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INFLAMMATORY PSEUDOTUMOR OF THE LIVER: 3 CASE REPORT AND LITERATURE REVIEW

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ABSTRACT

Inflammatory pseudotumor of the liver (IPTL) is a rare benign lesion characterized by chronic infiltration of inflammotory cells and an areas of fibrosis that sometimes mimics a malignant lesion, first reported by Pack and Baker in 1953. The etiology and pathogy still remain unknown. Clinical and laboratory features are not specific. The treatment attitude is still controversial. We report 3 cases of IPTL who were treated surgically with preoperative diagnosis of ruptured liver abscess or a malignant liver tumor. The postoperative patient was safe and the pathological results were inflammotory pseudotumor of the liver. Conclusion: IPTL is a benign lesion that can be confused with other diagnoses of the liver. The treatment of choice is still surgical resection, and this is especially true for patients with severe symptoms or an indeterminate diagnosis.

Keywords: Inflammatory pseudotumor, the liver, case report

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1. INTRODUCTION

Inflammatory pseudotumors (IPT) is rare lesion and first described in the lung in 1939 [1]. In addition, this type of lesion can be observed in other organs such as: central nervous system, endocrine glands, kidney, liver, ovary, bladder, breast, pancreas, spleen, lymph nodes,… [2]. Inflammatory pseudotumor of the liver (IPTL) is a rare benign lesion characterized by chronic infiltration of inflammotory cells and an areas of fibrosis that sometimes mimics a malignant lesion, first reported by Pack and Baker in 1953 [2]. As of 1998, there were only about 80 cases recorded worldwide [3].

The etiology and pathogy still remain unknown. Clinical and laboratory features are not specific. The differential diagnosis between IPTL and other focal lesions is controversial. Surgery remains the primary option, especially in patients with symptoms or other diagnoses in doubt.

From 06/2022 to 07/2022, at National Hospital of Tropical Diseases, we treated surgically 3 cases of IPTL with preoperative diagnosis not excluding cancerous lesions or abscesses. In this article, we would like to review the literature on the clinical features and management attitude of IPTL in the liver.

2. CASE REPORTS

Case 1

Nguyen Van D, a 48-year-old man, was admitted to the hospital on June 15, 2022 with a high fever (highest temperature 40 degrees), pain in the right hypochondriac region spread to the right shoulder, relief when lying on the side. The abdomen was soft. The liver and spleen were not palpable.

Laboratory findings revealed an elevated WBC count 11.1 x 109/L (71,2% neutrophil); CRP 45.5mg/l. HbsAg (-), HCV (-), HIV (-). Liver, renal function and electrolyte tests were within normal limits. The liver fluke antibody test: Clonorchis (+); Fasciola (+); Toxocara (+); Echinococcus (-). Computed tomography (CT): many foci of hypoattenuation were located at segment VII (5-12HU), uneven and clear boundary, largest dimension of 44x22mm. After contrast injection, masses had borderline enhancement, thick wall, non-enhanced liquefaction center. Chest X-Ray: right pleural effusion. The patient was diagnosed preoperatively with a ruptured liver abscess.

Surgery was performed to resect liver segment 7 and clean the abscess. The abscess ruptured into the right diaphragm but did not perforate the diaphragm. Macroscopic findings: a mass of 12x8x7cm in size; 1cm from the cut area, there was a 6cm mass with soft yellow-gray at the cross-section, ill-defined boundary. It resembles hepatocellular carcinoma. Microscopic findings: about 15% liver fatty degeneration, ill-defined boundary lesions predominantly fibroblasts, chronic inflammatory infiltrates (lymphocytes, plasma cells). The center of lesion contains many fat-eating macrophages, degenerating neutrophils, and neovascularization. No specific inflammation, parasites and malignant cells were found. Conclusion: Inflammatory pseudotumor of the liver. The patient was discharged 7 days after surgery.

Case 2

Ngon Duc T, a 54-year-old man, was admitted to the hospital on May 10, 2022 with an

abdominal distension and pain in the right hypochondriac region. At the National Cancer Hospital, the patient was diagnosed with a left liver tumor/cirrhosis and transferred to National Hospital of Tropical Diseases. On admission to the hospital, the abdomen was soft and the liver was not palpable; the spleen was below the costal margin.

Laboratory findings revealed an elevated WBC count 21.4 x 10^9/L (87.9% neutrophil); CRP 177.60mg/L. HbsAg (-), HCV (-), HIV (-). AFP 2.3ng/mL; PIVKA 46.9ng/mL. Stool culture: C. tropicalis positive. MRI scan: Segment III had a mass of 43x43mm, increased signal on T2W, slightly decreased signal on T1, mild restricted diffusion on DWI. After contrast injection, the mass was relatively uniform in the arterial phase, and washout in the portal venous phase or late phase. MR image conclusions: left liver tumor with the nature of hepatocellular carcinoma.

