The Klatskin Tumor That Wasn’t: An Unusual Presentation of Sarcoidosis

Priya D. Farooq, MD and Darryn R. Potosky, MD

ABSTRACT

We present the case of a patient who presented with signs and symptoms associated with a Klatskin tumor. After endoscopic retrograde cholangiopancreatography (ERCP) and biopsy, she was found instead to have granulomatous infiltration of the extrahepatic biliary tree consistent with biliary sarcoidosis. The patient was treated successfully with systemic corticosteroids and azathioprine. She later developed cutaneous, lymphatic, and pulmonary granulomatous disease. Isolated biliary disease is a rare initial presentation of systemic sarcoidosis.

INTRODUCTION

Sarcoidosis is a disease characterized by granulomatous infiltration and can affect any organ system.1-3 Isolated extrapulmonary involvement in the absence of lung disease is only seen in 2%-13% of patients.4,5 Gastrointestinal involvement is not uncommon, but isolated involvement of the biliary system in the absence of hepatic disease is rare. There have been only a few reports of similar cases in the medical literature.6-15

CASE REPORT

A 41-year-old African American woman presented with new-onset jaundice and pruritus. She endorsed a 13-pound weight loss over the prior few months but denied additional symptoms, including fevers, chills, night sweats, and other gastrointestinal symptoms. Physical examination found scleral icterus but was otherwise unremarkable. Laboratory studies showed serum alkaline phosphatase (ALP) 1440 U/L, total bilirubin 2.4 mg/dL, aspartate aminotransferase 205 IU/L, alanine aminotransferase 152 IU/L, albumin 3.2 g/dL, international normalized ratio 1.0, and platelets 286 000/mcL. Computed tomography (CT) demonstrated an ill-defined, infiltrative mass consistent with a Klatskin tumor (Figure 1), with magnetic resonance cholangiopancreatography (MRCP) demonstrating significant upstream intrahepatic biliary ductal dilatation (Figure 2). Carcinoembryonic antigen was normal and cancer antigen 19-9 (CA19-9) was mildly elevated at 53 U/mL. ERCP revealed a tight stricture at the common hepatic duct extending into the takeoff of the right and left ducts, which are associated with malignancy (Figure 3). Stents were placed in the right and left systems. Duct brushings were negative for malignancy. Biopsies of the stricture showed extensive granulomatous inflammation in the wall of the bile duct (Figure 4). Stains were negative for mycobacteria or fungus.

Alternative diagnoses, including sarcoidosis, biliary inflammatory pseudotumor, and atypical primary sclerosing cholangitis, were considered. MRCP was repeated later that month and again demonstrated persistent intrahepatic biliary ductal dilatation. Chest x-ray for evidence of pulmonary sarcoidosis revealed no hilar lymphadenopathy or pulmonary infiltrates.

Subsequent testing showed a mildly elevated serum angiotensin converting enzyme (ACE) level; c-ANCA, p-ANCA, IgG4, purified protein derivative (PPD) and anti-mitochondrial antibody (AMA) were all normal. Given the
lack of malignant pathology and the presence of granulomas, the patient was started on a prednisone taper. During treatment, her ALP improved from 1440 to 398 U/L, and transaminases and total bilirubin normalized. After completion of the steroid taper, her serum ALP rose again to 849 U/L. Repeat ERCP found improvement in the strictures and intrahepatic ductal dilatation without complete resolution. Repeat brushings were negative, and the stents were removed. Prednisone was restarted, again leading to an improvement in ALP. Soon after, azathioprine was added as a steroid-sparing agent. Subsequent liver biopsy found mild nonspecific portal inflammation and no evidence of granulomatous disease; stain for
IgG4 was negative. Her doses of prednisone and azathioprine were adjusted over several months to near resolution of her liver tests. A third MRCP after 6 months of medical therapy showed resolution of the ductal dilation (Figure 5). Soon after, she became pregnant, and self-discontinued all medications. After a planned abortion, she was restarted on monotherapy with ursodeoxycholic acid for biliary sarcoidosis. Her ALP remained near normal.

Three years after her initial presentation, she was noted to have small erythematous papules and plaques on her face and scalp. Skin biopsy was consistent with cutaneous sarcoidosis. She was treated successfully with topical and intraleSIONAL therapies. Three months later, she developed inguinal lymphadenopathy also biopsy proven to be sarcoidosis. Nearly 4 years after her diagnosis, she developed a severe cough and shortness of breath. Chest CT and bronchoscopy with biopsy confirmed pulmonary sarcoidosis. She had an excellent response to steroid therapy, but due to a quick relapse when tapered, was again started on azathioprine with good response.

