CASE REPORT

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A case report: Nasobiliary drainage inducing remission in benign recurrent intrahepatic cholestasis

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Benign recurrent intrahepatic cholestasis is a rare hereditary disorder characterized by recurrent episodes of cholestasis and pruritus without anatomical obstruction. Generally, medical therapy is not effective in benign recurrent intrahepatic cholestasis. Here, we report the case of a young male patient with benign recurrent intrahepatic cholestasis who presented with cholestatic jaundice and pruritus, refractory to standard therapies. He improved on treatment with temporary endoscopic nasobiliary drainage. We propose that temporary endoscopic nasobiliary drainage should be considered in cholestatic benign recurrent intrahepatic cholestasis patients. A 36-year-old male patient admitted to our outpatient clinic with the complaint of pruritus. His anamnesis revealed that he experienced the same symptoms and signs in 2006. He was hospitalized in a hepatology clinic and was thoroughly examined. Liver biopsy was performed, and he was finally diagnosed as having benign recurrent intrahepatic cholestasis. Medical therapy options all proved to be ineffective and we were able to achieve remission in this patient only with the help of nasobiliary drainage. For this patient, we tried nasobiliary drainage in addition to the standard medical therapies. He improved on nasobiliary drainage. In conclusion, we propose that temporary endoscopic biliary drainage should be considered in cholestatic benign recurrent intrahepatic cholestasis patients. We hope that this case report contributes to the topic, since only a few nasobiliary drainage case experiences have been reported to date.

Key words: Benign recurrent intrahepatic cholestasis, endoscopic nasobiliary drainage, remission

Bir vaka sunumu: Nazobiliyer drenajın, benign tekrarlayıcı intrahepatik kolestazda remisyona sokucu etkisi

Benign tekrarlayan intrahepatik kolestaz, anatomik bir tıkanma olmaksızın gerçekleşen tekrarlayıcı kolestaz ve kaşıntı atakları ile karakterize, nadir bir kalıtsal bozukluktur. Benign tekrarlayan intrahepatik kolestazda tıbbi tedavi, genellikle etkisiz kalmaktadır. Bu yazıda, bize tıbbi tedavilere dirençli kolestatik sarılık ve kaşıntı ile başvuran genç bir erkek benign tekrarlayan intrahepatik kolestaz hastasını takdim ediyoruz. Hasta, geçici endoskopik nazobiliyer drenajdan fayda gördü. Dolayısıyla, geçici endoskopik nazobiliyer drenajın kolestatik benign tekrarlayan intrahepatik kolestaz hastalarının tedavisinde mutlaka akla gelmesini önermekteyiz. Otuz altı yaşında erkek hasta, kaşıntı yakınması ile polikliniğimize başvurdu. Anamnezi alınınca, 2006 yılında da aynı yakınma ve belirtilerin ortaya çıktığı, bir hepatoloji kliniğinde yatırılarak tetkik edildiği, karaciğer biyopsisinin yapıldığı ve neticede benign tekrarlayan intrahepatik kolestaz tanısı aldığı anlaşıldı. Tıbbi tedavi seçeneklerinin pek etkili olmadığı hastayı, nazobiliyer drenaj yardımıyla remisyona soktuk. Bu hastada, standart tıbbi tedavilere ek olarak nazobiliyer drenajı da uyguladık ve olumlu sonuç aldık. Buna dayanarak, kolestatik benign tekrarlayan intrahepatik kolestaz hastalarının tedavisinde geçici endoskopik biliyer drenajın düşünülmesi gerektiği kanaatindeyiz. Bugüne dek bildirilen vaka sayısı çok az olduğundan, konuya katkıda bulunabileceğimizi umuyoruz.

Anahtar kelimeler: Benign tekrarlayan intrahepatik kolestaz, endoskopik nazobiliyer drenaj, remisyon

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INTRODUCTION

Cholestasis is a liver disease caused by impaired bile secretion, associated with and often secondary to the intracellular accumulation of bile acids in the hepatocytes. Bile acids are natural detergents that are secreted from the liver to facilitate emulsification and absorption of fats in the intestine (1). Benign recurrent intrahepatic cholestasis (BRIC) is a rare hereditary disorder characterized by recurrent episodes of cholestasis and pruritus without anatomical obstruction (2). BRIC type 1 is associated with mutations in ATP8B1, encoding FIC1, while BRIC type 2 is caused by mutations in ABCB11, encoding BSEP (3,4). More severe mutations are associated with progressive familial intrahepatic cholestasis (PFIC) type 1 and 2, respectively (3,5). Generally, medical therapy is not effective in BRIC. However, in PFIC, surgical partial biliary diversion (PBD) or ileal exclusion has been employed successfully (6-9). Although PBD may also be effective in BRIC (10), its permanent character makes it less suitable to be used in a disorder that is only episodic.

Here, we report the case of a young male patient with BRIC who presented with cholestatic jaundice and pruritus, refractory to standard therapies. He improved on treatment with temporary endoscopic nasobiliary drainage (NBD). We propose that temporary endoscopic NBD should be considered in cholestatic BRIC patients.

