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【 CASE REPORT 】

Inflammatory Pseudo-tumor of the Liver Accompanied by Eosinophilia

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Abstract:
A 28-year-old woman was referred to our hospital for liver dysfunction and neck pain. Blood tests revealed elevated liver enzymes and eosinophilia. Ultrasonography, computed tomography, and magnetic resonance imaging showed a mass lesion near the hepatic hilus. The tumor was considered to be an inflammatory pseudo-tumor or malignancy. A liver-mass biopsy was performed and led to a diagnosis of inflammatory pseudo-tumor. In the present case, a markedly elevated eosinophil count was a characteristic clinical feature, and the patient underwent steroid therapy. Treatment resulted in a reduced eosinophil count, improved neck symptoms, and disappearance of the inflammatory pseudo-tumor.

Key words: inflammatory pseudo-tumor, eosinophilia, liver dysfunction

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Introduction

Inflammatory pseudo-tumor of the liver is a rare, benign lesion characterized by chronic infiltration of inflammatory cells and an area of fibrosis. As it sometimes mimics a malignant tumor (1-3), an inflammatory pseudo-tumor may be misdiagnosed and resected as a metastatic or primary liver tumor.

Eosinophilia occurs in three main scenarios: Reactive eosinophilia, caused by allergy or a parasitic infection, clonal myeloid disorders, such as eosinophilic leukemia, and hypereosinophilic syndrome (HES), which is persistent eosinophilia of unknown origin. HES is also characterized by eosinophilic infiltration of several organs (4, 5). Hypereosinophilia may be complicated by neurological disease. However, cases of idiopathic HES-related inflammatory pseudo-tumor or liver dysfunction are sporadic (6-14).

We herein report a case of inflammatory pseudo-tumor and liver dysfunction associated with possible eosinophilia due to HES.

Case Report

A 28-year-old woman with an unremarkable medical history was referred to our hospital for liver dysfunction and neck pain. The patient was not taking any regular medication, including oral contraceptives. In addition, the patient had no allergic episodes. The patient had been aware of the pain in her right neck region for 10 days before the hospital visit. Furthermore, she had development numbness in both legs a few days before the hospital visit.

Blood tests revealed an elevated white blood cell (WBC) count (11,600/μL); in particular, the level of eosinophils was markedly increased (6,148/μL, 53%). A liver function test revealed elevated levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and gamma-glutamyltransferase (γ-GTP) (44 IU/L, 86 IU/L, 561 IU/L, and 125 U/L, respectively).

Table shows the laboratory data obtained on admission. Ultrasound sonography (US) showed a low-echoic mass with a size of 28×27 mm near the porta hepatis. The tumor borders were relatively indistinct, and the internal echoes were slightly heterogeneous. The tumor was located near the portal vein and the hepatic vein. The tumor was found to be

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Table. **Laboratory Data Obtained on Admission.**

WBC	8,700 /μL	AST	42 U/L	AFP	1.3 ng/mL
Neutrophil	14 %	ALT	65 U/L	PIVKAII	13 mAU/mL
Eosinophil	52 %	ALP	384 U/L	ANA	80 ×
Basophil	1 %	LDH	197 U/L	AMA-M2	(-)
Monocyte	4 %	T-Bil	1.2 mg/dL	MPO-ANCA	<0.5 U/mL
Lymphocyte	29 %	D-Bil	0.2 mg/dL	PR3-ANCA	<0.5 U/mL
Hb	12.7 g/dL	I-Bil	1 mg/dL	s-IL2-R	901 U/mL
Plt	319,000 /μL	γ-GTP	89 U/L	IgG-4	47.6 mg/dL
		CK	90 U/L	IgA	190 mg/dL
		BUN	16.8 mg/dL	IgG	142.2 mg/dL
		Cre	0.64 mg/dL	IgM	128 mg/dL
		Na	139 mEq/L	HBs Ag	(-)
		K	4.3 mEq/L	HBs Ab	(-)
		Cl	104 mEq/L	HBc Ab	(-)
		CRP	0.02 mg/dL	HCV Ab	(-)

ALP: alkaline phosphatase, ALT: alanine aminotransferase, AMA-M2: anti-mitochondrial M2 antibodies, ANA: antinuclear antibodies, AST: aspartate aminotransferase, BUN: blood urea nitrogen, CK: creatine kinase, Cre: creatinine, CRP: C-reactive protein, D-Bil: direct bilirubin, γ-GTP: γ-glutamyl transpeptidase, Hb: hemoglobin, HBc Ab: hepatitis B core antibody, HBs Ag: hepatitis B surface antigen, HCV Ab: hepatitis C virus antibody, MPO-ANCA: myeloperoxidase-antineutrophil cytoplasmic antibody, Plt: platelets, PR3-ANCA: proteinase-3-antineutrophil cytoplasmic antibody, T-Bil: total bilirubin

