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Single Case

Spontaneous Resolution of IgG4-Related Hepatic Inflammatory Pseudotumor Mimicking Malignancy

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Keywords

Inflammatory pseudotumor · IgG4-related diseases · Lymphoplasmacytic infiltrate · Storiform fibrosis · HIV-positive patient

Abstract

Hepatic inflammatory pseudotumor (IPT) is characterized by a well-circumscribed benign tumor mimicking or often mistaken for a malignant lesion. A 48-year-old male presented to the hospital with complaints of epigastric pain, with initial laboratory findings showing mildly elevated alkaline phosphatase (140 U/L) with normal AST, ALT, bilirubin, and lipase, a CD4 count of 384, and an HIV viral load of >10 million copies. The total IgG level was elevated to 2,228 mg/dL (normal IgG4 level 114 mg/dL). Contrast-enhanced MRI of the abdomen showed heterogeneous mass-like infiltration in the right lobe of the liver measuring 9.6 cm. The liver mass was biopsied which showed dense collagenous fibrosis with abundant lymphoplasmacytic infiltrates with 18 IgG4-positive plasma cells per high-power field. The patient was not given any treatment for this IPT. For more than 1 year of follow-up triple-phase CT scan of the liver was repeated, which showed no liver mass. As radiological images of hepatic IPTs, including IgG4-

related hepatic IPT, mimic liver malignancy, histological analysis of the biopsy remains the cornerstone for the diagnosis. Symptomatic patients with IgG4-related hepatic IPT have shown improvement with corticosteroid use; however, spontaneous resolution has also been reported like in the present case.

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Introduction

Inflammatory pseudotumor (IPT) was initially observed in the lung in the 1930s with its quasi-neoplastic characteristics of tumor-like masses consisting of inflammatory and myofibroblastic spindle cells [1, 2]. In a large pathological series of 84 extrapulmonary IPTs, Coffin et al. [3] reported that approximately 8% were located in the liver. Now hepatic IPT is a well-known entity; however, IgG4-related hepatic IPT is rare. From our review of the literature, we present the first case of IgG4-related hepatic IPT in a human immunodeficiency virus (HIV)-positive patient, in whom the mass spontaneously regressed without any intervention.

Case Presentation

A 48-year-old Hispanic male presented to the emergency department with a chief complaint of epigastric pain. Two days prior to the presentation, the patient had started to experience epigastric pain, non-radiating, associated with three episodes of non-bloody emesis. His medical history includes hypertension, diabetes mellitus type 2, and gallstone pancreatitis complicated with pseudo-cyst, which had been drained via cyst-gastrostomy 4 years prior to this presentation. On admission, his home medication included enalapril and insulin. Vital signs were within normal limits and physical examination showed mild epigastric tenderness. Laboratory findings showed a mildly elevated alkaline phosphatase level (140 U/L) with normal AST, ALT, total bilirubin, indirect bilirubin, and lipase. [Table 1](#) provides additional laboratory data on admission. The patient had a history of high-risk sexual behavior; therefore, an HIV profile was ordered that turned out to be positive. Additional laboratory data revealed: cluster of differentiation 4 count of 384, HIV viral load of >10 million copies, total immunoglobulin G (IgG) 2,228 mg/dL, and IgG4 114 mg/dL. Contrast-enhanced computed tomography (CT) scan of the abdomen showed a questionable necrotic mass that was followed with magnetic resonance imaging (MRI) of the abdomen showing heterogeneous mass-like infiltration in the right lobe of the liver, measuring 9.6 cm and focal fibrosis in the head of the pancreas with dilatation of the pancreatic duct in the body and the tail of the pancreas ([Fig. 1](#)). The liver mass was biopsied for which the pathology described dense collagenous fibrosis with abundant lymphoplasmacytic infiltrate ([Fig. 2a](#)). IgG4 immunostaining of the biopsy specimen revealed 18 positive plasma cells per high-power field ([Fig. 2b](#)). Endoscopic ultrasound showed pancreatic calcifications with no pancreatic tumor. The patient's pain was attributed to chronic pancreatitis. It improved over the course of hospitalization, and therefore he was discharged home. The patient was recommended to be followed up in the affiliated clinic; however, he was lost to follow-up. A year after discharge, the patient was followed up and had a triple-phase CT scan of the liver, which did not show the previous liver mass. Taking

into consideration the diagnostic modalities, histological finding and spontaneous regression, the final diagnosis of IgG4 hepatic IPT was made.