CASE REPORT

A 36-year-old male patient admitted to our outpatient clinic with the complaint of pruritus. On physical examination, he had jaundice, with dark urine and light stool, and was therefore hospitalized. His anamnesis revealed that he had experienced the same symptoms and signs in 2006. He was hospitalized in Cerrahpasa Medical Faculty Hepatology Clinic and was thoroughly examined. Liver biopsy was performed, and he was finally diagnosed as having BRIC. That was his first attack, and it took nearly six months to achieve remission.

Biochemically, he had hyperbilirubinemia with direct bilirubin dominance. Abdominal ultrasonography (USG) was performed and found to be within normal limits. Markers for acute viral hepatitis and serology for brucella-syphilis-Ebstein-Barr virus were found negative.

His total bilirubin level was 20 mg/dl at first admittance; when it increased to 28 mg/dl, he was started on cholestyramine three times a day, in addition to the ursodeoxycholic acid (UDCA) therapy. Bilirubin levels continued to increase, reaching a total of 38.5 mg/dl. He was consulted with a hepatologist, and the cholestyramine dosage was increased. It was also advised to place a NBD catheter if hyperbilirubinemia persisted.

A magnetic resonance cholangiopancreatography (MRCP) imaging was performed as the first and noninvasive diagnostic step, which revealed a normal choledochus and normal intrahepatic biliary ducts without mechanical obstruction. Then, an endoscopic retrograde cholangiopancreatography (ERCP) was performed. We obtained a normal cholangiogram, but a 5 mm sphincterotomy was nevertheless performed for better drainage of bile. Unfortunately, hyperbilirubinemia persisted, and the patient's liver functions worsened, as indicated by prolonged prothrombin times and emerging upper gastrointestinal hemorrhage at the sphincterotomy site. Thus, therapeutic upper endoscopy and sclerotherapy, intravenous (iv) administration of vitamin K, and transfusion of fresh frozen plasma and erythrocyte suspensions were performed. A few days later, a second ERCP was performed to place a 7 French nasobiliary catheter, providing 100 ml of bile drainage daily.

Meanwhile, human albumin perfusions for correction of emerging severe hypoalbuminemia (1.9 g/ml) and iv administration of 40 mg methylprednisolone daily for the next three days were also performed in order to diminish the severity of intrahepatic edema. At the end of the first month, total bilirubin levels had dropped to a level of 20 mg/dl; this was the third week of the NBD. The patient was discharged a few days later. At the follow-up tests two weeks later, total bilirubin level had dropped to 10 mg/dl, and considering the risk of catheter infection, the NBD catheter was removed. The patient is currently taking only a low dose of prophylactic UDCA and had normal biochemical values on follow-up. He returned to work without any problems. We plan to perform an earlier NBD procedure and iv steroids for diminishing intrahepatic edema as the first-line therapy on the next attack.

DISCUSSION

This patient presented with features of a syndrome termed BRIC. BRIC is characterized by recurrent attacks of pruritus and jaundice, which may start at any age (11-14) and which resolves spon-

taneously in most cases. The 'classical' form of BRIC was first described in 1959 by Summerskill and Walshe (15). It is due to mutations of the FIC-1 gene (3) and a P-type ATPase. Cholestatic episodes of the patients are triggered by infections (14,16,17). These infections might induce cell stress (18,19), which might be the cause of the protein instability and improper trafficking.

Treatment for BRIC includes corticosteroids, phenobarbital, cholestyramine, decreased fat diet (20), plasmapheresis (21), and rifampin (22). Bijleveld et al. (20) proposed that the increase in lithocholates in the serum contributes to cholestasis (being cholestatic itself). Therefore, treatment with cholestyramine and reduction of intestinal bacteria may reduce these secondary bile acids in the serum. Brenard et al. (21) described a number of treatments used in their patient cohort with varied success. The treatments without success were phenobarbital, UDCA and cholestyramine. Plasmapheresis was also performed (21,23), with some improvement in pruritus and biochemical results. These studies highlight the ineffectiveness of the current treatments, and no treatment other than endoscopic NBD has yet been reported for the management of cholestatic episodes or prevention of recurrences.

Endoscopic NBD elicited a faster remission in this patient, who was otherwise refractory to the other therapy modalities. Stapelbroek et al. (24) reported complete and long-lasting disappearance of pruritus and normalization of serum total bilirubin levels in cholestatic BRIC patients within 24 hours after endoscopic NBD. He proposed that temporary endoscopic NBD should be considered in cholestatic BRIC patients.

Because the first attack lasted nearly six months, we were not expecting the patient to achieve remission quickly after his second attack, but worsening liver functions forced us to establish a faster remission period. Therefore, we tried NBD in addition to the standard medical therapies, and he improved on NBD.

In conclusion, we propose that temporary endoscopic biliary drainage should be considered in cholestatic BRIC patients. We hope that this case report can contribute to the topic, regarding which only a few NBD case experiences have been reported to date.

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