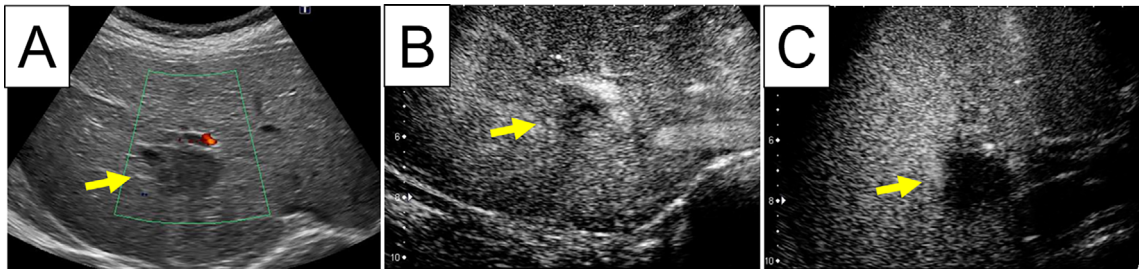

Figure 1. **Abdominal ultrasonography (US) image showing a low-echoic mass lesion (arrow) (A), sonazoid-enhanced US image showing a high-echoic mass lesion at the early vascular phase (B), and sonazoid-enhanced US image showing a hypoechoic mass lesion at the post-vascular phase (C).**

compressing blood vessels, but there was no evidence of invasion.

The mass was hypovascular on color Doppler. Sonazoid-enhanced US showed that the tumor was hyperechoic at the early vascular phase (within 1 minute after intravenous injection of sonazoid) and hypoechoic at the post-vascular phase (more than 5 minutes after injection) (Fig. 1). Computed tomography (CT) showed that the tumor exhibited a lower density than the surrounding liver parenchyma (plain CT). Dynamic CT in the arterial phase showed a poorly defined peripheral enhancement with an internal hyperattenuating area, and dynamic CT in the equilibrium phase showed a homogeneously hypoattenuating lesion (Fig. 2). Based on the CT findings, the mass was considered an inflammatory pseudo-tumor or a malignant tumor. Magnetic resonance imaging (MRI) revealed mild hypo-intensity on T1-weighted imaging compared with the surrounding hepatic parenchyma. T2-weighted imaging showed a slightly higher signal intensity than the surrounding liver parenchyma. Dynamic gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid-enhanced magnetic resonance imaging (EOB-MRI) showed a poorly defined peripheral rim-like enhancement with hepatic arterioportal shunt in the early phase. In contrast, dynamic EOB-MRI showed a poorly defined hyperintensity with an internal hypointense area in the hepatobiliary phase (Fig. 3). As in the other imaging studies, MRI indicated an inflammatory pseudo-tumor of the liver; however, differentiation from malignancy was difficult. Therefore, we biopsied the tumor for further clarification.

We noted fibroblast hyperplasia and infiltration by inflammatory cells, and the primary lesion exhibited chronic inflammation with bile duct hyperplasia and inflammatory pseudo-tumor pathology. Although there were eosinophils in the tumor, large numbers of eosinophils that could be considered direct eosinophil infiltration were not detected. Immunohistochemistry indicated vimentin, histiocytosis, and fibrosis, but there was no involvement of SMA or IgG4 and no evidence of malignancy (Fig. 4). The evaluation of the tumor biopsy specimen led to the diagnosis of inflammatory pseudo-tumor of the liver.

