Infarcted Giant Liver Hemangioma Presenting with Signs of Acute Inflammation

Sherif Saadeh, Kevin D. Mullen, William Carey, David Barnes, Mark Baker, Terry Gramlich, and David Vogt

Liver hemangioma is generally benign and asymptomatic. In this case report, we describe a patient who presented with giant liver hemangioma (GLH) and signs of acute inflammation. The patient had a 3-month history of right upper quadrant pain, fever, and abnormal liver enzymes. Imaging studies revealed GLH, and careful workup ruled out infectious etiology and malignancy. After surgical resection, the patient’s symptoms disappeared and biochemical markers returned to normal. Histological examination revealed GLH with extensive necrosis and thrombosis. Clinicians should consider in their differential diagnosis that GLH, while usually silent, may present with acute inflammatory symptoms and abnormal liver enzymes. Surgical resection is curative.

INTRODUCTION

Liver hemangioma is the most common benign tumor of the liver (1–6). It is composed of cavities lined with endothelial cells and filled with blood (4). Giant liver hemangioma (GLH) is defined as a lesion greater than 4 cm in diameter (1). Most cases with liver hemangioma are asymptomatic and discovered incidentally on a liver ultrasound or computed tomography scan (2–4). Most patients with liver hemangioma have normal liver function tests (1,3–6). Infrequently, patients may complain of abdominal pain. There are few reported cases in the literature of patients with GLH who present with a triad of right upper quadrant abdominal pain, fever, and abnormal liver enzymes (3–6). After careful workup, these cases had no evidence of infection, malignancy, or other causes of acute inflammation. Biochemical and clinical manifestations disappeared after surgical resection. We describe a patient with infarcted GLH presenting with the same triad of signs and symptoms, which normalized after surgical resection.
CASE REPORT

A 47-year old male was referred to the Cleveland Clinic Foundation from outside hospital with 3-months history of right upper quadrant pain, fever, and persistently elevated levels of alkaline phosphatase and γ-glutamyltransferase. During his previous hospitalization, a laparoscopic cholecystectomy was performed but failed to resolve his symptoms; the intraoperative cholangiogram was negative. Post-operatively, the patient remained febrile, and multiple repeated blood cultures were negative for organisms. An endoscopic retrograde cholangiopancreatography (ERCP) revealed mild biliary leak for which a stent was placed. Pathologic evaluation of surgical specimen was inconclusive and tissue from gall bladder revealed candidal fungal growth. Intravenous amphotericin was given for 18 days. In spite of the above management, the patient had persistent fluctuating fever, abdominal pain and elevated liver enzyme levels. At this point, he was transferred to the Cleveland Clinic.

On admission, the patient had a temperature of 38°C and the liver was palpable at the right costal margin. Otherwise, he had no stigmata of chronic liver disease. Laboratory workup revealed a normal white blood cell count, hemoglobin level, platelet count, kidney function, prothrombin time, α-fetoprotein level, and serum bilirubin. Serum alkaline phosphatase was 2–11 times and γ-glutamyltransferase 2–7 times the upper limit of normal. Bacterial, fungal, and amebic cultures were all negative.

Computed tomography (CT) of the abdomen (Fig. 1) showed low attenuated large mass (14.1 × 12.1 × 12 cm) with peripheral irregular nodular enhancement occupying the left lateral segment of the liver. Magnetic resonance imaging (MRI) of the abdomen showed a complex heterogenous mass in the left hepatic lobe, with mixed areas of decreased and slightly increased signal intensity on T1 weighted images (Fig. 2), and increased signal intensity on T2 weighted images (Fig. 3). Fine-needle aspiration of the central complex part of the mass was consistent with infarcted cavernous hemangioma. A left lateral segmentectomy of the liver was performed. The weight of the removed liver was 570 grams. Histological examination showed cavernous hemangioma (Fig. 4) with areas of extensive necrosis and infarction (Fig. 5). Biopsy specimens from the unaffected liver were consistent with mild steatosis and negative for malignancy. The patient had a smooth post-operative course. Biochemical and clinical symptoms normalized soon after the surgery. An ERCP was repeated in two

Figure 1. Computed tomographic scan (CT) of the abdomen displaying left lobe liver mass with peripheral enhancement not typical of a cavernous hemangioma.

