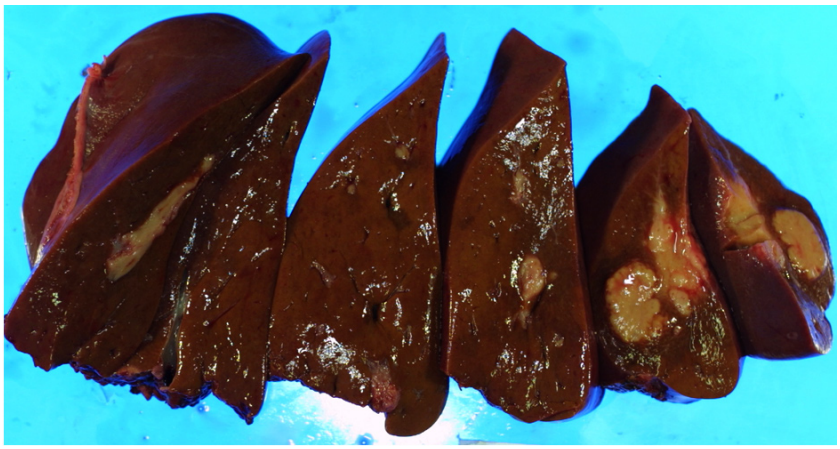

Fig. 5. Macroscopic findings of excised specimens: A white well-demarcated tumor mass approximately 4 cm in diameter can be seen.

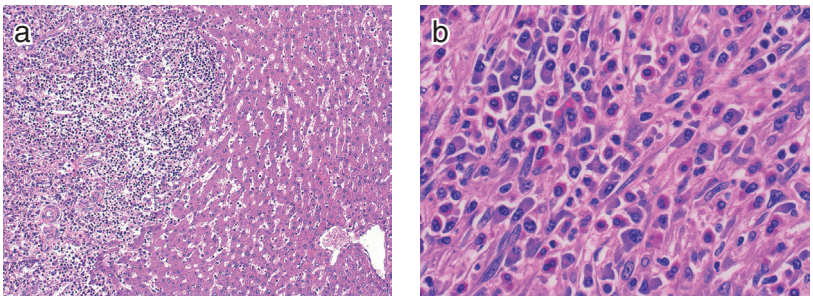

Fig. 6a b. Microscopic findings (high magnification). The nodules were mainly composed of lymphocytes, eosinophils, and plasma cells with fibrosis

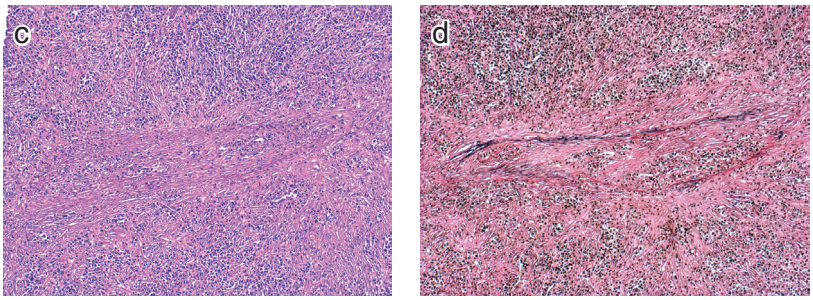

Fig. 6c(H&E). and Fig. 6d(Elastica Van Gieson).
Some foci of obstructive phlebitis were found in the nodules.

tions, tumor marker measurements, and so on were conducted. There were either no abnormal findings or only very slightly abnormalities, suggesting malignant tumors (including metastasis). On needle biopsy, only findings of inflammation were recognized, i.e. no features of malignancy. IPT of the liver was thus suspected, and the course was observed.

Since the tumor mass had increased to approximately 6 cm in diameter on abdominal CT 4 m onths after needle biopsy confirmation of the mass, excision biopsy was planned (Fig. 4a). Another abdominal CT conducted 2 months later revealed regression to approximately 2 cm in diameter (Fig. 4b). The possibility that the mass was malignant could not be ruled out, and the patient himself requested surgical removal of the mass. For these reasons, laparotomy was undertaken.

Laparotomy showed a white well-demarcated tumor mass lesion approximately 4 cm in diameter in a Lateral hepatic Segment. The rapid operative pathological examination revealed no malignant cells. The Lateral hepatic Segment was excised (Fig. 5).

Pathological findings: Macroscopically, the resected liver revealed multiple nodules (Figure 5). On cross section, the nodules were well-circumscribed, solid, and white. The size of the main nodule was 2.5 × 2.0 cm. Some lesions were located around the large bile ducts.

Microscopically, the nodules were composed of diffuse infiltration of lymphocytes, eosinophils, and plasma cells with fibrosis (Figure6a 6b). Some foci of obstructive phlebitis were identified in the nodules (Figure 6c

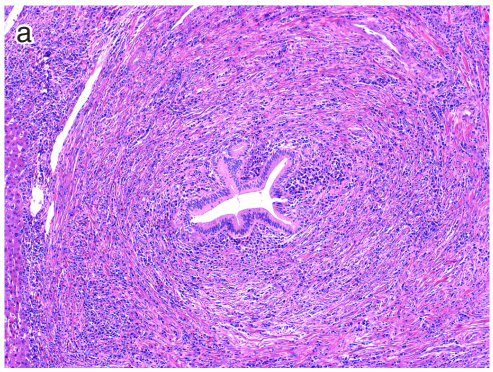

Fig. 7a. Sclerosing cholangitis was found in the large bile ducts.

