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CASE REPORT

Regression of Inflammatory Pseudotumor of the Liver Under Conservative Therapy

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Inflammatory pseudotumor (IPT) is a rare benign lesion of the liver, histologically characterized by a mixture of inflammatory cells (predominantly plasma cells, lymphocytes, and foamy histiocytes and occasionally polymorphonuclears) in a stroma consisting of interlacing bundles of fibroblasts and collagenous tissue (1–13). Due to clinical presentation and morphological appearance, liver IPTs are often misdiagnosed (1, 3, 4, 6, 7, 9, 11, 12), especially as primary liver carcinoma. Hepatic resection is therefore usually performed (1, 3, 4, 6–9, 11, 12) and the prognosis under conservative treatment remains unclear.

We report a new case of liver IPT with special focus on its regression under antibiotic therapy. Further morphological and histological features are described and may facilitate recognition. This opportunity and the possible effectiveness of conservative treatment should serve to keep IPT in mind in the differential diagnosis of liver tumors.

CASE REPORT

A 56-year-old Vietnamese man, without previous significant medical history, developed, in December 1993, moderate left iliac pain, progressive weakness, and intermittent fever. Abdominal ultrasonography (US) and computed tomography (CT) disclosed a solid heterogeneous and ill-defined tumor in the left lobe of the liver. The morphological pattern of the lesion was hypoechogenic at US and hypodense at CT scan, with slight enhancement after contrast injection. CT scan showed left portal vein collapse without thrombus visualization. In addition, left pleural, perihepatic, and perisplenic effusions were noted. As pleural centesis disclosed an aseptic puriform fluid, draining and antibiotic therapy, with cefotaxime 1 g four times a day and metronidazole 500 mg three times a day, were initiated.

The patient was subsequently admitted in our unit for further investigation. Initial clinical findings were limited to intermittent fever (37–38.5°C) and weight loss of 8 kg without hepatomegaly or abdominal tenderness. On admission, blood exams showed a white cell count of 16,500/mm^3 with 90% neutrophil polymorphs, an increase of erythrocyte sedimention rate (106 mm/hr), hyperfibrinogenemia (6.9 g/liter), and an increase of α_2 globulin (6 g/liter). Total bilirubin was 10 μmol/liter, serum albumin 25 g/liter, alkaline phosphatase 439 units/liter, gamma-glutamyltranspeptidase 201 units/liter. Aminotransferase and α-fetoprotein were normal. Blood culture and monotest were negative. Anti-HBs and anti-HBc were positive. Antibody to HVC was negative. Magnetic resonance imaging showed an hypointense, poorly margined liver lesion on T1 weighted sequence; T2 weighted sequence revealed a slight increase of intensity of the lesion and the surrounding parenchyma (Figure 1A). Hepatic and splenic effusion had almost disappeared. Occlusion of the left portal branch was confirmed with thickening of vein margins without thrombus visualization. Although morphologic patterns remained nonspecific, the association of portal vein occlusion and liver tumor led to the initial suspicion of hepatocellular carcinoma. US-guided percutaneous hepatic biopsy was performed. The lesion was surrounded by hyalinized fibrosing bundles, which infiltrated normal hepatic tissue. The core exhibited compact proliferation of regular foamy cells, mixed with scattered plasma cells and some inflammatory cells: lymphocytes, neutrophils, and foreign body giant cells (Figure 2A and 2B). No organisms could be demonstrated in the lesion (Gram and Ziehl-Nieelsen stainings were negative). Immunohistochemistry enhanced the macrophagic origin of the foamy cells (antibody against CD68 was positive) and polyclonal characteristics of the plasma cells. These lesions were morphologically comparable to the inflammatory pseudotumors found elsewhere in other organs (lung, soft tissues). Because of the reactive nature of the IPT, associated infectious diseases were researched. Digestive