Discussion

Hepatic IPT is characterized by a well-circumscribed benign tumor predominantly in the right lobe of the liver mimicking or often mistaken for a malignant lesion requiring invasive interventions. The etiology and pathogenesis of IPT remains unknown; however, possible etiologies have been reported including infections, trauma, vascular causes, gallstones, congenital diseases, chronic biliary inflammation, and autoimmune disorders such as IgG4-related disease (IgG4-RD) [4–8]. Hepatic IPTs have been increasingly recognized in Asian countries in recent years [9]. In 2007, Zen et al. [10] proposed a classification of hepatic IPT into two major types based on clinical and histological features: fibrohistiocytic and lymphoplasmacytic. The fibrohistiocytic IPT type was characterized by xanthogranulomatous inflammation, multinucleated giant cells, and neutrophilic infiltration, while the lymphoplasmacytic IPT type has features of the inflammatory neoplastic process with infiltration of lymphocyte cells and IgG4-positive plasma cells. IgG4-related hepatic IPTs fall under the lymphoplasmacytic type of IPTs. IgG4-RD is defined as a fibroinflammatory condition characterized by tumefactive lesions, dense lymphoplasmacytic infiltrate, storiform fibrosis, rich in IgG4-positive plasma cells with or without elevation of serum IgG4 levels [11]. Like IPT, IgG4-RD has been described affecting almost every organ system including the liver, with strikingly consistent histological features denoting to be a systemic disease. In the consensus guidelines, serum IgG4 (>135 mg/dL) was bundled as part of the diagnostic criteria for IgG4-RD as the marker of the disease, although its utility remains inconclusive as 40% of histologically diagnosed IgG4-RD cases had normal serum IgG4 [11–14]. As radiological images of hepatic IPT including IgG4-related hepatic IPT mimic liver malignancy, histological analysis of the biopsy remains the cornerstone for the diagnosis [10, 11]. In 2012, Deshpande et al. [11] proposed a set of guidelines on histopathological features for the diagnosis of IgG4-RD for different organs. Although there is no guideline on the clinical characteristics of IgG4-related hepatic IPT, as per the consensus guideline for histopathology, liver tissue should have dense lymphoplasmacytic infiltrate with IgG4 infiltrate (>10 cells per high-power field), storiform fibrosis, and obliterative phlebitis [11]. A recent systemic review of hepatic IPT revealed only 10 patients with IgG4-related hepatic IPT with a mean age of 60.8 years, a higher predilection in males, and a mean size of the tumor of 2.76 cm [12]. Symptomatic patients with IgG4-related hepatic IPT have shown improvement with corticosteroid use, which remains the first-line therapy with a recommended dose of 0.6 mg/kg of body weight per day for 2–4 weeks, and subsequently tapered over 3–6 months [9, 11–14]. Clinicians should be cautious about the use of corticosteroids in patient with diabetes as there is a risk of hepatic abscess while treating IgG4-related hepatic IPT with corticosteroids [15]. There are numerous case reports of hepatic IPT without IgG4-RD having undergone spontaneous regression of the mass and resolution of symptoms [15, 16]. Chougule and Bal [12] reported only 1 patient with IgG4-related hepatic IPT who had spontaneous resolution upon follow-up. These findings suggest that watchful waiting could be a sensible option in some cases; however, the ultimate management decision should rest on the clinician's evaluation. Previously, there was only one case reported

of hepatic fibrohistiocytic type IPT in a HIV-positive patient [17]. We report the first case of IgG4-related hepatic IPT in an HIV-positive patient with spontaneous resolution of the tumor and symptoms. Our case report explains the importance to include IgG4-related hepatic IPT as part of the differential diagnosis of any liver lesion seen on imaging study.

Statement of Ethics

The patient gave permission to publish his case.

Disclosure Statement

There are no conflicts of interest.