The patient was indicated for left hepatectomy with preoperative diagnosis of left liver tumor, monitoring for HCC. Macroscopic findings: The left lobe was 20x15x5cm in size, the visceral surface had a 3cm diameter tumor close to the capsule, the capsule had not been ruptured. Microscopic findings: lesions were clustered, clear boundary, mainly rhabdoid cells small nuclei, lymphocytes, plasma cells, centers of many fat-eating macrophages at the center. No hepatocellular and cholangiocarcinoma were found. Conclusion: Inflammatory pseudotumor of the liver. The patient was discharged 8 days after surgery.

Case 3

Hoang Thi N, a 57-year-old woman, was admitted to the hospital on June 2, 2022 with a high fever (39-40 degrees) and pain in the epigastric region. At the National Cancer Hospital, the patient was diagnosed with a suspected HCC on left liver and transferred to National Hospital of Tropical Diseases. On admission to the hospital, the abdomen was soft adn the liver and spleen were not palpable.

Laboratory findings revealed an elevated WBC count 30.8 x 10^9/L (85.2% neutrophil); CRP 239.3mg/l. HbsAg (-), HCV (-), HIV (-), AFP 2.6 ng/mL. The liver fluke antibody test: Clonorchis (unknown); Fasciola (-); Toxocara (-); Echinococcus (-). CT scan: The left liver had a heterogeneous mass of 8x10.5cm. After contrast injection, the central area decreased in density equivalent to fluid density, no enhancement.

After 3 weeks of medical treatment, the mass reduced in size to 4x6 cm. There were many walls inside the mass with ill-defined boundary. Left liver resection due to abscess was indicated after medical treatment with little improvement. Postoperative gross pathology: The left lobe was 12x10x6cm in size; there was an area of size 6x6x6cm with yellow white mixed with soft brown right beyond the liver capsule. Microscopic findings: multifocal fibrous lesions infiltrating chronic inflammatory cells (lymphocytes, plasma cells and macrophages). No specific inflammation, parasites and malignant cells were found. Conclusion: Inflammatory pseudotumor of the liver. The patient was discharged 8 days after surgery.

3. DISCUSSION

IPTL is more common in children and adolescents. In adults, the male/female ratio is from 1/1 to 3.5/1. IPTL is common in non-European populations. The disease is quite rare

and accounts for about 8% of extrapulmonary IPT lesions. Some recent studies show that IPTL accounts for about 0.7% of benign liver lesions [2].

The etiology and pathogenesis of IPTs remain unknown. IPT lesions differ in different IPTs, but IPTL is considered to be closely associated with the hepatitis response. Hypotheses based on infectious agents causing IPTL include: infection, trauma, vascular causes, and autoimmune disorders [2]. Several recent studies have documented some common bacteria in IPTL including: Bacteroides caccae, Actinomyces, Klebsiella, Escherichia coli, Gram-positive cocci, and b-hemolytic Streptococcus [4]. In other studies it has been reported that autoimmune liver diseases such as IgG4-related sclerosing cholangitis may also be the cause of IPTL [4]. Of our 3 cases, case 1 tested for flukes in the blood and was positive for small liver flukes, large liver flukes, dog and cat roundworms; case 3 was positive for small liver fluke and large liver fluke. All 3 were not tested for IgG4.

Based on histopathology, IPT is divided into 3 groups: xanthogranulomatous pseudotumor; plasma cell granuloma; pseudosarcomatous fibromatosis [4]. Macroscopically, the lesions resemble malignant lesions and may exist with one or more lesions at the same time. The largest tumor size recorded was 25cm. Microscopically, IPT is characterized by cylindrical cells, myofibroblasts, and interspersed by inflammatory cells (plasma cells, lymphocytes, macrophages).

Clinical features

The most common manifestations of IPTL are inflammation and infection. Lesions often develop against the background of an abscess or hepatitis. Common clinical symptoms are abdominal pain, fever, and weight loss. IPTL is usually primary with a good prognosis [5]. Clinical symptoms of 3 cases in this report were very diverse, but mainly included high fever (2 cases), abdominal pain in the right hypochondriac region, liver tumor on examination (2 cases). But due to elevated liver enzymes and fever, the patients were transferred to our hospital. Clinical examination did not reveal any cases of liver and spleen enlargement.

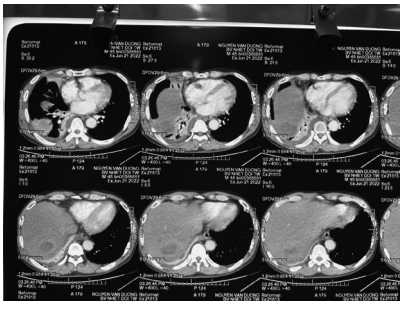
Diagnosis

IPTLs are difficult to diagnose. Ultrasound and CT features are nonspecific and similar to malignancy or liver abscess. On CT scan, the mass is hyperattenuating, accompanied by a hypoechoic margin due to fibrosis, and presents at a late phase similar to liver metastases or cholangiocarcinoma [6]. On MRI, lesions have a decreased signalon T1, average or increased signal on T2 [3]. To confirm the diagnosis of IPT, biopsy and pathology are required.

