

[ CASE REPORT ]

## Hepatic Inflammatory Pseudotumor Protruding from the Liver Surface and Directly Penetrating the Colon

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### Abstract:

A 69-year-old man was diagnosed with a liver abscess and received antibiotics at a local hospital. He was referred to our hospital due to a persistent fever. He had hepatic masses protruding from the liver surface toward the transverse colon. We reached a diagnosis of inflammatory pseudotumor (IPT) by a percutaneous liver biopsy. Colonoscopy showed direct invasion of IPT to the colon. His condition improved by the intravenous administration of antibiotics. Hepatic IPT is often misdiagnosed as a malignant tumor. We should consider IPT when we encounter hepatic tumors, and a percutaneous liver biopsy is useful for avoiding unnecessary excessive treatments.

**Key words:** inflammatory pseudotumor, hepatic tumor, liver abscess, liver biopsy

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### Introduction

Inflammatory pseudotumor (IPT), which is also called inflammatory myofibroblastic tumor, is a rare benign disease. Its common organ is the lung, but it has also been observed in the central nervous system, salivary glands, larynx, breast, pancreas, spleen, lymph nodes, skin and liver (1). Hepatic IPT accounts for about 8% of IPTs among extrapulmonary IPT (2-4), and the incidence was reported to be around 0.7% among 405 resected liver tumors (5). It is very difficult to make an accurate preoperative diagnosis of hepatic IPT, as it shows nonspecific symptoms and various image findings. We herein report a patient with two hepatic IPTs that protruded from the liver surface and directly penetrated the hepatic flexure of the colon.

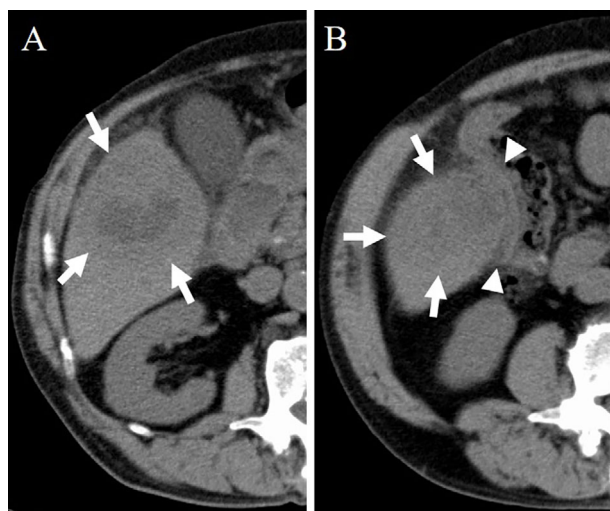
### Case Report

A 69-year-old man visited a local hospital after suffering from a fever for two weeks. He had consumed about 100 g/day of alcohol for 49 years. He had been taking amlodipine besilate since 45 years of age and theophylline and pranlukast hydrate since 60 years of age because of hypertension

and chronic obstructive pulmonary disease, respectively. He had no history of diabetes mellitus, a disease that induces ischemia of the liver, cholestatic liver disease, autoimmune diseases (including IgG4-related disease or inflammatory bowel disease), or abdominal surgery. He had been hospitalized three months earlier due to a liver abscess and had undergone percutaneous transhepatic drainage at a local hospital. The drainage had been purulent-like, and *Fusobacterium spp.* had been detected in bacterial culture, although blood cultures were negative. An examination of the blood showed a white blood cell (WBC) count of 14,900/ $\mu$ L and C-reactive protein (CRP) of 16.52 mg/dL. Plain computed tomography (CT) showed 2 consecutive masses with a central low-attenuation area and a maximum size of 6 cm in diameter in liver segments 5 to 6 (Fig. 1A). He was therefore diagnosed with a liver abscess and emergently admitted to another local hospital (day 1).

Despite treatment with intravenous infusion of antibiotics sulbactam/cefoperazone (SBT/CPZ), the fever did not disappear. He was transferred to our hospital on day 7. On admission, a hard and tender mass was palpable 3 cm below the costal arch in the right anterior axillary line. Laboratory findings showed a WBC count of 12,300/ $\mu$ L, CRP of 12.59 mg/dL, mild elevation of liver enzymes and carcinoembry-

onic antigen (CEA), and negative for anti-amoebic antibody (Table). After reviewing CT findings on day 1, the border



**Figure 1.** Plain computed tomography (CT) images at a local hospital on day 1. Two consecutive masses with central low attenuation were observed in liver segments 5 to 6 (arrows). (A) The cranial lesion was 6 cm in diameter. (B) The border between the caudal mass and hepatic flexure of the colon was ill-defined, and the neighboring mesenteric adipose tissue showed stranding (arrowheads).

