CASE REPORT

A surprising cause of acute right upper quadrant pain

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SUMMARY

A 42 year-old African-American woman was admitted for severe acute right upper quadrant pain. Her liver function tests showed a cholestatic pattern of hepatitis. She had no known history of liver disease or sarcoidosis. Imaging of her liver and biliary tree did not reveal any apparent cause for her right upper quadrant pain. A liver biopsy was performed which showed granulomatous disease. This prompted a CT chest that showed mediastinal lymphadenopathy. Biopsy of the mediastinal lymphnode revealed non-caseating granulomas. Despite having no pulmonary symptoms or history of pulmonary sarcoidosis, she was diagnosed with systemic pulmonary sarcoidosis. She was treated with corticosteroids and had complete resolution of symptoms over the next several weeks.

BACKGROUND

Sarcoidosis is a multisystem inflammatory disease characterised by non-caseating granulomas. The cause of sarcoidosis is unknown with a higher prevalence in the African-American population. Hepatic sarcoidosis is typically asymptomatic and found incidentally on routine hepatic function tests with a cholestatic pattern of hepatitis in those already diagnosed with pulmonary sarcoidosis. There are few cases of symptomatic hepatic sarcoidosis reported in the literature. Hepatic sarcoidosis can be a cause of acute right upper quadrant pain and should be in the differential diagnosis, especially in a patient with high-risk demographics. Also, patients may not have a diagnosis of pulmonary sarcoidosis at time of presentation.

CASE PRESENTATION

A 42-year-old African-American woman was admitted through the emergency department for severe right upper quadrant pain. Associated symptoms included nausea, frequent vomiting, pruritus and a 45 pound unintentional weight loss over a period of 3 months. She had a medical history of uncontrolled type 2 diabetes mellitus, cholecystectomy 10 years prior to admission for cholecystitis, and two previous admissions for similar symptoms without a definitive diagnosis. During the previous two hospitalisations, she was evaluated with multiple imaging studies (listed below). A thorough laboratory evaluation revealed a cholestatic pattern of hepatitis and a liver biopsy was scheduled to evaluate this finding. She did not drink alcohol, smoke tobacco, use illicit drugs or take over the counter supplements. Family history was unremarkable. Vital signs were within normal limits. Physical

examination was remarkable for right upper quadrant tenderness without peritoneal signs. Her liver was not palpable below her right costal margin. A Murphy's sign was positive.

INVESTIGATIONS

The comprehensive metabolic panel showed glucose 159 mg/dL, blood urea nitrogen 6 mg/dL, creatinine 0.5 mg/dL, sodium 132 mmol/L, potassium 4.0 mmol/L, chloride 96 mmol/L, bicarbonate 27 mmol/L, calcium 8.9 mg/dL, total protein 7.6 g/dL, albumin 3 g/dL, aspartate aminotransferase 56 U/L, alanine transaminase 61 U/L, alkaline phosphatase 931 U/L, and total bilirubin 0.7 mg/dL. White cell count was 9000/mm³, haemoglobin 11.3 g/dL, haematocrit 33.5%, mean corpuscular volume 81.1 femtoliters, and platelets 541 000/mm³ (table 1).

Chest radiograph (figure 1), right upper quadrant ultrasound, and MR cholangiopancreatography were normal.

An evaluation for possible infections was negative for tuberculosis, viral hepatitis, and cytomegalovirus. The patient was not taking any drugs known to be hepatotoxic. A working diagnosis of primary biliary cirrhosis was made and there was no improvement in symptoms with ursodiol treatment.

DIFFERENTIAL DIAGNOSIS

- ▶ Hepatic Sarcoidosis
- ▶ Primary biliary cirrhosis
- ▶ Autoimmune hepatitis
- ▶ Primary sclerosing cholangitis
- ▶ Choledocholithiasis

TREATMENT

Prednisone 40 mg daily.

OUTCOME AND FOLLOW-UP

Serum antimitochondrial antibody (Ab) later returned negative (table 2). Antinuclear Ab screen was negative along with tissue transglutaminase. Both antiproteinase3 and myeloperoxidase antibodies were negative. Parietal C Ab was non-reactive. Antismooth muscle Ab was reactive with a low titre. Her liver biopsy showed a large number of portal and periportal non-caseating granulomas with notable ductopenia (figure 2). This prompted a further diagnostic evaluation for sarcoidosis with a contrast-enhanced chest CT despite a normal chest radiograph and no pulmonary symptoms. CT chest demonstrated mediastinal lymphadenopathy (figure 3). Fine-needle aspiration of an enlarged

