CASE REPORT

IgG4-related inflammatory pseudotumour mimicking a hepatic abscess impending rupture

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SUMMARY

A 50-year-old man presenting with sudden onset right upper quadrant pain and no constitutional symptoms was found to have two necrotic liver masses on imaging, consistent with hepatic abscesses unresponsive to systemic antibiotics and percutaneous drainage. The patient deteriorated and developed symptoms consistent with impending rupture. He therefore subsequently underwent right hepatic segmentectomy. All cultures were negative and histopathology confirmed IgG4 related disease/inflammatory pseudotumour of the liver. Postoperatively, the patient was asymptomatic with no IgG4 disease activity in other organs.

BACKGROUND

Immunoglobulin G4-related disease (IgG4-RD) is a relatively newly recognised fibroinflammatory condition histopathologically characterised by tumefactive lesions, dense lymphoplasmacytic infiltrate with abundance of IgG4 positive plasma cells, storiform fibrosis and obliterative phlebitis. IgG4-RD affects virtually every organ system, often in association with autoimmune pancreatitis. It commonly presents as sclerosing cholangitis (SC), inflammatory pseudotumor (IPT) or chronic active hepatitis. Our focus will be on the unique presentation of IgG4-related IPT (IgG4-IPT) of the liver. These disease entities present with an array of clinical manifestations, however, common histopathological findings, elevated serum and tissue levels of IgG4, and demonstration of a response to corticosteroids helps researchers in classifying these diseases under a common umbrella of IgG4-RD.

CASE PRESENTATION

A 50-year-old man presented to the emergency department with a 1-week history of right upper quadrant abdominal pain and anorexia. The pain was sharp and stabbing, non-radiating with no aggravating factors and not associated with nausea, vomiting or other gastrointestinal symptoms. There were no constitutional symptoms such as fever, weight loss and night sweats. There was no history of recent sick contacts, incarceration, intravenous drug abuse or travel to tuberculosis endemic countries. The patient had similar symptoms 1-month prior; he was hospitalised and found to have a liver mass concerning for a liver abscess, but the patient left against medical advice and was subsequently lost to follow-up. His family history was non-contributory. On physical examination, he was tachycardic (110 bpm), and had a low-grade fever (37.8°C) with stable blood pressure. He exhibited

epigastric and right upper quadrant tenderness to palpation, with marked hepatomegaly (liver span 16–18 cm). The rest of his physical examination was unremarkable.

INVESTIGATIONS

Laboratory testing revealed evidence of leucocytosis with neutrophilic predominance, whereas other tests including alkaline phosphatase, bilirubin, alanine aminotransferase, aspartate aminotransferase, amylase and lipase were all within normal limits. An abdominal ultrasound (day 1 of hospital admission) was performed initially, which revealed two liver masses within the right lobe of the liver. The first mass, measuring 6.6×4.5×4.0 cm and having a heterogeneous appearance, was located in the inferoposterior segment of the liver; the other was 2.3×2.3 cm, with a similar appearance, and was located in the anterosuperior segment of the right lobe. The gallbladder and biliary system were unremarkable. Subsequent abdominal CT scan (day 1 of hospital admission) was performed, and confirmed the above findings, with a thrombus in the hepatic veins (figure 1).

DIFFERENTIAL DIAGNOSIS

Owing to the above presentation, a concern for multifocal necrotic hepatic abscesses with a septic thrombus in the hepatic vein was raised; however, an underlying malignancy could not be completely ruled out. Therefore, a decision was made to send the patient for ultrasound-guided aspiration and to biopsy (day 2) the liver masses. The aspiration demonstrated 45 cc of green purulent material, which was sent for cytological analysis and cultures. A pigtail catheter was placed in the abscess for further drainage. Meanwhile, the patient was started on broad-spectrum antibiotics with

Figure 1 Sagittal section of CT of the abdomen with intravenous and oral contrast showing a heterogeneous mass in the right hepatic lobe.

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anaerobic coverage while awaiting the results of fluid analysis and pathology.

TREATMENT

During the hospital stay, on day 4 of hospital admission (post-operative day 2), the patient developed a high-grade fever (39.8°C), worsening right upper quadrant pain, and his white cell count was trending upwards. The catheter had minimal output hence repeat imaging (day 4 of hospital admission) was performed, which revealed reaccumulation of the abscess and a new subcapsular extension, raising concern for an impending hepatic rupture (figures 2 and 3). The patient was immediately taken to the operating room for a liver resection of the mass.

OUTCOME AND FOLLOW-UP

Grossly, a 6.5×4×3 cm subcapsular haemorrhagic mass was identified with three additional satellite nodules 0.4–0.8 cm in greatest dimension. Histologically, the mass was a confluence of mass-like nodules rich in plasma cells and other inflammatory components, including macrophages and myofibroblasts (figure 4). No epithelial elements were demonstrated histologically or with cytokeratin immunostains. Anaplastic lymphoma kinase (ALK) immunostain was negative in myofibroblasts, and IgG4 immunostain was positive in numerous plasma cells (figure 5). A diagnosis of IgG4-IPT was rendered. The patient tolerated the procedure well and remained asymptomatic during the rest of the hospital course; his antibiotics were deescalated to oral antibiotics. The cultures, including blood and aspirated fluid from the abscess, and from the liver tissue, were sterile. The patient had no residual disease or symptoms after surgery so was not started on immunosuppression.

DISCUSSION

IgG4-RD is a newly recognised fibroinflammatory condition that affects multiple organs; it has a specific histopathological picture with or without elevation of serum IgG4 levels. IgG4-RD involving the liver and biliary tree exhibits variable morphological changes. It is classified into SC, hepatic IPT or chronic active hepatitis.

