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Idiopathic Adulthood Ductopenia: 'It Is Out There'

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Keywords

Idiopathic adulthood ductopenia · Elevated alkaline phosphatase · Cholestasis

Abstract

Idiopathic adulthood ductopenia (IAD) is a chronic cholestatic entity of unknown origin characterized by loss of inter-lobular bile ducts that was first described two decades ago. Although the diagnostic criteria have been described in detail, IAD continues to be a rare diagnosis. Our thorough literature search revealed less than a hundred cases of IAD reported. Here we present a 34-year-old female with no significant past history who was evaluated for persistent elevation of serum alkaline phosphate levels. Serology was negative for all viral hepatitis, and a chronic liver disease workup was unremarkable. Magnetic resonance cholangiopancreatography and endoscopic retrograde cholangiopancreatography did not reveal any abnormalities in the biliary tree. Finally, a liver biopsy demonstrated ductopenia involving greater than 50% of the portal triads, making a diagnosis of IAD. Since the disease can progress rapidly, close follow-up is warranted, so liver transplantation can be pursued if deemed necessary.

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Introduction

Idiopathic adulthood ductopenia (IAD) is a rare chronic cholestatic entity of unknown origin characterized by loss of inter-lobular bile ducts that was first described over two decades ago [1]. Since its initial description, less than a hundred cases have been reported.

Abnormalities in liver function tests are routinely seen in clinical practice and at times are transient secondary to acute illnesses or drugs. Isolated elevation in serum alkaline phosphatase levels is often encountered and mostly occurs secondary to cholestasis. Since impairment of bile secretion can be at any point from the hepatocytes to the second part of the duodenum, the differential diagnosis for cholestatic disorders is usually broad. Primary biliary cirrhosis and primary sclerosing cholangitis are the most common causes of chronic cholestasis [2]. IAD is another cause of chronic cholestasis that involves the small bile ducts. Since the symptoms and presentation of IAD can be nonspecific, it continues to be a diagnosis of exclusion. To date, no specific test has been found to be solely related to IAD. Here we report an interesting case of IAD that was diagnosed after extensive workup.

Case Report

A 34-year-old female with a past medical history of cervical dysplasia was referred to our Hepatology Clinic by her primary care physician for persistent elevation of her serum alkaline phosphatase levels. On review of records, the patient was found to have the following laboratory values; total bilirubin, 0.4 mg/dl (normal: 0.2–1.2 mg/dl), direct bilirubin, 0.2 mg/dl (normal: 0.0–0.4 mg/dl), serum alanine transaminase, 32 IU/l (normal: 9–52 IU/l), serum aspartate transaminase, 23 IU/l (normal: 13–35 IU/l), serum alkaline phosphatase, 295 IU/l (normal: 38–126 IU/l), serum albumin, 4.4 g/dl (normal: 3.5–5.0 g/dl), international normalized ratio, 1.0 (normal: 0.9–1.1). The patient's other laboratory abnormalities were only significant for elevation of serum gamma-glutamyl transpeptidase levels at 279 IU/l (normal: 12–58 IU/l). She did not have any symptoms. She was on no medications at home. Serology results for hepatitis A, B and C were negative. Results were also negative for anti-mitochondrial, anti-nuclear, anti-smooth muscle, anti-liver-kidney microsomal and anti-neutrophil cytoplasm antibodies. Serum alpha fetoprotein, alpha-1-antitrypsin, ceruloplasmin and ferritin levels were in the normal range. Magnetic resonance cholangiopancreatography was done which was normal. Endoscopic retrograde cholangiopancreatography was performed which showed diffuse pruning of the biliary tree with no dominant strictures or extra-hepatic biliary tree abnormalities. Finally, a liver biopsy was done which revealed ductopenia involving 60% of the portal triads, METAVIR stage II portal fibrosis and mild steatosis. No granulomas or florid bile duct lesions were appreciated. (fig. 1, fig. 2) The patient was diagnosed as having IAD based on the criteria defined by Ludwig. The patient was started on ursodiol 500 mg three times a day and continues to be stable to date. She has been closely monitored over the past 3 years.