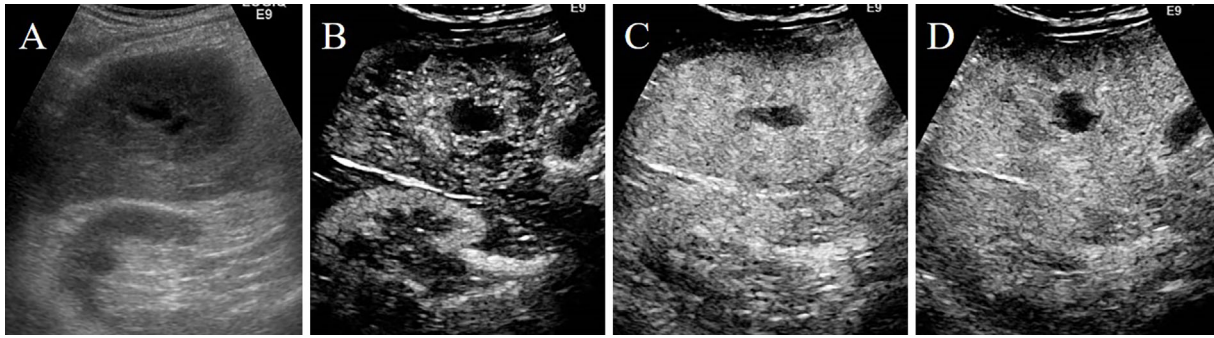
between the caudal mass and hepatic flexure of colon was found to be ill-defined, and the neighboring mesenteric adipose tissue showed stranding (Fig. 1B). On B-mode ultrasonography (US) performed on day 7, the liver lesions were hypoechoic with a central anechoic area (Fig. 2A). On contrast-enhanced US, the lesions were hypervascular at the arterial phase, isovascular at the portal phase, slightly hypovascular at the equilibrium phase (Fig. 2B-D), and hypoechoic at the Kupffer phase. The central areas were avascular at all phases. Contrast-enhanced CT showed that the cranial lesion had increased to 8 cm in diameter and that both peripheral lesions were slightly enhanced (Fig. 3A). In addition, the caudal lesion protruded from the liver surface, and the border with the colon was indistinct (Fig. 3B).

Although we considered liver abscesses with central necrotic lesion, it was difficult to completely exclude malignant neoplasms, including metastases. Therefore, we performed a US-guided percutaneous aspiration biopsy of the hypoechoic area around the anechoic area of the cranial nodule using a 21-gauge needle twice. The section showed infiltration of inflammatory cells, such as lymphoid and plasma cells, and the proliferation of spindle-like fibroblasts that were positive for  $\alpha$ -smooth muscle actin ( $\alpha$ -SMA) according to an immunohistochemical analysis (Fig. 4). We also performed aspiration of the central fluid of the mass and aspirated 50 mL of purulent-like liquid that was nega-

**Table.** Laboratory Data on Admission to Our Hospital on Day 7.

|              |   |                       |                |
|--------------|---|-----------------------|----------------|
| Hematology   |   | Serology              |                |
| WBC          | 12,300 / $\mu$ L                        | CRP                   | 12.59 mg/dL    |
| Neutro       | 74.8 %                                  | Endotoxin             | <3.0 pg/mL     |
| Lympho       | 18.5 %                                  | HBsAg                 | (-)            |
| RBC          | 440 $\times$ 10 <sup>4</sup> / $\mu$ L  | HCV-Ab                | (-)            |
| Hb           | 12.1 g/dL                               | Anti-amoebic antibody | (-)            |
| Plt          | 41.3 $\times$ 10 <sup>4</sup> / $\mu$ L |                       |                |
| Biochemistry |   | Coagulation           |                |
| Alb          | 3.2 g/dL                                | PT%                   | 82.3 %         |
| T-bil        | 0.4 mg/dL                               | APTT                  | 39.4 Sec       |
| AST          | 35 U/L                                  | Fibrinogen            | 851 mg/dL      |
| ALT          | 37 U/L                                  | FDP                   | 9.6 $\mu$ g/mL |
| LDH          | 178 U/L                                 |                       |                |
| ALP          | 331 U/L                                 | Tumor maker           |                |
| $\gamma$ GTP | 174 U/L                                 | AFP                   | 2.3 ng/mL      |
| BUN          | 10 mg/dL                                | CEA                   | 4.4 ng/mL      |
| Cre          | 0.72 mg/dL                              | CA19-9                | 6.6 U/mL       |
| FPG          | 105 mg/dL                               |                       |                |
| HbA1c        | 5.8 %                                   |                       |                |

