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CASE REPORT | LIVER

A Case of Erdheim-Chester Disease Causing Secondary Sclerosing Cholangitis

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ABSTRACT

Erdheim-Chester disease (ECD) is an exceedingly rare and aggressive disease characterized by foamy CD68 + CDa-histiocytic infiltration into multiple tissues and organs. Only 1,500 cases have been diagnosed since 1930 when ECD was first described. Biliary tract involvement of ECD has only been reported in the literature once. We report a case of ECD causing extrahepatic biliary obstruction without significant bile duct dilation, mimicking primary sclerosing cholangitis or IgG4 disease.

KEY WORDS: myeloid neoplasms; histiocytosis; IgG4 disease; obstructive cholangiopathy

INTRODUCTION

Erdheim-Chester disease (ECD) is a rare myeloid neoplasm characterized by tissue infiltration of CD68 + CD1a-histiocytes. It frequently involves the long bones, heart, vasculature, central nervous system, retroperitoneum, skin, and lungs.[1,2] Bile duct involvement is extremely rare.[3] We report a case of an unusual case of ECD causing secondary sclerosing cholangitis.

CASE REPORT

A 65-year-old man presented with a 1-year history of fatigue and was found to have elevated liver enzymes: alkaline phosphatase 1,805 IU/L, gamma-glutamyl transferase 2,007 IU/L, aspartate aminotransferase 47 IU/L, and alanine aminotransferase 81 IU/L. Bilirubin, platelet count, albumin, international normalized ratio, and creatinine were normal. Hepatitis and autoimmune liver disease markers were negative. Serum IgG4 (41 mg/dL) and CA19-9 (121 IU/mL) were both unremarkable.

An MRI/MRCP demonstrated subtle multifocal short segment intrahepatic biliary dilation, mild perihilar duct wall thickening with enhancement, and a normal extrahepatic biliary tree. Abdominal computed tomography (CT) showed bilateral perinephric fat stranding and diffuse large vessel inflammation (Figure 1). Differentials for the radiographic findings included ECD, lymphoma, IgG4 disease, or other large vessel vasculitis. Lower extremity x-ray showed diffuse sclerotic changes of the long bones—nonspecific but compatible with ECD. Taken together, the pattern was nonspecific but most suggestive of large duct obstruction. Positron emission tomography/CT showed no abnormal uptake in the vasculature or bone but demonstrated an FDG avid left hilar mass, with subsequent biopsy revealing low-grade follicular lymphoma. Observation for asymptomatic disease was recommended.

A tentative diagnosis of primary sclerosing cholangitis (PSC) was made, and the patient was started on ursodeoxycholic acid, with some improvement of pruritis. He had 3 hospitalizations in the next 4 months for clinically suspected cholangitis, and his total bilirubin fluctuated around 2 mg/dL during this period.

Approximately 16 months after symptom onset, the patient noticed the appearance of dome-shaped skin lesions over the face, hands, and legs. In addition, the patient developed worsening jaundice with a bilirubin of 10.7 mg/dL. ERCP showed common hepatic duct stricture with nonfilling of the right intrahepatic duct system (Figure 2). The narrowed segments at the hilum were dilated, and a plastic biliary stent was placed. Biliary brushing and biopsy from the stricture showed benign reactive tissues. One of the skin lesions was ultimately biopsied

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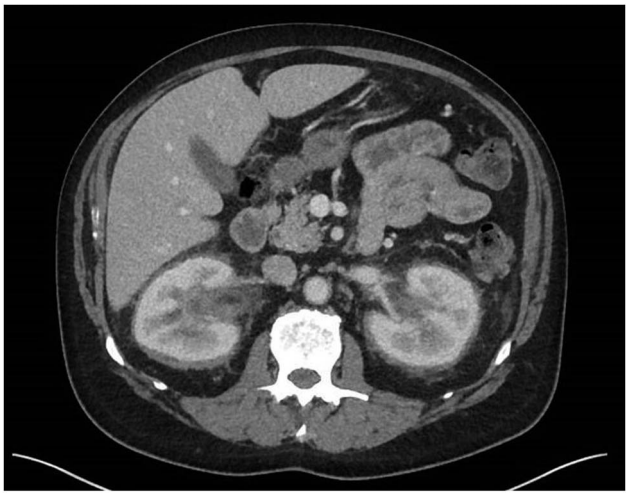

Figure 1. "Hairy kidney," a nonspecific but classic radiographic finding for ECD. ECD, Erdheim-Chester disease.

and revealed CD68+CD1a-histiocytic proliferation, consistent with ECD. Cancer mutation analysis of skin biopsy tissue identified BRAF (v-raf murine sarcoma viral oncogene homolog B1) V600E, CBL R420Q, and TET2 T556fs variants.