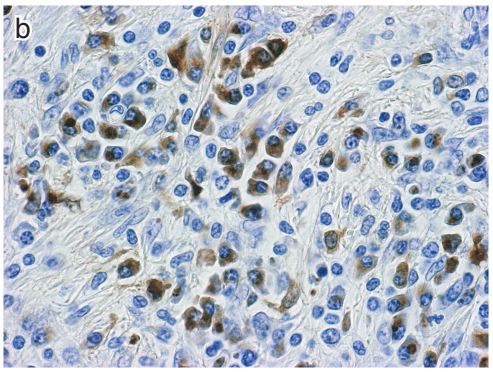

Fig. 7b. IgG4 was expressed in the cytoplasm of plasma cells.

and 6d). There was sclerosing cholangitis in the large bile ducts around the main nodular lesion (Figure 7a). Immunohistochemically, a lot of plasma cells were positive for IgG4 (Figure 7b). Anaplastic lymphoma kinase was not expressed. No EBER-positive cell was detected by in situ hybridization. No bacterial infection was identified.

DISCUSSION

IPT is a tumorous lesion composed of granulation tissue. Its etiology remains unknown, but infections (bacteria and parasites), autoimmunity, and so on are been considered to be involved in the development of IPT[1]. Biphasic peaks are recognized in the infantile period and the 40s to 60s age group. The mean age of patients with IPT of organs other than the lung is reportedly as low as 9.7 years, and females accounted for approximately 60% of these patients[3]. In 1953, Pack et al. reported the first case of IPT of the liver, which involved systemic symptoms such as pyrexia and general malaise and was distinctly diagnosed from pathological findings[2]. IPT of the liver is a rare disease, which usually develops in men of middle or advanced age[1].

It is difficult to make the diagnosis of IPT of the liver, because this disease shows variable imaging findings and lacks specific findings. Many cases are detected based on hypoechoic findings on ultrasonography, but these features are non-specific. The inside of the tumor mass is non-homogeneous. The mass includes neither necrosis nor cysts, but frequently shows a mosaic pattern. It may be difficult to differentiate from hepatocellular carcinoma[4]. On plain CT, the mass is frequently hypodense and on contrast-enhanced CT is frequently hyperdense in the equilibrium phase. Close observation revealed one case, in which the overall tumor mass was deeply stained, and another case, in which a broad, ill-demarcated deeply stained area was recognized in the margin of the tumor mass while the inside of the tumor mass was hypo- to hyperdense. These cases reportedly correspond to fibrosis of the entire inside of the tumor and marginal fibrosis with remarkable cell infiltration of the internal portion[5]. In our present patient, the inside of the tumor mass was hypoechoic with internal non-homogeneity on echography, and the lesion was hypodense with a slightly stained peripheral area on contrast-enhanced CT. Thus, these observations were consistent with the above-described findings.

IPT of the liver shows variable non-specific findings on MRI as well. The tumor mass is frequently hypo- to hyperintense on T1-weighted images and hyperintense on T2-weighted images. However, these findings are non-specific[6]. One report described a hyperintense tumor mass margin during observation of the course by T1-weighted imaging[7]. Since this high signal band is enhanced by super-paramagnetic iron oxide (SPIO)-enhanced MRI, the tumor mass must be differentiated from metastatic cancer of the liver[8]. Another report showed incorporation of SPIO into the tumor mass to be recognizable on SPIO-enhanced MRI[9]. This finding is useful for making the diagnosis. In general, the lesion is frequently visualized as an ischemic tumor mass by angiography, but there are also cases in which the margin of the tumor mass may be deeply stained and in which hepatic parenchyma other than the tumor mass may be irregularly deeply stained[9]. Inflammatory changes in the hepatic artery and biliary system and a shadow of soft tissue in the vicinity of the portal vein have also been reported[9]. The tumor lesion may be difficult to differentiate from carcinoma of the bile duct in some cases[9].

Thus, IPT is difficult to differentiate clinically from malignant tumors, because it shows variable imaging findings, and excision biopsy is frequently needed to make the diagnosis. The postoperative prognosis of IPT of the liver is favorable. To our knowledge, there have been no reports of recurrence. Some reports have shown that percutaneous needle biopsy is efficient for making the diagnosis, but the rate of making the correct diagnosis of IPT of the liver by needle biopsy is only 40–50%[11]. When malignant tumors are suspected, needle biopsy is not necessarily recommended, because there is a risk of dissemination of tumor cells[12].

Microscopically, the nodules were composed of diffuse infiltration of lymphocytes, eosinophils, and plasma cells with fibrosis. Immunohistochemically, a lot of plasma cells were positive for IgG4. The above mentioned this case is plasema cell type [19),20),21)]

It has also been reported that some cases showed regression of IPT in response to conservative treatment; an IPT of the liver, measuring 7 cm in diameter, showed spontaneous regression[17]. Another report described lesions of 3 cm or less in diameter as showing spontaneous regression. A deceased case without response to antibiotics has also been reported[16], while some cases responded to steroids, antibiotics, or non-

steroidal anti-inflammatory drugs. Patients with symptoms such as abdominal pain and jaundice, cases in whom the tumor mass tends to increase, and those in whom making the diagnosis is difficult, should be recommended to undergo surgical excision[18]. However, the fact that many cases show spontaneous regression or can be conservatively treated must also be taken into consideration in determining treatment policies. In our present case, the tumor mass had increased 4 months after detection, but showed regression on CT immediately before the operation. In accordance with the patient's wishes, laparotomy was undertaken. However, there was also a possibility that the tumor mass would have regressed spontaneously during observation of the course. Thus, meticulous assessment is needed to determine operative indications for IPT of the liver.

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