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Table 1

Glucose (mg/dL)	159
Blood urea nitrogen (mg/dL)	6.0
Creatinine (mg/dL)	0.5
Sodium (mmol/L)	132
Potassium (mmol/L)	4.0
Chloride (mmol/L)	96
Bicarbonate (mmol/L)	27
Calcium (mg/dL)	8.9
Total protein (g/dL)	7.6
Albumin (g/dL)	3.0
Aspartate aminotransferase (U/L)	56
Alanine transaminase (U/L)	61
Alkaline phosphatase (U/L)	931
Total bilirubin (mg/dL)	0.7
White blood count (per mm ³)	9000
Haemoglobin (g/dL)	11.3
Haematocrit (%)	33.5
Mean corpuscular volume (femtolitres)	81.1
Platelets (per mm ³)	541 000
Hepatitis A IgM	Negative
Hepatitis B surface Ag	Negative
Hepatitis B surface Ab	Negative
Hepatitis C Ab	Negative

Ag, antigen; Ab, antibody.

mediastinal lymph node showed non-caseating granulomatous lymphadenitis consistent with pulmonary sarcoidosis (figure 4). Fungal and acid-fast bacilli cultures were negative. ACE level was elevated at 101 U/L (table 2). Her cholestatic pattern of hepatitis, low antismooth muscle Ab titre with negative

Figure 1 Normal chest X-ray without parenchymal lung abnormality or evidence of hilar lymphadenopathy.

Table 2

Antimitochondrial Ab	Non-reactive
ACE (U/L)	101 (9–67)
Antinuclear Ab screen	Negative
Antismooth muscle Ab	Reactive, 1:20 titre
Parietal C Ab	Non-reactive
TTG IgA	<1 U/mL
Proteinase 3 Ab	Negative
Myeloperoxidase Ab	Negative

Ab, antibody.

antinuclear Ab screen, and the absence of significant elevation in transaminases or other systemic sequelae of autoimmune disease was not consistent with diagnosis of autoimmune hepatitis. A diagnosis of systemic sarcoidosis with hepatic involvement was performed.

The patient experienced significant resolution of her symptoms over the course of several days and complete resolution within several weeks.

DISCUSSION

Sarcoidosis is a multisystemic disease of unknown aetiology characterised by non-caseating granulomas believed to be a result of a cell-mediated immune response and is typically asymptomatic. The epidemiology of hepatic sarcoidosis is largely unknown. Ayyala *et al*¹ reports an incidence of 11.5% in a study of 736 patients with known pulmonary sarcoidosis enrolled in the ACCESS (A Case Controlled Etiologic Study of Sarcoidosis) study while Turhan *et al*² diagnosed hepatic sarcoidosis in approximately 5% of 86 liver biopsies that contained granulomatous disease. Other smaller case series have reported incidences of up to 70%.³

The diagnosis of hepatic sarcoidosis can be challenging. The disease may be suspected if there is a chronic cholestatic pattern of hepatitis in a patient with known pulmonary sarcoidosis or in a patient belonging to a high-risk demographic population.⁴ ACE

Figure 2 Liver biopsy showing prominent granulomatous inflammation of varying age and size involving the portal areas.

Figure 3 CT chest revealing a pretracheal lymph node measuring 2.2×0.9 cm as well as an aortopulmonary window lymph node measuring the same size.

Figure 4 Groups of epithelioid histiocytes, lymphocytes and benign bronchial epithelial cells, non-caseating, from pretracheal lymph node.

may be elevated but is not sensitive or specific. The diagnosis is confirmed with a liver biopsy and exclusion of other aetiologies for granulomatous hepatitis.

There is no established or US Food and Drug Administration-approved treatment for sarcoidosis, although glucocorticoid therapy is the standard of care. Most patients have a rapid response in symptoms and hepatic enzymes with initiation of corticosteroid therapy. The decision to treat hepatic sarcoidosis is based on symptoms or evidence of liver dysfunction such as portal hypertension or chronic cholestatic disease. If glucocorticoid therapy fails, other immunomodulators such as azathioprine, methotrexate or infliximab can be used. Despite improving laboratory findings of cholestatic hepatitis, treatment has not been shown to slow progression of hepatic disease or time to transplant. Progression to liver failure is rare.

Our patient presented with a cholestatic pattern of hepatitis and a clinical picture consistent with acute biliary pathology, as opposed to the typical indolent nature of hepatic sarcoidosis. Even more unusual, she did not carry a diagnosis of pulmonary sarcoidosis nor have any pulmonary symptoms. The cholestatic pattern of hepatitis with unremarkable imaging prompted a liver biopsy for further diagnostic evaluation which showed numerous non-caseating granulomas. Other aetiologies for granulomatous hepatitis such as infection and drug reactions were excluded. Hepatic sarcoidosis was then suspected but without pulmonary symptoms, the diagnosis remained tentative. This prompted the CT chest which discovered mediastinal lymphadenopathy and a subsequent fine-needle aspiration, showing non-caseating granulomas consistent with sarcoidosis, solidifying the diagnosis.

Learning points

- ▶ Sarcoidosis is a multisystem disease with an unclear aetiology.
- ▶ Hepatic sarcoidosis should be in the differential diagnosis of a patient with a cholestatic pattern of hepatitis and right upper quadrant pain, especially in a patient with high-risk demographics.
- ▶ Patients with hepatic sarcoidosis may not have a diagnosis of pulmonary sarcoidosis at time of presentation.

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