AFP: alpha-fetoprotein, Alb: albumin, ALP: alkaline phosphatase, ALT: alanine aminotransferase, APTT: activated partial thromboplastin time, AST: aspartate aminotransferase, BUN: blood urea nitrogen, CA19-9 carbohydrate antigen 19-9, CEA: carcinoembryonic antigen, Cre: creatinine, CRP: C-reactive protein, FDP: fibrinogen degradation product, FPG: fast plasma glucose,  $\gamma$ GTP: gamma glutamyltranspeptidase, Hb: hemoglobin, HbA1c: hemoglobin A1c, HBsAg: hepatitis B surface antigen, HCV-Ab: hepatitis C virus antibody, LDH: lactate dehydrogenase, Lympho: lymphocyte, Neutro: neutrophils, Plt: platelet, PT: prothrombin time, RBC: red blood cell, T-bil: total bilirubin, WBC: white blood cell



**Figure 2.** Ultrasonography (US) images on day 7. (A) B-mode US showed the mass as a hypoechoic lesion with a central anechoic area. On contrast-enhanced US, it was hypervascular at the arterial phase (B), isovascular at the portal phase (C) and slightly hypovascular at the equilibrium phase (D). The central areas were avascular at all phases.

tive on bacterial culture and a cytological examination. We therefore made a diagnosis of IPT.

Because the fever and inflammatory reaction persisted, we changed the antibiotics from SBT/CPZ to tazobactam/piperacillin (PIPC/TAZ). The fever and blood inflammation markers immediately improved, and we discontinued PIPC/TAZ on day 14 (Fig. 5). Total colonoscopy was performed on day 14 because of the CT findings and mild elevation of serum CEA values. It showed a smoothly elevated erythematous lesion at the hepatic flexure (Fig. 6A). A white mass also appeared at the top of the lesion, which was thought to be infiltration from the outside of the colon. We performed 2.8-mm forceps biopsy (Radial Jaw™ 4; Boston Scientific, Boston, USA). However, it was difficult to obtain an adequate pathological specimen from the white mass, as it was composed of fibrotic scleroid tissue. The specimen from the erythematous membrane around the white mass showed mild-to-moderate chronic inflammatory changes and epithelial regeneration. Finally, we diagnosed the patient with hepatic IPT with bacterial infection and direct penetration to the hepatic flexure of the colon. CT on day 18 showed that the hepatic IPTs had decreased in size and that the border with the colon had become clear (Fig. 3C, D). He was discharged from our hospital on day 21. The IPTs had almost completely disappeared on CT (Fig. 3E, F), and the colonic lesion was completely healed on colonoscopy two months after the discharge (Fig. 6B).