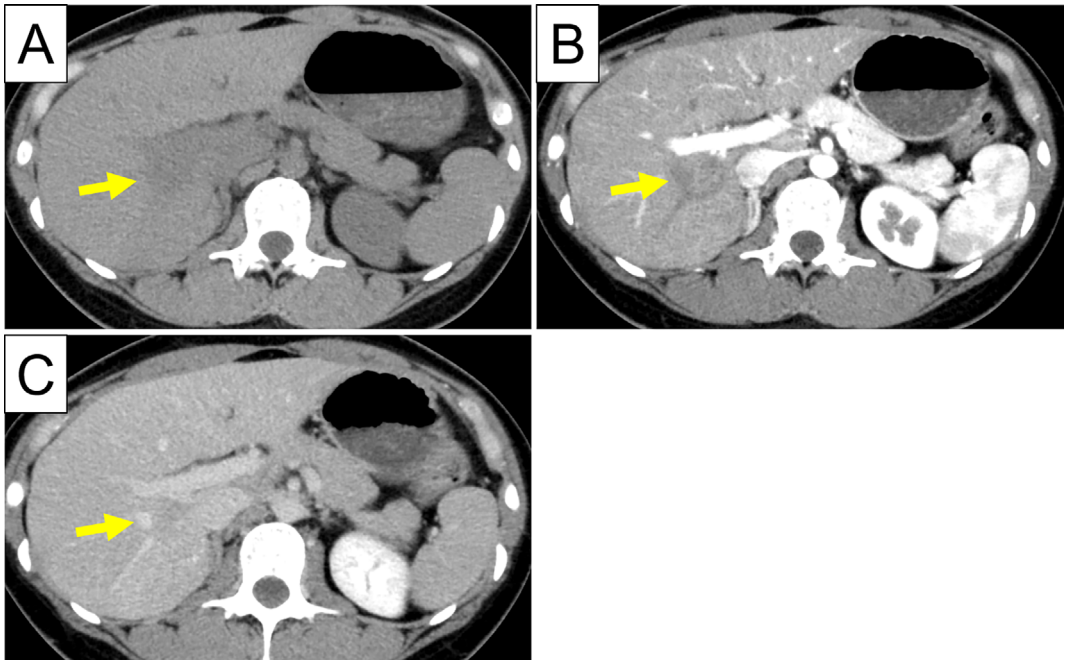

Figure 2. **Computed tomography (CT) image of the abdomen showing a mass located near the porta hepatis (arrow) in the plain image (A), the arterial phase (B), and the equilibrium phase (C).**

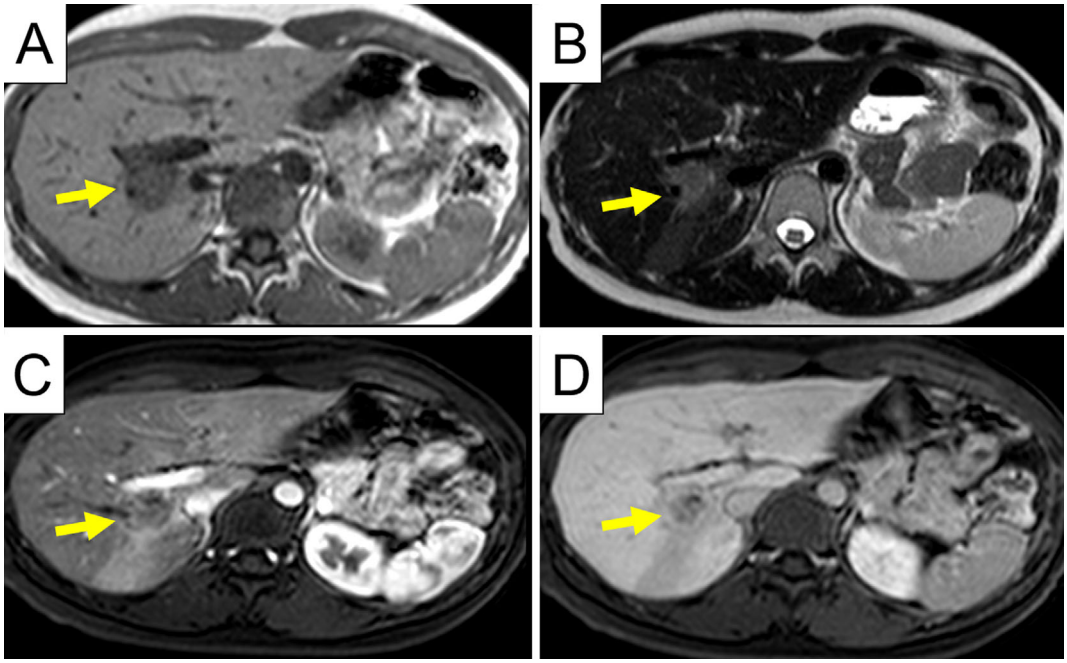

Figure 3. **Abdominal magnetic resonance imaging (MRI) showing a mild hypointense mass (arrow) on T1-weighted imaging (A), a slightly higher-signal-intensity mass on T2-weighted imaging (B), a mass with rim-like enhancement on dynamic gadolinium ethoxybenzyl diethylenetriamine pentaacetic acid-enhanced MRI (EOB-MRI) (early phase) (C), and a hyperintense mass with an internal hypointense area on dynamic EOB-MRI (hepatobiliary phase) (D).**

As the patient's symptoms were not improved by conservative supportive care, the clinical findings were considered to indicate a syndrome associated with eosinophilia. Treatment was required for the eosinophilia. The patient was thus administered 40 mg/day of prednisolone (PSL). The eosinophil levels and cervicodynia improved with treatment, suggesting that the cervicodynia might reflect eosinophilic fasciitis. Even with the tapering of PSL, there was no symptom relapse, and the tumor gradually disappeared on diagnostic imaging. PSL treatment was discontinued after seven months, after which there was no tumor recurrence, and the clinical course was uneventful.