IPTs are rare well-circumscribed benign tumour-like masses occurring throughout the body, with the most common site being the lung. Other documented sites include the central nervous system, major salivary glands, kidney, liver, omentum, ovary, larynx, bladder, breast, pancreas, spleen, lymph nodes, skin, soft tissues and the orbit.¹ Hepatic IPT is rare, and was first described by Pack and Baker in 1953.² In a large series of 84 extrapulmonary IPTs reported by Coffin *et al*,³ 7 (8%) were

Figure 2 Coronal sections of CT of the abdomen demonstrating an interval increase in the size of the irregular heterogeneous mass in the inferior aspect of the right hepatic lobe.

Figure 3 Sagittal sections of CT of the abdomen showing an interval increase in the size of the hepatic mass. The inferior aspect of the right hepatic lobe demonstrates a subcapsular and extracapsular extension suggestive of impending liver rupture.

located in the liver. Although the aetiology and pathogenesis is not well understood, it has been suggested that bacterial or viral infections, as well as autoimmune reactions, may play a role in the development of some hepatic IPTs.

Hepatic IPT is often mistaken for a primary malignant tumour of the liver, leading to more radical and invasive procedures. The concept of IgG4-RD that has been proposed by Kamisawa *et al*⁴ has caused more cases of hepatic IPT being identified as IgG4-RD. Zen *et al*⁵ classified hepatic IPT into two major subtypes based on histological features, namely, lymphoplasmacytic and fibrohistiocytic types. The lymphoplasmacytic type was defined by an inflammatory process, mainly involving lymphoplasmacytic infiltration and corresponded to IgG4-RD. The fibrohistiocytic type was defined as having abundant histiocytic infiltration involving foamy cells or multinucleated giant cells. The two distinct types of IPT proposed by Zen *et al* were not only different with regard to their histopathological findings, but also in their clinical presentations. The lymphoplasmacytic type predominantly involved males with an average age of 67 years, mostly presenting with liver dysfunction on laboratory testing, as opposed to subjective symptoms with the fibrohistiocytic type. IgG4-IPT is distinct from IPT/inflammatory myofibroblastic tumour of soft tissue, due to the former's strong

Figure 4 Tissue sections from the resected liver mass demonstrate a confluence of tumour-like areas rich in myofibroblasts, macrophages and plasma cells (H&E; ×400).

Figure 5 The plasma cells demonstrate strong positivity for IgG4 (immunoperoxidase; ×400).

expression of IgG4 positive plasma cells and the latter's expression of ALK protein in spindle cells by immunohistochemistry.

The diagnosis of IgG4-IPT represents a challenge to the treating physician, due to multiple disease conditions with a similar clinical picture, and marked difference in the treatment and prognosis. Usually, laboratory findings in IPT are subtle, but, occasionally, mildly elevated alkaline phosphatase levels with normal bilirubin are not an uncommon finding in these patients. Other laboratory abnormalities commonly seen are high serum IgG4 levels; levels >182 mg/dL indicate significant IgG4-RD activity. Imaging findings of hepatic IPT are non-specific. They can manifest as a single or multifocal mass. On ultrasound images, they appear as hypoechoic or hyperechoic masses with increase through transmission and septation.⁶ On unenhanced CT images, they are low in attenuation relative to the surrounding liver. Contrast-enhanced imaging shows several patterns of enhancement.⁷ On MRI, these lesions are usually T1 hypointense and T2 hyperintense with heterogeneous enhancement.^{8,9} Furthermore, needle biopsy findings may not be sufficient for diagnosis, and resection may be required. Histopathological analysis of biopsy specimens remains the cornerstone for the diagnosis of IgG4-RD in general, demonstrating a dense lymphoplasmacytic infiltrate that is organised in a storiform pattern, obliterative phlebitis and mild-to-moderate eosinophil infiltrate with positive IgG4 plasma cells demonstrated on tissue sections.

The major differential diagnoses of IgG4-IPT include lymphomas, hepatic abscesses and other malignancies such as hepatocellular carcinoma and metastatic disease. The closest histopathological mimickers of IgG4-RD in general are lymphomas. An early clue to the diagnosis of B-cell lymphoma is the presence of a predominantly B-cell infiltrate without isolated IgG4 deposits.

All symptomatic patients should be treated. The indications, dosing and duration of therapy are not fully understood; at this time, most recommendations are from case reports. Patients should be offered a 2–4-week course of prednisone therapy followed by a prednisone taper. Patients who have failed to respond to prednisone therapy, or who have side effects from the latter, could benefit from B-cell depletion with rituximab, based on several case reports.^{10–12}

Our case was a diagnostic dilemma, as the clinical presentation suggested an infectious aetiology, whereas imaging supported a neoplastic process and a complicated clinical course

including post-drainage deterioration of the patient and impending rupture resulting in radical treatment. Hence, keeping IgG4-IPT in the differential diagnosis of unusual liver masses with complex presentation can decrease mortality and morbidity as a result of invasive procedures.

Learning points

- ▶ Hepatic inflammatory pseudotumor (IPT) is a part of the spectrum of immunoglobulin G4-related disease (IgG4-RD).
- ▶ IgG4-IPT has become a fourth distinct clinical entity of IgG4-RD.
- ▶ Imaging findings of IPT of the liver are non-specific. They can manifest as a single or multifocal mass that can be confused with lymphomas, tumour, malignancy or abscess.
- ▶ Histopathological analysis of biopsy specimens remains the cornerstone in the diagnosis of IPT. IPT should be carefully diagnosed based on a combination of characteristic clinical, serological, morphological and histopathological features after tissue biopsy, and ruling out other close differential diagnoses.
- ▶ Patients should be offered a 2–4-week course of prednisone therapy followed by a prednisone taper. The role of other immunosuppressive therapy is not yet established.

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