Idiopathic adulthood ductopenia (IAD) is a rare chronic small duct cholestatic biliary disease of unknown origin characterized by the loss of interlobular bile ducts. IAD was first described in 1988 by Ludwig et al, and since then, fewer than 100 cases have been published in the literature. IAD is a diagnosis of exclusion in adults in which there is biochemical evidence of cholestatic liver disease, ductopenia on liver biopsy, and no other identifiable cause of cholestasis. The etiology for IAD is unknown, and the only definitive treatment is liver transplantation.

CASE REPORT

A 67-year-old white man with a medical history of prostate cancer status postradioactive seed implant presented with 10 days of abdominal pain, jaundice, and worsening liver function tests as an outpatient. He had no history of liver disease, autoimmune disease, herbal supplement use, acetaminophen use, or intravenous drug use. He was not on any home medications before admission. He did not demonstrate signs or symptoms of portal hypertension before presentation, including no history of gastrointestinal (GI) bleed, no varices on esophagogastroduodenoscopy, and no ascites. His laboratory report revealed total bilirubin of 27.5 mg/dL, aspartate aminotransferase of 154 U/L, alanine aminotransferase of 103 U/L, alkaline phosphatase of 195 U/L, and international normalized ratio of 1.9, with normal lipase. He did not demonstrate evidence of metabolic syndrome. Abdominal ultrasound and computed tomography were demonstrative of patent hepatic vasculature, no visualized gallstones or cholecystitis, but with cirrhotic morphology with perihepatic ascites. Cirrhosis workup was negative, including f-actin, α-1-antitrypsin, antimitochondrial antibody, ceruloplasmin, iron, acetaminophen, and ethanol studies within normal limits. Hepatitis A, B, and C, as well as human immunodeficiency virus and cytomegalovirus (CMV), were ruled out with serologic studies. Liver biopsy demonstrated vanishing bile duct syndrome, with bile ducts present in 2 of 10 portal tracts, and stage IV cirrhosis, hepatocyte ballooning, and cholestasis (Figure 1). In addition, the biopsy demonstrated the absence of granulomas, intracytoplasmic hepatocellular globules, and iron, as well as a lack of significant inflammatory infiltrate (Figure 2). The patient’s liver function tests continued to uptrend, and he was subsequently listed for liver transplant. His course was complicated by renal failure, spontaneous bacterial peritonitis, and severe coagulopathy. Unfortunately, his clinical status quickly deteriorated and he died from septic shock in the setting of underlying cirrhosis from vanishing bile duct syndrome.

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DISCUSSION

IAD is a rare, chronic progressive cholestatic disease that was first described by Ludwig et al.\(^1\) in 1988. IAD diagnosis is made with adult onset of biochemical evidence of cholestatic liver disease, evidence of ductopenia on biopsy, and the exclusion of other common etiologies.\(^6\) As aforementioned, the hallmark histologic finding in IAD is ductopenia, a condition characterized by interlobular and septal bile ducts that disappear in ≥50% of portal tracts.\(^7\) There exist several causes for ductopenia that must be ruled out before IAD diagnosis, including primary biliary cirrhosis, autoimmune cholangitis, and adverse drug reactions.\(^1,2,8\) In addition, several viral infections have been linked to cholestasis and ductopenia, most notably CMV, hepatitis B, and hepatitis C.\(^9\)

The underlying etiology is unknown, although several causes have been suggested, which include late-onset nonsyndromic paucity of the intrahepatic bile ducts, small duct primary sclerosing cholangitis without large duct involvement and without evidence of inflammatory bowel disease, nonsuppurative viral cholangitis, and autoimmune cholangitis.\(^2\) In addition, unique underlying host factors that point to an immunogenic basis of susceptibility have also been proposed.\(^10\) IAD clinically presents with cholestatic pattern symptoms, including jaundice, pruritus, and fatigue; however, IAD has also been observed in patients without symptoms of liver disease.\(^11\) There are 2 distinct courses of the disease that are recognized, which vary histologically and by prognosis. Type 1 IAD has less than 50% loss of biliary ducts on biopsy and is characterized with a more benign clinical course and better prognosis. Type 2 IAD has more widespread ductopenia and usually progresses to decompensated biliary cirrhosis.\(^4,5,11\) Treatment for IAD is dependent on the underlying presentation. The more benign type 1 IAD has been shown to have improvement in liver function tests with ursodeoxycholic acid, whereas patients with the type 2 IAD will ultimately require liver transplantation.\(^11,12\) Finally, although immunosuppressed states are associated with IAD, there have been anecdotal reports of improvement in IAD with immune suppression and controlled trials for immune modulation could be considered in the future.\(^6\)

**Figure 1.** Masson trichrome stain showing bridging fibrosis and fibrotic expansion of the portal tract. Also evident is the significant periportal ballooning degeneration.

**Figure 2.** Liver biopsy using (A–C) hematoxylin and eosin and (D) periodic acid-Schiff with diastase showing minimal inflammatory infiltrate, with mild expansion of the portal triad and a stark paucity of bile ducts. The venules and arterioles are intact with no evidence of vascular inflammation.
In this unfortunate case, our patient appeared to have had a relatively acute presentation of cholestasis. However, in reviewing the literature, IAD has a variable time to presentation and there have been published cases of IAD within 2 weeks of onset of the symptoms.13 Our patient was likely developing this condition for some time, as evidenced by the development of cirrhosis. He had demonstrated elevated liver function tests for at least 2–3 weeks before admission and likely had subclinical elevation in liver function tests for some time. Although IAD is more commonly seen in patients in immunosuppressed states, such as in whole organ transplant and chemotherapy, our patient was not immunosuppressed. He had a remote history of prostate cancer that was only treated with radiation. The possibility of drug injury was considered, but a detailed history demonstrated that the patient had not been taking any new medications or over-the-counter supplements before presentation. Viral etiology was considered, but serologic studies for a variety of viruses were within normal limits. In addition, the biopsy did not demonstrate any significant inflammatory infiltrate, making infection less likely in this immunocompetent host.

In summary, IAD is a rare but serious cause of cholestatic disease. The underlying etiology is unknown, and the clinical presentation can be subtle, making the diagnosis difficult. In patients with chronic cholestasis in which more common etiologies have been excluded, IAD should be considered in the differential diagnosis.

DISCLOSURES

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