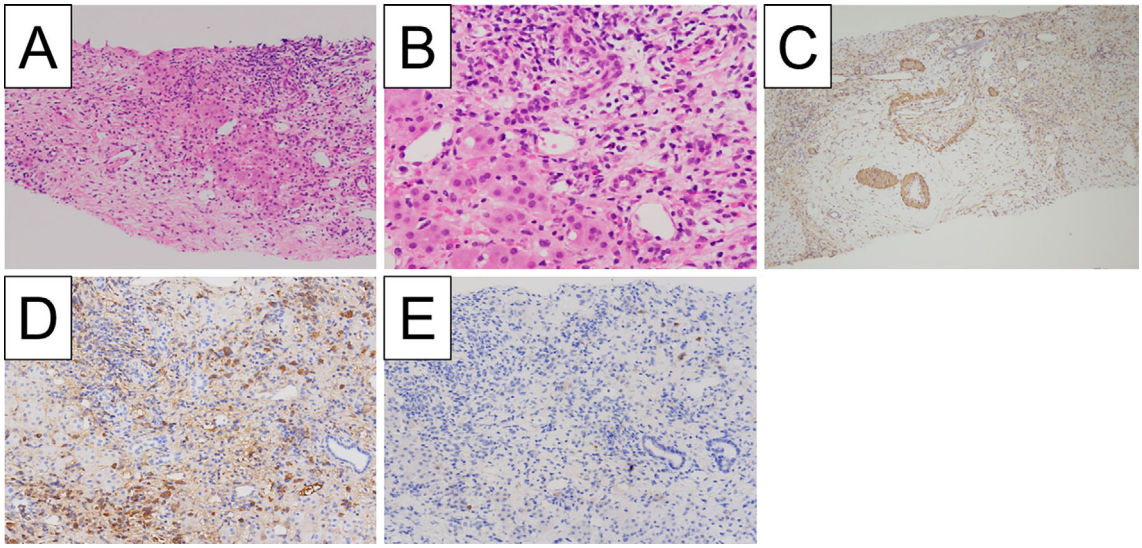

Figure 4. **Hematoxylin and Eosin staining showing the presence of inflammatory cell infiltration (A, low-power field; B, high-power field). Immunohistochemistry showing alpha-SMA (C), IgG (D), and IgG4 (E).**

Discussion

An inflammatory pseudo-tumor, also known as an inflammatory myofibroblastic tumor, is a rare, benign disease. A 1939 report identified an inflammatory lung pseudo-tumor (15), and a 1953 report discussed an inflammatory liver pseudo-tumor (16). The epidemiology of inflammatory liver pseudo-tumors remains unclear because of the rarity of the disease, but possible etiologies include infection, congenital diseases, chronic biliary inflammation, vascular conditions, gallstones, trauma, and autoimmune disorders, such as IgG4-related disease (17-21). The definitive diagnosis of inflammatory pseudo-tumor depends on needle biopsy findings. While there are no established treatment guidelines, conservative therapy may be used, such as antibiotics, non-steroidal anti-inflammatory drugs, or steroids (3). However, because of the variety of imaging findings, such as those obtained by CT or MRI, combined with the lack of characteristic features, some tumors are misdiagnosed as metastatic liver tumors or primary liver tumors and thus resected (3). In our case, the imaging findings indicated an inflammatory pseudo-tumor of the liver, but differentiation from malignancy was difficult, which led to a tumor biopsy being performed. We suspected a link between the marked peripheral eosinophilia, liver injury, and inflammatory pseudo-tumor of the liver; therefore, the patient began steroid therapy.

Eosinophilia may develop either as reactive eosinophilia, eosinophilic leukemia, or HES; the latter may involve eosinophilic infiltration of several organs (4, 5). HES represents features of prolonged eosinophilia of >1,500 eosinophils/μL peripheral blood observed over 6 months (22). However, in the presence of end-organ damage, treatment should not be withheld in patients with hypereosinophilia lasting for less than six months (22). The present patient had liver dysfunction, inflammatory pseudo-tumor of the liver, neck pain, and numbness in both legs. Urgent treatment was deemed indispensable because of the organ disorder, so treatment was initiated without waiting for six months to rule out HES. Since all findings improved markedly after steroid therapy, the clinical findings were considered a syndrome associated with eosinophilia. Hepatic injury and inflammatory pseudo-tumor of the liver associated with serum eosinophilia are rare. In such cases, steroid therapy may be effective.

Conclusion

The present case presented with an inflammatory pseudo-tumor and liver dysfunction associated with eosinophilia potentially linked to HES. In the absence of standard treatment for inflammatory pseudo-tumor, PSL therapy may be effective in patients with peripheral blood eosinophilia.

The authors state that they have no Conflict of Interest (COI).

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