The patient's jaundice did not improve after the stent placement. Treatment with interferon alpha or BRAF/mitogen-activated extracellular signal-regulated kinase inhibitors were suggested by hematology/oncology faculty but declined by the patient and family because of his severe deconditioning, rapidly progressive jaundice and kidney failure. The patient pursued hospice and passed away shortly after the ECD diagnosis.

DISCUSSION

In retrospect, the patient's liver disease diagnosis was modified to secondary sclerosing cholangitis caused by ECD. Because of the infiltrative and fibrotic nature of the disease and the rapid disease progression, there was no significant bile duct dilation on cross-sectional imaging, leading to a delay in diagnosis. ERCP had a higher spatial resolution of the bile duct than MRI or CT and alluded to the right diagnosis, although an attempt at reopening the ducts mechanically was unsuccessful. The diagnosis of ECD was also delayed because of the lack of an easily accessible biopsy target before the skin lesions appeared, the patient's frequent hospitalizations for cholangitis, and the new diagnosis of PSC and follicular lymphoma, both acting as a confounder. IgG4 disease was another consideration, but in the absence of a biopsy target, the diagnostic criteria were not met. Unlike IgG4 disease, which frequently involves the biliary tract, ECD has only been reported to have biliary manifestation once in the literature, causing a mass-forming lesion in the hilum, mimicking Klatskin tumor.[3]

Mutations activating the mitogen-activated protein kinase pathway have been found in >80% of patients with ECD, mainly BRAF V600E in 57%–70%.[1] Treatment with BRAF and mitogen-activated extracellular signal-regulated kinase inhibitors are highly effective and recommended for most patients.[2] The disease is aggressive and can progress within a few months without treatment, and early diagnosis is key in improving prognosis. Last, in patients who present with sclerosing cholangitis, secondary causes, such as an infiltrative disorder (eg, ECD), should be excluded before a diagnosis of PSC is made.

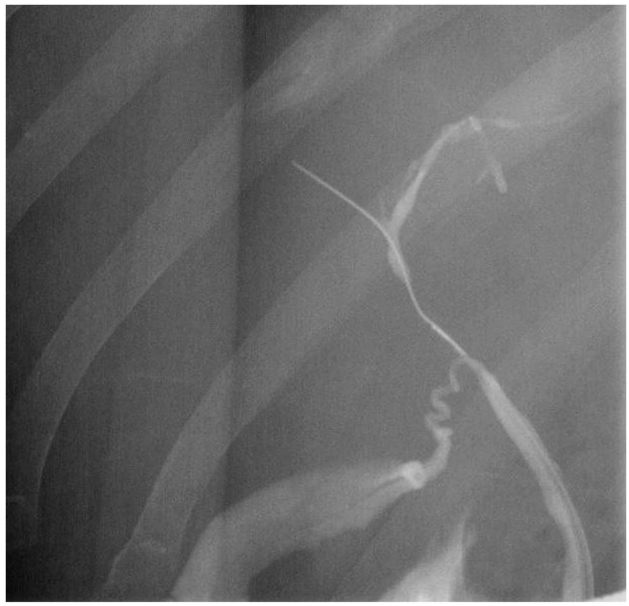

Figure 2. ERCP image showing common hepatic duct stricture and nonfilling of the right intrahepatic duct system.

DISCLOSURES

Author contributions: V. Kamalumpundi, J. Rieth, and X. Zhang drafted the initial manuscript. H. Tran, M. Ashat, and X. Zhang critically revised the manuscript for intellectual content. X. Zhang is the article guarantor.

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