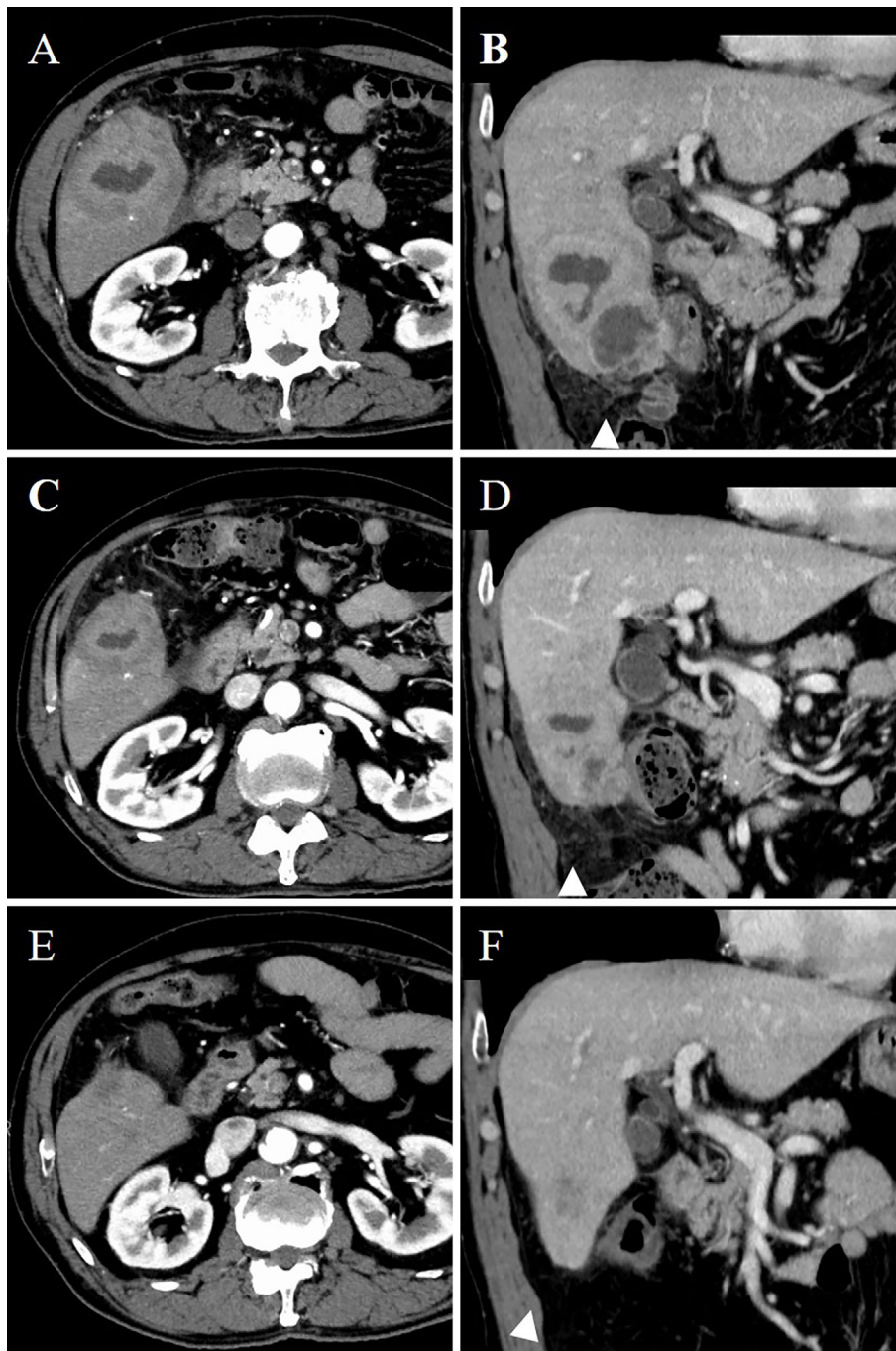
## Discussion

IPT was first described in the lung in 1939 (6), and hepatic IPT was first reported in 1953 by Pack and Baker (7). The epidemiology of hepatic IPT remains unclear because it is a rare disease. Some previous studies from Asia, Europe and the USA have reported that men accounted for about two-thirds of total hepatic IPT cases (4, 8, 9). Although the common age described in those studies ranged widely, from the 30s to 60s, one study from Korea in 45 cases of histologically proven hepatic IPT reported a median age of 65 years old (9), and our patient was also near this age.

The present patient showed a fever and elevation of serum inflammatory markers and hepatobiliary enzymes. The most common symptoms of hepatic IPT are abdominal pain, a fever, malaise, and weight loss (4, 5, 9, 10). However, about 20% of the patients are asymptomatic. In addition, the most common abnormal laboratory findings were elevation of serum inflammatory markers, including the erythrocyte sedimentation rate (ESR), CRP level and leukocyte count (2, 9, 11). Mild elevation of hepatobiliary enzymes is sometimes observed. However, these symptoms and laboratory findings are nonspecific and are also seen in patients with other hepatobiliary infections and malignancies.

The etiology of hepatic IPT remains unknown. However, several factors, such as infection, trauma, biliary obstruction and cholangitis, autoimmune disorders, hepatitis B virus, hepatitis C virus, IgG4-related cholangitis and primary sclerosing cholangitis, are thought to be closely related to hepatic IPT (12-14). The present case had undergone percutaneous transhepatic liver abscess drainage six months earlier. This traumatic procedure may have been related to his hepatic IPT. In addition, hepatic IPT in the present case may have been caused by liver abscess, as purulent-like liquid was detected in the central lesion, and blood examinations showed marked inflammation. Unfortunately, we did not examine the autoantibody, IgG and IgG4 presence. There were no biliary or pancreatic abnormalities on imaging or physical findings suggesting autoimmune disease. Although he was not an immunocompromised host, we should have considered the possibility of cytomegalovirus (CMV) infectious liver abscess. An instructive report described a case of CMV colitis affecting an immunocompetent patient complicated with liver abscess and subsequent colorectal stenosis requiring surgical resection (15).