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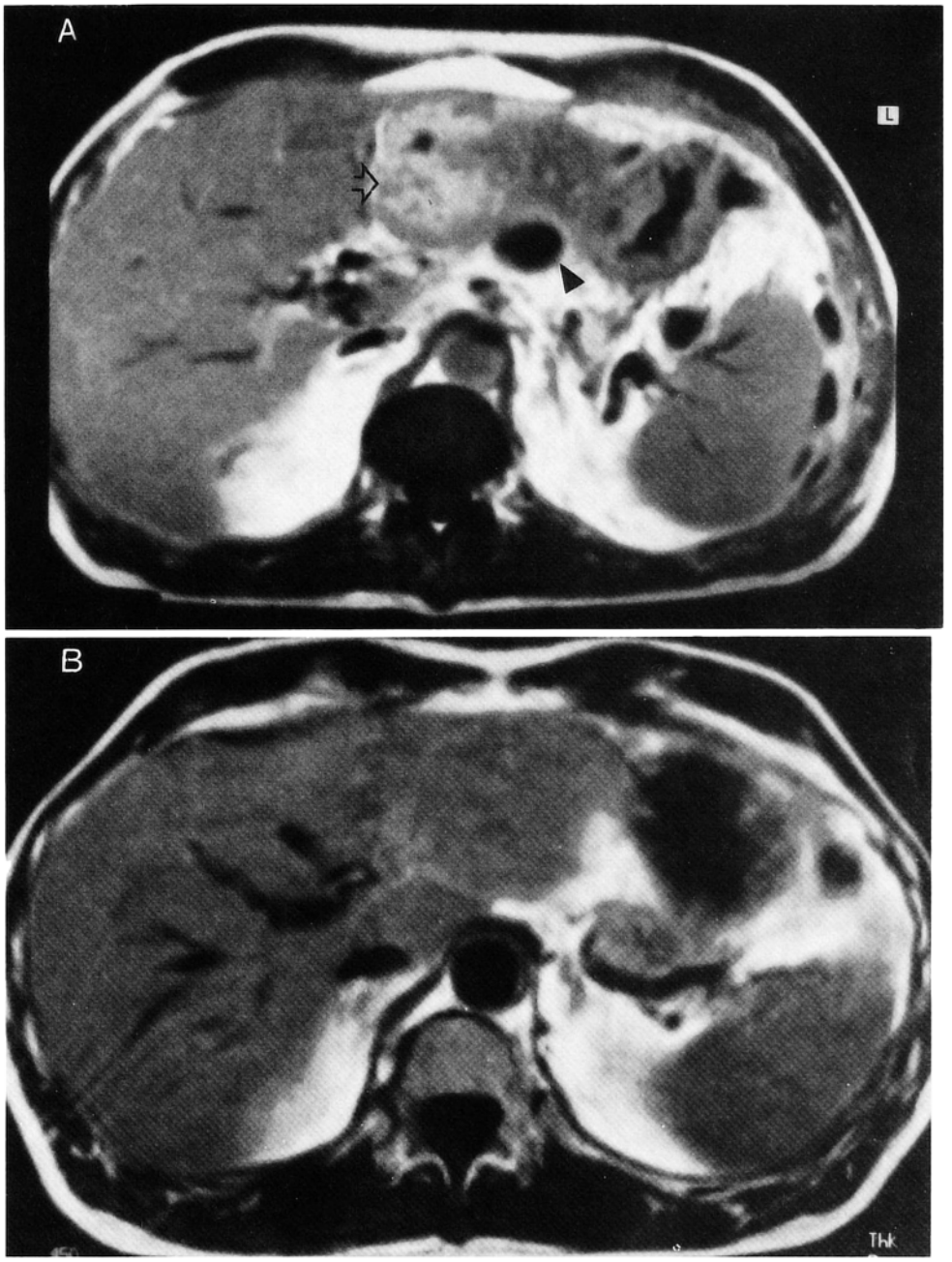

Fig 1. (A) Initial MR imaging (T1 SE weighted sequence after injection) showed a heterogeneous lesion in the left lobe of the liver (white arrow). Hepatic effusion (arrow head). No enhancement of the left portal vein is observed. (B) MR imaging performed two months later showed vanishing of the focal liver lesion.

endoscopy, endoscopic US of the bile duct, and cardiac echography were normal. Colon fiberscopic examination and barium enema showed a diverticular stenosis.

During the following months, the condition responded well to a conservative treatment with metronidazole and cefotaxime for one month, then ceftriaxone alone for another month. Fever disappeared within four days, cholestasis and inflammatory syndrome within one month. Radiological studies, performed one and two months later, showed vanishing of the focal liver tumor and recanalization of the left portal vein (Figure 1B). The patient was completely free of symptoms six months later.