Contrast-enhanced MRI imaging plays an important role in avoiding missed small lesions and distinguishing between benign and malignant lesions (hepatocellular carcinoma and liver metastases). An important feature for differential diagnosis from angiogenic HCC is not hypervascular on the arterial phase. In cases of non-angiogenic HCC, the following MRI features may help in the differential diagnosis: (1) Peripheral infiltrative lesions in in the delayed phase; (2) septum in the lesion center this is not seen in HCC; (3) deformable and non-massive lesions, and may be associated with several other lesions; (4) isoattenuated lesions on T2WI, but more than 90% of HCC lesions present hyperattenuation on T2WI. Contrast-

enhanced MRI can help differentiate between IPTL and HCC [7]. Peripheral hypoechoic border can easily misdiagnose with liver metastases. Among our 3 patients, there were 2 patients with preoperative diagnosis of ruptured liver abscess, insignificant improvement after medical treatment and 1 case of suspected malignant liver tumor.

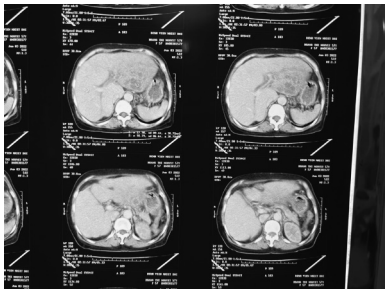
Figure 1: Some diagnostic images of 3 cases



Case 1: Ruptured liver abscess



Case 2: Suspected hepatocellular carcinoma



Case 3: Left liver abscess

Other laboratory tests are also nonspecific in IPTL. Recent studies all agree that it is difficult to distinguish between the diagnosis of IPTL and other localized liver lesions. If atypical liver lesions are found, IPTL may be suggested for diagnosis when this mass is clinically characterized by an inflammatory process: evidence of an existing infection, upper abdominal pain, and/or intermittent fever, presenting with chronic liver disease, hypersplenism, liver dysfunction tests, and non-specific imaging findings. All of our patients had an infection with elevated white blood cells and increased PCR. Especially, there were 2 patients with positive antibody test for Clonorchis and Fasciola.

In clinical and imaging terms, IPTL is easily confused with other liver lesions such as lymphoma, melanoma, hepatocellular carcinoma, liver metastases, tuberculosis or sarcoid disease leading to indicated for surgical treatment [2].

Liver biopsies have an important role in the in definitively diagnosing and determining the origin of liver metastases, but are controversial because of possible risks in cases of malignancy-like lesions. The main histopathological features are the presence of cytoskeleton, plasma cells, macrophages, and lymphocytes without multiple irregular nuclei [8]. Biopsy is not necessary if hepatectomy including lesions is indicated. Unfortunately, none of our 3 patients had preoperative biopsies. But in many studies, it has been shown that if the biopsy is negative, do we question surgery or continue medical treatment and follow-up.

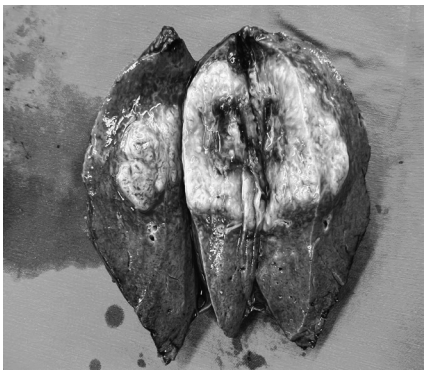
Treatment

Treatment options are still controversial. IPTLs are benign lesion. The effectiveness of medical or surgical treatment has not been clearly proven because the number of patients is not large enough.

The goal of treatment is radical. Different treatment options have similar prognosis. Some patients are treated with antibiotics and corticosteroids, but the lesions remain

unchanged. In contrast, several studies have reported that liver resection was performed, mainly because of suspected malignancy based on preoperative imaging. After surgery, the tumor did not recur [8]. All 3 of our patients had a favorable surgery, stable postoperatively. Re-examination after 1 month did not detect postoperative complications.

Figure 2: Macroscopic image of liver lesions



Case 1: Ruptured liver abscess



Case 2: Suspected hepatocellular carcinoma



Case 3: Left liver abscess

In addition, there are some reports that IPTL can be reduced on its own or with antibiotic treatment. But surgical treatment remains the method of choice after medical therapy fails, especially in patients with severe symptoms or an unspecified diagnosis. In the last 20 years, hepatectomy has become increasingly safe in non-cirrhotic patients with almost 0% mortality. Therefore, the treatment of choice in these cases is surgical resection of the liver with lesions [8]. This option reduces biopsy complications (malignant cell spread) and eliminates the possibility of IPTL recurrence. However, this treatment option has not yet been fully agreed upon by clinicians.

4. CONCLUSION

IPTL are rare benign lesions. Differential diagnosis from other liver lesions is important. IPTL may resolve spontaneously and may be confused with other tumors of the liver. Surgery remains the primary option, especially in patients with symptoms or other diagnoses in doubt.

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