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EDITORIAL

Hepatic pseudotumor: A diagnostic challenge

Arghya Samanta, Moinak Sen Sarma

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Abstract

Hepatic pseudotumors are rare lesions of unknown origin, characterized by the proliferation of fibrous connective tissue and inflammatory cell infiltrates. They mimic malignant lesions clinically, and radiologically, given their non-specific clinical and imaging features. The pathophysiology of hepatic pseudotumor is incompletely understood and there are no standardized criteria for diagnosis. Pseudotumors have been reported to develop in various organs in the body with the lung and liver being the most common site. Hepatic pseudotumors develop in patients with underlying triggers of liver inflammation and injury, including infections, autoimmune liver diseases, bile duct injury, or surgery. Hepatic pseudotumors respond well to conservative treatment with antibiotics, and steroids and some may regress spontaneously, thus avoiding unnecessary resection. This condition is rewarding to treat. It is important to recognize pseudotumor as a distinct clinical entity and include it in the differential of liver masses with atypical imaging features.

Key Words: Hepatic pseudotumor; Infection; Stroglyloides; Hepatic resection

Core Tip: Hepatic pseudotumors may mimic malignant lesions clinically and radiologically and often result in unnecessary invasive procedures. Both clinicians and pathologists should consider this differential in patients with hepatic mass lesions, especially if the patient has a clinical history of infection or injury of the biliary tree and/or hepatic parenchyma.

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INTRODUCTION

The term "pseudotumor" describes a heterogeneous group of benign, non-neoplastic, non-metastasizing masses that can involve many organs[1]. This entity has been described by several names and histologic presentations. In 1954, Umiker and Iverson coined the term "inflammatory pseudotumor" as the clinical and imaging findings of the lesion mimic those of malignant tumors[2]. Pseudotumor is characterized by the presence of myofibroblastic spindle cells, infiltrated plasma cells, and mixed inflammatory cells without atypical mitoses or anaplasia[3,4]. The lesions are known to have extensive variability in histologic features, and no uniform criteria have been recommended for diagnosis and classification[5,6]. The most commonly involved organ is the lung followed by the liver, central nervous system, major salivary glands, kidney, omentum, ovary, larynx, urinary bladder, breast, pancreas, spleen, lymph nodes, skin, soft tissues, orbit *etc*[7]. In this editorial, we discuss the etiopathogenesis, differentiating radiological and histological features of this unique disease entity and currently available treatment modalities.

ETIOPATHOGENESIS OF HEPATIC PSEUDOTUMOR

An inflammatory pseudotumor of the liver is an uncommon, benign, tumor-like lesion that clinically, radiologically, and histologically mimics a malignant tumor, particularly hepatocellular carcinoma, cholangiocarcinoma, or metastatic tumors[8]. Tang *et al*[9] found that these lesions were more common in men than women and most common in young adults. The most frequent presenting symptom is abdominal pain, followed by fever[9]. Biliary obstruction or portal hypertension may also be present. The pathogenesis of hepatic pseudotumor is poorly understood but it has been associated with infection, autoimmune liver disease, or recent trauma or surgery of the liver[10-12]. In the majority of cases, these inflammatory pseudotumors are infectious in origin[12]. *Mycobacterium tuberculosis*, Brucella, Strongyloides, Bartonella, syphilis, Candida, and Actinomyces have been reported as causative agents[13,14].

The lesions often appear to develop from a healing abscess or an inflammatory condition resulting from rupture of the bile duct and extravasation of bile into the tissue, which provokes a xanthogranulomatous inflammatory response that heals with scarring.