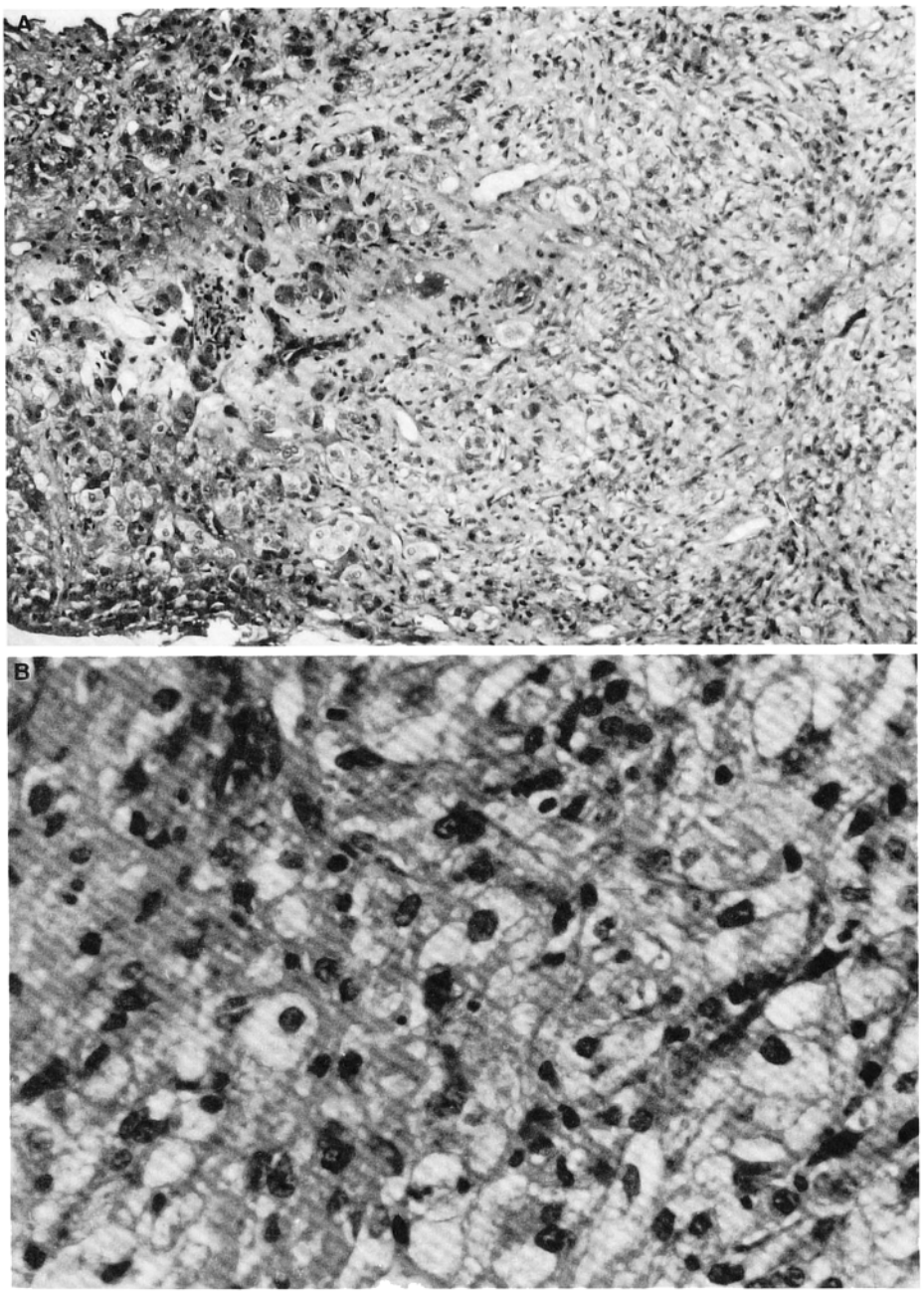

Fig 2. (A) On the left, scattered hepatic cells trapped by fibroblasts and collagenous tissue. In the center, compact clusters of foamy histiocytes with some mononuclear cells and fibroblats (×25). (B) Foamy histiocytes mixed with scattered mononuclear cells (×400).

DISCUSSION

Inflammatory pseudotumors are rare benign diseases which have been mainly reported to occur in the orbit and lung (14). A wide variety of additional anatomic locations have also been described, including gastrointestinal tract, pancreas, heart, brain, ovary, and retroperitoneum. The liver is a rare site, with only 51 reported cases since Pack and Baker's first description in 1953 (9). Liver IPT predominantly affects children, adolescents and young adults with a male-to-female ratio of 3 to 1 (4, 11).