It has been reported that most cases with hepatic IPT were diagnosed after surgical resection (14). This is because of the lack of accurate diagnostic imaging methods. The US findings of hepatic IPT show various echogenicity patterns or lesions mimicking an abscess or a hepatocellular carcinoma (16). On contrast-enhanced CT, hepatic IPT often shows late enhancement of the peripheral region (3). How-



**Figure 3.** Contrast-enhanced CT images. (A, B) On day 7, the cranial lesion had increased to 8 cm in diameter and was slightly enhanced with non-enhanced low attenuation foci in the center. The caudal lesion protruded from the liver surface, and the border with the colon was indistinct (arrow). (C, D) On day 18, the two lesions had decreased in size. However, the border with the colon became slightly clearer (arrow). (E, F) Two months after the discharge, the two liver lesions had almost disappeared, and the border with the colon had become clear (arrow).

ever, this enhancement pattern is also seen in adenocarcinoma, such as cholangiocarcinoma or metastatic tumors. In addition, one study found that hepatic IPT sometimes showed early enhancement with washout at the late phase, like hepatocellular carcinoma (17). In the present case, the mass was enhanced from the arterial to equilibrium phase on contrast-enhanced US. The image findings of hepatic IPT are thus variable and nonspecific. This is because the en-

hancement patterns created by the contrast medium represent the distribution proportions of inflammatory cells and fibrosis, and this distribution varies depending on the cause and inflammatory phase (18).

Hepatic IPT is usually a single lesion localized to the liver and does not protrude from the liver surface. In rare cases, multiple hepatic IPTs are reported (4, 9). In addition, there are some case reports of hepatic IPT extrahepatic

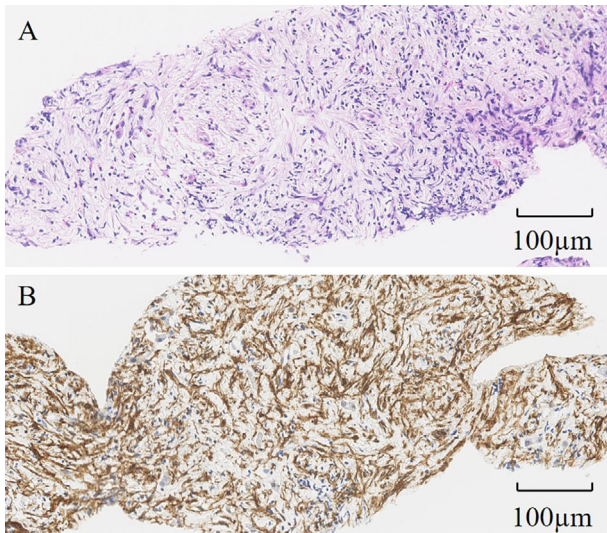
growth patterns mimicking the present patient (19-21). The present case also had two lesions that directly invaded the colon, mimicking malignant tumors. These findings made it difficult for us to discriminate hepatic IPT from malignant tumors.

The typical pathological findings of IPT are the presence of myofibroblastic spindle cells, plasma cells, macrophages, and lymphocytes without cellular atypia or atypical mitotic

