Benign recurrent intrahepatic cholestasis—25 years of follow-up

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Summary: Only 70 cases of recurrent intrahepatic cholestasis have been reported in the literature since the original description of this entity in 1959.

The benign nature of the disease has been questioned, some authors suggesting progression to biliary cirrhosis. We report our follow-up of one such patient for over 25 years with no adverse physical consequences or histological deterioration. Sequential liver biopsies were obtained during this period. A conservative approach to diagnosis and treatment is therefore indicated.

Introduction

Benign recurrent intrahepatic cholestasis (BRIC) is a rare aetiology of jaundice, only some 70 cases being reported since the original description by Summerskill & Walshe in 1959.¹ The clinical features include early onset of recurrent attacks of cholestatic jaundice, lasting up to months in duration and eventually resolving spontaneously.^{2,3} This disease is thought to be benign in nature, without progression to chronic liver dysfunction. However, development towards biliary cirrhosis has been documented.^{2,4} In addition, most of the literature concerning BRIC is in the form of case reports, with few papers reporting long term follow-up.⁵ We wish to report the course of our patient with no evidence of chronic liver disease after over 25 years of follow-up.

Case report

A 28 year old female was admitted to our department for evaluation of pruritus and jaundice of 3 weeks duration. From the age of two to twelve (1959–1969) she was repeatedly hospitalized for recurrent bouts of extreme pruritus and deep jaundice. Plasma biochemical evaluation consistently revealed direct hyperbilirubinaemia with markedly elevated alkaline phosphatase and increased transaminase and cholesterol levels. Radiological studies and, finally, explorative laparotomy excluded extrahepatic obstruction. Repeated liver biopsies were virtually identical, showing cholestasis of various degrees, bile plugs, mild fibrosis at the portal spaces, few multinu-

cleate hepatocytes, and some lymphocytic infiltration of the portal spaces. Six years after her first bout of jaundice, she was diagnosed as suffering from BRIC, the case report being one of the first to be published.⁶

After an asymptomatic interval of 16 years, she again presented with a 3 week history of identical symptoms. An additional liver needle biopsy was obtained. No progression of liver histology towards cirrhosis was found. The lobular architecture was preserved, and only some inflammatory infiltrate was present. Fibrosis was almost unnoticeable. The patient was discharged on cholestyramine, which was discontinued after a few weeks on return of liver function to normal.

Discussion

Tygstrup & Jensen⁷ proposed the following criteria for the diagnosis of BRIC: (1) several episodes of pronounced jaundice with severe pruritus and biochemical evidence of cholestasis; (2) bile plugs on liver biopsy; (3) normal intra- and extrahepatic bile ducts on direct cholangiography; (4) absence of a factor known to produce intrahepatic cholestasis; (5) symptom-free intervals of several months or years.

Our patient met the above criteria and presented a clinical picture compatible with the reported cases in the literature. Detailed features of this entity, laboratory abnormalities found, differential diagnosis, presumed aetiology and suggested therapy are discussed in various excellent reviews.^{2,3,5–9}

Our patient was notable in several ways: asymptomatic intervals generally last from one month to several years, with very long intervals (over 15 years) reported only thrice – the longest being 23 years.^{9,10}

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Our patient remained asymptomatic from the age of 12 to her latest attack at 28 years of age.

In addition, we had the unique opportunity to examine liver histology 25 years after the original biopsy. No progression towards chronicity was noted. Portal space fibrosis has been reported as a pathological finding in BRIC.^{2,8,11} In fact, in this case fibrosis had significantly regressed in comparison to previous biopsies. Liver function tests between attacks have been consistently normal, with no physical impairment or retardation, though jaundice attacks

began in early childhood.

The case reported above reaffirms the essentially benign nature of this disease. Clinicians should be aware of this entity, its clinical features and diagnostic criteria. Once the diagnosis is made, the patient may be saved costly and time consuming diagnostic manoeuvres even when long intervals separate attacks of jaundice. The patient can also be reassured that recurrent intrahepatic cholestasis is indeed benign in the long term.

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