Discussion

IAD is a rare disorder which was first described by Ludwig and colleagues in 1988 [1]. Although the diagnostic criteria have been well described, the presentation of the disease is rare. The diagnostic criteria include the following. (i) The patient must be an adult or at least

an adolescent. (ii) Biochemical evidence of cholestatic liver disease and biopsy evidence of ductopenia. (iii) Biopsy should show a decrease in intrahepatic bile ducts in at least 50% of the portal tracts. (iv) No identifiable cause of cholestasis should be present [3]. It is important for medical practitioners to be aware of IAD because it has a very benign presentation and can be easily missed or neglected. The progression of this entity also varies from a benign course to serious outcomes [4, 5]. Ursodiol has been used in some case studies with symptomatic relief [5, 6]. The only definitive treatment is orthotopic liver transplantation [3, 7]. Since the disease can progress rapidly, it is important for physicians to closely monitor these patients, and liver transplantation can be pursued timely if deemed necessary.

This case highlights the fact that IAD may be more common than previously thought. The subtle presentation and rarity of this disease can make the diagnosis challenging. IAD should be considered in the differential diagnosis of persistent elevation of alkaline phosphatase levels, so that early referral to a dedicated hepatology center could be made to follow progression of disease.

Statement of Ethics

The published research is compliant with the guidelines for human studies and animal welfare regulations.

Disclosure Statement

The authors report no conflict of interest and no financial declaration.

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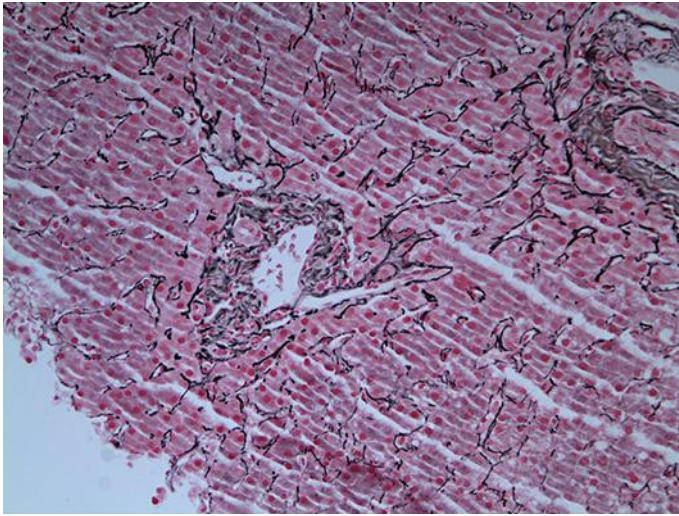


Fig. 1. Low-power magnification: portal tract showing absence of bile duct and ductular proliferation. Reticulin stain.

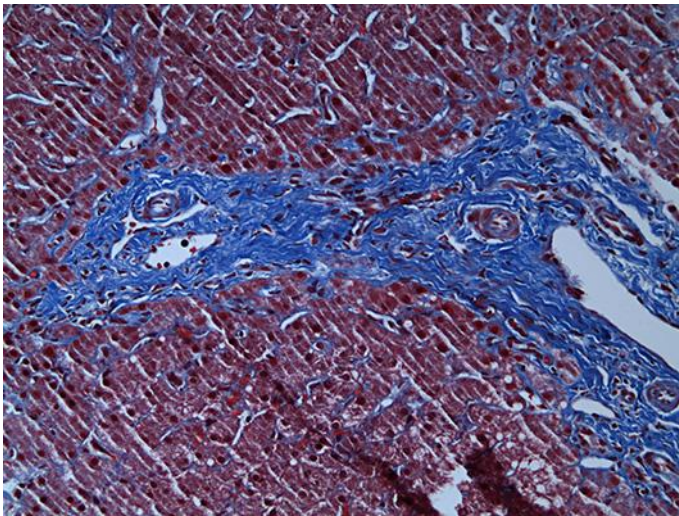


Fig. 2. High-power magnification: portal tract showing portal fibrosis and intrasinusoidal fibrosis. Masson's trichrome stain.