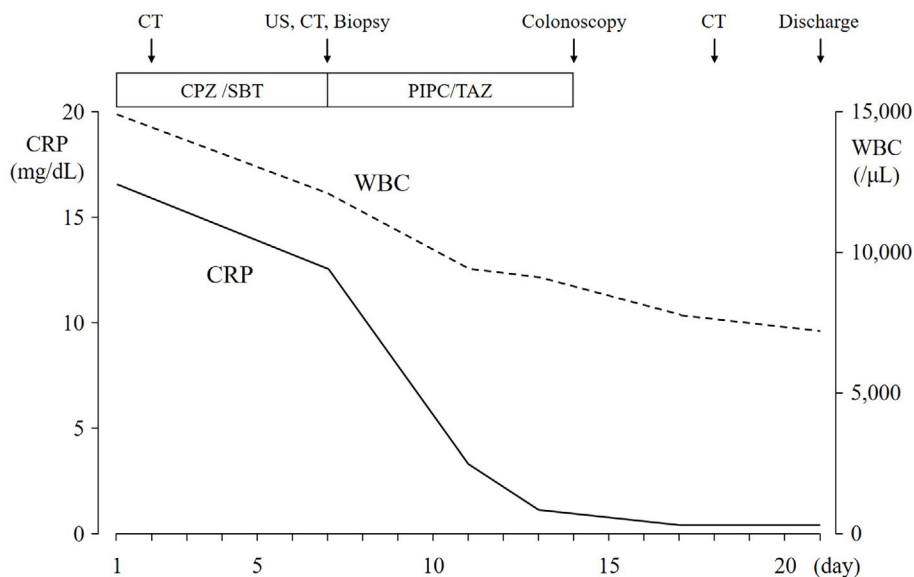
figures (22). These findings differ markedly from those of liver abscess and malignant tumors. Therefore, differentiation between hepatic IPT and other liver diseases seems to be easy. However, many cases with hepatic IPT are diagnosed postoperatively rather than preoperatively (14). Although a US-guided percutaneous biopsy plays an important role in making a diagnosis of liver lesions in general, its diagnostic accuracy regarding hepatic IPT is insufficient (23). The major reason for this lack of accuracy is thought to be sampling error. In most cases, hepatic IPT regresses spontaneously or after the administration of antibiotics. We believe that performing a US-guided percutaneous biopsy twice in the hypoechoic area, where viable tumor cells might remain, rather than the anechoic area helped avoid sampling error.

Surgical resection is a treatment option, but unnecessary resection should be avoided (24). A re-biopsy should therefore be considered if the histological findings fail to clearly distinguish among hepatic IPT, cholangiocarcinoma and metastases.

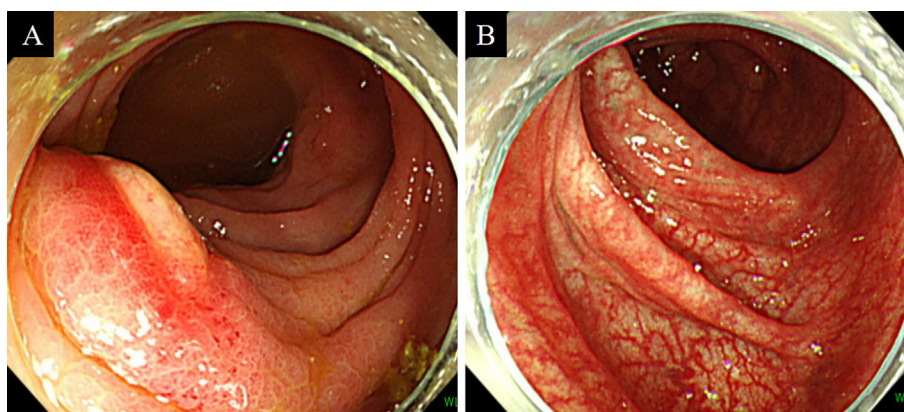
It is difficult to diagnose hepatic IPT because its symptoms are nonspecific and its imaging findings can mimic malignant tumors. In the present case, the spread of inflammation to the hepatic flexure on colonoscopy was noted, and no malignant tissue was detected by a colon biopsy. Colon cancer and liver abscess without liver metastasis have been reported to be simultaneously detected (25). Given the possibility of a discrepancy between the histopathology of the liver and the colon, it is important to perform both a liver and colon biopsy. We reached a diagnosis of hepatic IPT and avoided invasive surgical resection by performing a liver and colon biopsy with a careful immunohistochemical



**Figure 4.** Histopathological findings of the cranial nodule. (A) Hematoxylin and eosin staining showed infiltration of inflammatory cells, such as lymphoid and plasma cells, and proliferation of spindle-like cells. (B) The spindle-like cells were positive on  $\alpha$ -SMA immunohistochemical staining.



**Figure 5.** Clinical course. The patient was admitted to a local hospital on day 1 and treated with sulbactam/cefoperazone (SBT/CPZ) from days 1 to 6. He was transferred to our hospital, and a percutaneous aspiration biopsy was performed on day 7. Tazobactam/piperacillin (PIPC/TAZ) was administered from days 7 to 14. Blood inflammatory markers, such as the white blood cell (WBC) count and C-reactive protein (CRP) level, improved immediately. CT: computed tomography, US: ultrasonography



**Figure 6.** Colonoscopy images at the hepatic flexure of the colon. (A) On day 14, a hard, white mass infiltrated from the outside of the colon. (B) The colonic lesion had completely healed by two months after the discharge.

analysis.

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

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