DISCUSSION
Sarcoidosis is a systemic disease characterized by granulomatous infiltration of multiple organ systems, most commonly in the lungs and lymph nodes. It can also affect the liver, spleen, heart, skin, and eyes.1-3 Extrapulmonary sarcoidosis in the absence of lung involvement is uncommon; in a study of 736 patients enrolled within 6 months of diagnosis, only 2% had isolated extrapulmonary involvement.4 A separate retrospective study of 180 patients showed 13% had liver involvement without lung disease.5 Hepatic sarcoidosis is well reported; 50%-79% of liver biopsies in patients with sarcoidosis will show evidence of hepatic granulomas, with a smaller percentage demonstrating laboratory abnormalities.3,6,7 The most frequently reported symptoms are abdominal pain and pruritus.7

In contrast, jaundice is the presenting symptom in less than 5% of hepatic sarcoidosis patients and is more likely to be caused by intrahepatic cholestasis. Of those patients, isolated bile duct obstruction is a rarely documented cause.8

There have been 9 similar case reports published in the medical literature since 1978. Sarcoidosis can cause biliary obstruction via granulomatous inflammation within the bile duct or extrinsic compression by intraabdominal granulomatous lymphadenopathy. Lymphadenopathy was the attributed cause in at least 5 of the case reports. In addition, of the 6 patients with tissue from liver biopsy or resection, 4 had evidence of hepatic granulomas. Of the 9 patients, 7 of them underwent surgery to either diagnose or treat their condition, while 1 patient improved with stenting alone and the other required only corticosteroid therapy.8-15

In our case, the patient had granulomatous infiltration of the extrahepatic bile ducts, leading to stricture formation, in the absence of documented hepatic sarcoidosis. The area of narrowing at the confluence of the hepatic bile ducts was biopsied and demonstrated evidence of noncaseating epithelioid granulomas. The infiltrative mass was likely an outgrowth of the granulomatous tissue infiltration or pseudotumor, giving the appearance of an obstructing tumor. The mass resolved with steroid therapy.

A unifying diagnosis was initially difficult. The finding of granulomas on biopsy and robust response to steroids are non-specific. In addition, isolated biliary sarcoidosis is rare and usually reported in the context of previously diagnosed pulmonary sarcoidosis. The diagnosis of systemic sarcoidosis was finally confirmed only after the patient developed skin and pulmonary manifestations years after her initial presentation. This case highlights an unusual presentation of biliary sarcoidosis as the initial manifestation of systemic sarcoidosis, which has been managed medically with good outcomes.

DISCLOSURES
Author contributions: PD Farooq performed the literature and chart review and wrote the manuscript. DR Potosky reviewed and edited the manuscript and is the article guarantor.

Financial disclosures: None to report.

Informed consent was obtained for this case report.

Received November 28, 2015; Accepted April 15, 2016

REFERENCES
1. Newman LS, Rose CS, Maier LA. Sarcoidosis. N Engl J Med. 1997; 336(17):1224-34.
2. Iannuzzi MC, Rybicki BA, Teirstein AS. Sarcoidosis. N Engl J Med. 2007;357:2153-65.

Figure 5. A third MRCP after 6 months of medical therapy showing resolution of the intrahepatic ductal dilatation.
3. Karagiannidis A, Karavalaki M, Koulaouzidis A. Hepatic sarcoidosis. Ann Hepatol. 2006;5(4):251-6.
4. Baughman RP, Teirstein AS, Judson MA, et al. Clinical characteristics of patients in a case control study of sarcoidosis. Am J Respir Crit Care Med. 2001;164(10):1885-9.
5. Kennedy PTF, Zakaria N, Modawi SB, et al. Natural history of hepatic sarcoidosis and its response to treatment. Eur J Gastroenterol Hepatol. 2006;18(7):721-6.
6. Judson MA. Hepatic, splenic, and gastrointestinal involvement with sarcoidosis. Semin Respir Crit Care Med. 2002;23(6):529-41.
7. Ebert EC, Kierson M, Hagspiel KD. Gastrointestinal and hepatic manifestations of sarcoidosis. Am J Gastroenterol. 2008;103(11):2184-92.
8. Albu E, Saraiya RJ, Carvajal SJ, Sehonanda A, Balar N, Gerst PH. Sarcoidosis presenting as obstructive jaundice. Am Surg. 1995;61(6):516-7.
9. Baughman RP. Sarcoidosis: Usual and unusual manifestations. Chest. 1988;94(1):165-70.
10. Bloom R, Sybert A, Mascatello VJ. Granulomatous biliary tract obstruction due to sarcoidosis: Report of a case and review of the literature. Am Rev Respir Dis. 1978;117(4):783-7.
11. Buxbaum J, Papademetriou M, Klipfel N, Selby R, Fong T-L, Sharma O. Biliary sarcoidosis: Early diagnosis minimizes the need for surgery. Am J Respir Crit Care Med. 2013;187(5):556-9.
12. Kusielwicz D, Duchatelle V, Valeyre D, et al. Obstructive jaundice caused by granulomatous stenosis of the extrahepatic bile ducts in sarcoidosis [article in French]. Gastroenterol Clin Biol. 1988;12(8-9):664.
13. Pungpapong S, Steers JL, Wallace MB, Krishna M, Keaveny AP. Hepatobiliary sarcoidosis mimicking Klatskin’s cholangiocarcinoma. Gastrointest Endosc. 2006;64(1):124-5.
14. Rezeig MA, Fashir BM. Biliary tract obstruction due to sarcoidosis: A case report. Am J Gastroenterol. 1997;92(3):527-8.
15. Sotiropoulos GC, Dahmen U, Dirsch O, et al. Biliary tract obstruction due to sarcoidosis. Endoscopy. 2005;37(12):1262.