RADIOLOGICAL FEATURES OF HEPATIC PSEUDOTUMORS

Imaging studies of hepatic pseudotumors have revealed non-specific findings. Abdominal ultrasound shows variable echogenicity. Both hypoechoic, as well as hyperechoic lesions have been reported[7]. Computed tomography angiography of the abdomen shows hypoattenuating hepatic lesions, which show a hypodense peripheral halo with no significant enhancement on contrast images[15]. In contrast, hepatocellular carcinoma shows arterial phase hyperenhancement with rapid washout in the venous phase. On magnetic resonance imaging, hepatic pseudotumors are typically hypointense on T1-weighted images and hyperintense on T2-weighted images, with variable enhancement patterns[16].

HISTOPATHOLOGICAL FEATURES AND DIAGNOSTIC DILEMMA

Given the lack of uniform diagnostic criteria for diagnosing inflammatory pseudotumors, it is difficult to obtain clear data from the literature regarding the incidence, anatomic distribution, natural history, and malignant potential of these lesions. Not surprisingly, this difficulty has an impact on the understanding of the natural history of this condition as well as its prognosis and treatment.

No specific biomarker is available for diagnosing pseudotumors. A definitive diagnosis of inflammatory pseudotumor can be made *via* needle biopsy findings and, occasionally, fine-needle aspiration. It is well recognized that inflammatory pseudotumors have a wide variability in histologic features that may be reflected in different areas of the same lesion. Therefore, adequate sampling in multiple sections is essential for establishing an accurate diagnosis. Histological classification of hepatic pseudotumor has not been well established. Balabaud *et al*[1] conducted a study of 145 cases of liver pseudotumor and identified 5 histologic subgroups: a plasma cell–rich with discrete or diffuse lymphocytes, mixed inflammatory cell, granulomatous, granulomatous with eosinophils, and a predominantly purulent type. Although 2 of these 145 cases showed focally increased IgG4-positive plasma cells, these did not meet the currently accepted diagnostic criteria as too few plasma cells were observed in the tissue and none of the patients had elevated serum levels of IgG4[17,18]. A liver biopsy is recommended to avoid unnecessary liver resection.

TREATMENT: LESS IS MORE

It is common practice to excise a resectable liver tumor in the absence of a definitive diagnosis. However, if a preoperative diagnosis of pseudotumor can be made, there is no reason to advocate hepatic resection, as rightfully noted by Rosa *et al*[19]. Antibiotic treatment may be curative in infective cases, and hepatic resection can be avoided, as reported by Gialanella *et al*[20] and others[21]. Corticosteroids and non-steroidal anti-inflammatory drugs have been successfully

used in some cases[15,22-24]. If the patient presents with biliary obstruction, biliary stents may be placed[25]. Occasionally, the pseudotumor spontaneously regresses[20,26].

In this issue, Gialanella *et al*[20] presented the case of a 45-year-old female with tender hepatomegaly, who was diagnosed with a hepatic pseudotumor with the help of imaging and serology. The lesion resolved completely following treatment with an antihelminthic agent for 2 wk. The case report by Gialanella *et al*[20] is a good example of the necessity to consider the diagnosis of hepatic pseudotumor if an atypical mass is found in the liver with non-specific clinical and imaging features.

FUTURE DIRECTIONS

Given its rarity, more data should be collected to better classify pseudotumors and further understand their natural history; speci-fic areas of future research should involve culturing the infectious agents, testing for aberrant expression of anaplastic lymphoma kinase-1 and its gene translocation, and testing for the expression of IgG4-positive plasma cells. Further research is needed to determine which clinical settings warrant increased suspicion for this diagnosis.

CONCLUSION

Hepatic pseudotumor is a rare, benign space-occupying lesion of the liver with non-specific clinical and radiological features that pose diagnostic challenges. This entity remains a diagnosis of exclusion without any definitive diagnostic criteria. Despite its rarity, pseudotumor should be considered in the diagnosis of focal hepatic space-occupying lesions with atypical/non-specific radiological features, especially in the setting of co-existing inflammatory conditions or infection of the liver. Histopathological diagnosis of these conditions is crucial to avoid unnecessary surgical intervention.

FOOTNOTES

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