Figure 2. T1 weighted magnetic resonance imaging (MRI) of the left lobe liver mass after enhancement showing heterogeneous peripheral enhancement not typical of a cavernous hemangioma. Delayed scans did not demonstrate any central enhancement.
months after surgical resection of the giant hemangioma, and the stent was removed with no evidence of biliary leak.

DISCUSSION

Although GLH is most often asymptomatic, there have been few case reports of GLH associated with inflammatory manifestations (3–7). Bornman, et al (3) described two cases with GLH who experienced a triad of acute inflammatory process (fever, chills, right upper quadrant tenderness), a normal white blood cell count, and normal liver function tests. Pateron, et al (4) described two similar cases, but with associated abnormal liver tests. Pol, et al (5) reported three cases with inflammatory process complicating GLH. Smyrniotis, et al (6) reported one case of GLH associated with clinical and laboratory manifestations of an underlying inflammatory process (elevated fibrinogen, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), tumor necrosis factor (TNF), and interleukin-6).

The underlying pathophysiology of the inflammatory process in patients with GLH is not fully understood (3–6). One theory suggests that cytokines released from hepatic macrophages and endothelial cells are responsi-

Figure 3. T2 weighted magnetic resonance imaging (MRI) of the left lobe liver mass shows heterogenous increased signal not typical for a cavernous hemangioma.

Figure 4. (H&E stain ×200). Cavernous hemangioma consisting of dilated vascular channels lined by flat endothelial cells.

Figure 5. (H&E stain ×100). Area within the hemangioma (central part) shows ischemic necrosis (infarct).

ble for the inflammatory process (6,9). Others consider the key mediators to be interleukin-1 and -6 (9). The most likely explanation for the pain and increased ESR, CRP and fibrinogen is thrombosis within the tumor (6,8). The elevated levels of alkaline phosphatase and γ-glutamyltransferase could be the result of compression of bile ducts (Fig. 6), secondary to either the growing GLH itself, or to the rigid thrombosis and fibrosis that occur within the structure of the GLH (6–8). From an

(continued on page 72)
Infarcted Giant Liver Hemangioma

A CASE TO REMEMBER

(continued from page 70)

Figure 6. (H&E stain x100). The hemangioma (left) entraps portal structure (right) including bile ducts. Non-tumorous hepatocytes contain lipid vacuoles at the periphery (right).

imaging standpoint, it is well known that GLH does not demonstrate the classic findings on either CT or MRI (4,10–12). Typically on CT, hemangiomas are low-density on pre-contrast CT and during enhancement demonstrate discontinuous, peripheral, nodular enhancement. On delayed scanning, the enhancement slowly fills in a centripetal fashion (11,12). On MRI, without contrast enhancement, these lesions are low signal on T1 weighted images and demonstrate very high signal, equal to cerebrospinal fluid or the gallbladder on T2 weighted pulse sequences. They are sharply defined relative to the adjacent liver and may demonstrate thin, internal septi. The enhancement after Gadolinium-DTPA is the same as on CT (12). The mass in this case as with other giant liver hemangiomas was atypical. The enhancement peripherally was very continuous, especially laterally, indicating a more neoplastic or inflammatory process.

CONCLUSION

Our patient had a giant liver hemangioma that presented with an unusual combination of signs and symptoms: right upper quadrant abdominal pain, fever, elevated serum alkaline phosphatase and γ-glutamyltransferase, and normal white blood cell count. Careful study excluded all other sources of inflammation except for the GLH. Clinical and biochemical abnormalities resolved after surgical resection of the tumor. Histologic examination confirmed the presence of giant cavernous liver hemangioma with extensive necrosis and infarction. GLH should be considered in the differential diagnosis of a liver mass that presents with signs and symptoms of inflammation, even though it is rare in this context.

References