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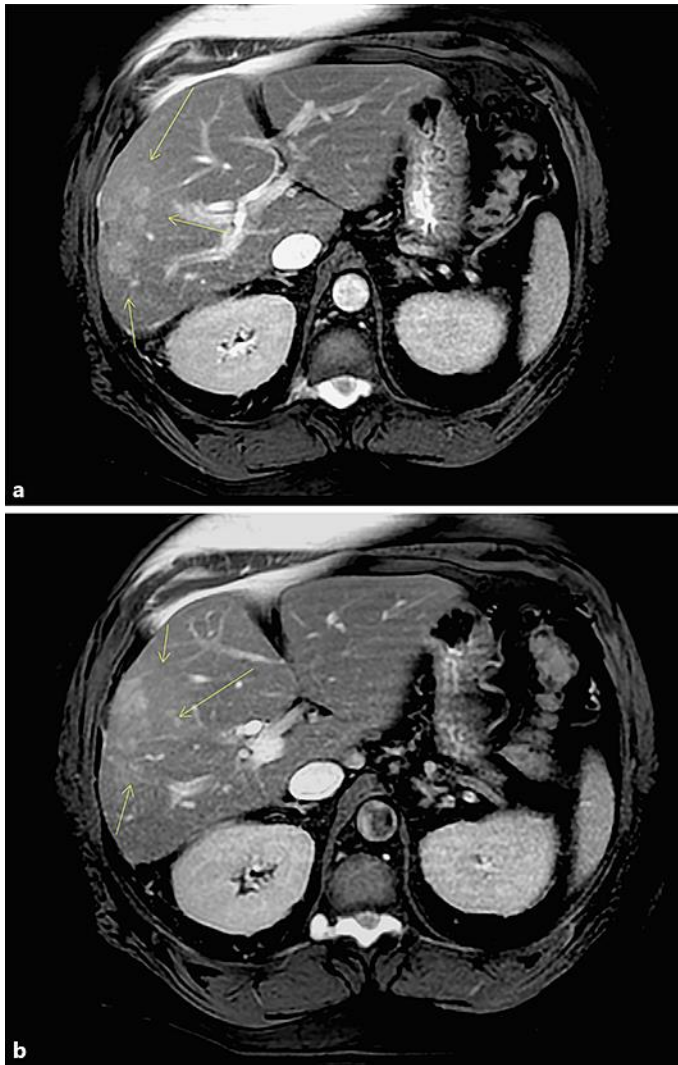


Fig. 1. a, b MRI of the abdomen showing a heterogenous, irregularly shaped mass infiltrating the right lobe of the liver, measuring 9.6 cm (yellow arrows).

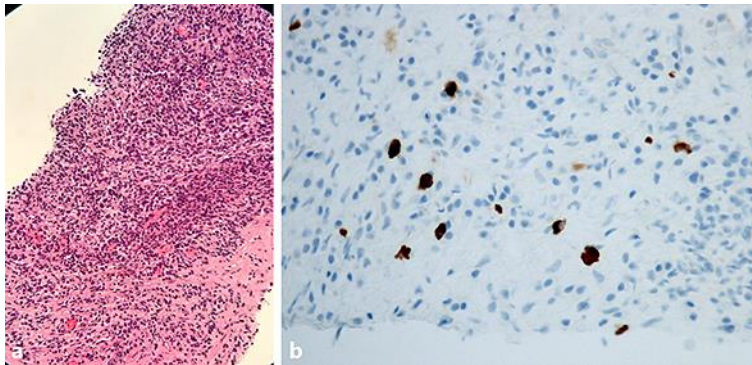


Fig. 2. Histological images of hepatic biopsy stained by hematoxylin and eosin. **a** Abundant lymphoplasmacytic reaction with dense collagenous fibrosis. **b** Immunostaining showing IgG4 infiltrating the tissue and 18 positive plasma cells per high-power field.

Table 1. Laboratory data on admission

Variable	Value on admission	Normal range
Lipase, U/L	12	11–82
Alkaline phosphatase, U/L	140	34–104
Alanine aminotransferase, U/L	19	7–52
Aspartate aminotransferase, U/L	26	13–39
Total bilirubin, mg/dL	0.5	0.3–1.1
Direct bilirubin, mg/dL	0.1	0–0.3
Total IgG4, mg/dL	2,228	700–1,600
IgG4, mg/dL	114	1–291