The etiology of liver IPT, as well as the other sites,

remains obscure. Although symptomatology strongly suggest a reactive infectious nature, no microorganisms are found in the majority the tumors (1–5, 9–12), but examination of a few liver IPTs disclosed microorganisms, including parasitic fragments (6), gram-positive cocci (7), *Klebsiella pneumoniae* (8) and *Escherichia coli* (13). Interestingly, luminal obliteration of the portal branch, associated with granulomatous inflammation of the portal margins and filling of the lumen with connective tissue, was found in our patient and several other cases (4, 6, 12). Portal phlebitis and the cellular constitution of the tumor strongly suggest that liver IPT is an atypical tissue response to microorganism infection of the liver parenchyma through the portal vein bloodstream. Most of the reported cases had a possible antecedent cause, for example, travel to the tropics (1, 4, 9), biliary disease (1, 4, 6, 11), or gastrointestinal infection (4, 6). In the present case, initial location of pain and colonic features suggest a relation with the diverticular disease.

Unlike the pulmonary counterpart (14), clinical symptoms of liver IPT are systemic and associated with low-grade fever, abdominal pain, and weight loss (1–12), whereas jaundice is observed only in the case of extrahepatic biliary obstruction (3, 10). Nevertheless, a few asymptomatic liver IPTs were found incidentally at laparotomy (4, 11). Imaging techniques disclose a solid focal liver tumor (1, 2, 4–8, 10–12) most often located in the right lobe of the liver (11). These features being nonspecific, liver IPT is often misdiagnosed as hepatoblastoma in children or liver abscess and hepatocellular carcinoma in adults (1, 3, 4, 6, 7, 9, 11, 12). In the present case, the association of a solid tumor and portal obstruction led to the diagnosis of hepatocellular carcinoma (15). Moreover, hepatic effusion, as shown on initial findings, may be encountered in case of hepatocellular carcinoma rupture. However, collapse of the portal lumen vein without thrombus is evocative of liver IPT, rather than hepatocellular carcinoma (15), providing a diagnostic clue to distinguish between them.

The gross and microscopic appearance of liver IPT is a mass with infiltrating borders. The histologic features of the lesion are characterized by connective tissue which exhibits foamy histiocytes, plasma cells, and variable neutrophils and lymphocytes (1–14). Our immunohistochemistry staining against CD68 clearly established the macrophagic origin of the foamy cells (16). Diagnosis is relatively easy in typical patterns, but a predominant whorl of fibroblasts and fibrosis is often present and may be misinterpreted as fibroma, leiomyoma, or malignant fibrous histiocytoma. Diagnostic difficulties have also been encountered where the presence of immature lymphoid cells led to the diagnosis of lymphoma or anaplastic carcinoma.

The prognosis and treatment of liver IPT remains unclear. The majority of published cases of hepatic IPT were surgically treated with a predominantly favorable outcome (1, 3–5, 11). To our knowledge, 10 patients in the literature (1–5, 10, 12) plus our patient were not treated surgically and only one of them received an antibiotic therapy (4). The outcome was favorable in nine of 11 cases (2, 4, 5, 10) and fatal in two (4). One of the latter had history of liver abscess six months before appearance of hepatic IPT and died during subsequent examinations without receiving antibiotics. The other patient received unspecified antibiotic therapy for a presumed liver abscess and died three months later in ill-defined circumstances. Because of the usually benign course of the disease, we suggest that the treatment should be as conservative as possible. A thorough investigation to identify the cause of liver IPT has to be performed because it could require a specific treatment. Since liver IPT may be an unusual tissue response to liver parenchyma infection through the portal vein bloodstream, antibiotic therapy efficient against gut flora should be used first. Subsequent evolution should be monitored, as in our case, by performance of a CT scan two weeks later and then every month until complete disappearance of the liver lesion. Limited hepatic resection appears to be indicated only when the conservative therapy is inefficient or when the diagnosis remains uncertain.

In conclusion, pseudotumor should be kept in mind in the differential diagnosis of liver masses and needle biopsy should be used. As conservative therapy may be effective, the surgical approach should be limited to cases that do not respond to this therapy.

SUMMARY

Inflammatory pseudotumors (IPT) of the liver are rare benign tumors of unknown origin. Most previously reported cases were initially misdiagnosed and treated surgically; thus, their course under medical treatment remains unclear. We report an additional case of hepatic IPT with a favorable outcome under medical treatment without surgical resection. New imaging and pathologic features of this disease are presented that may facilitate preoperative recognition and appropriate treatment.

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