Thyrotoxicosis-Associated Cholestasis in a Patient with Hepatitis B Cirrhosis

Hepatit B Siroz Hastasında Tirotoksikoz ile İlişkili Kolestaz

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Abstract

Abnormalities in liver function tests were reported in association with hyperthyroidism. Intrahepatic cholestasis is one form of this association. Reversal of hyperbilirubinemia upon correction of hyperthyroidism supports the causal relationship. Most reported cases have occurred in patients without previous liver disease. We report a case of marked cholestatic jaundice associated with hyperthyroidism caused by toxic adenoma in a patient with hepatitis B cirrhosis. Serum bilirubin returned to baseline level after correcting hyperthyroidism with radioiodine therapy. Hyperthyroidism should be considered in the differential diagnosis of cholestasis in association with chronic liver disease. *Turk Jem 2008; 12: 99-100*

Key words: Cholestasis, cirrhosis, hyperthyroidism, hepatitis B

Özet

Hipertiroidizm ile ilişkili karaciğer fonksiyon testi bozuklukları bildirilmiştir. Intrahepatik kolestaz bu ilişkinin bir türüdür. Hipertiroidizmin düzelmesi ile hiperbilirubineminin ortadan kalkması nedensel ilişkiyi destekleyen bir bulgudur. Bildirilen vakaların çoğu daha önce karaciğer hastalığı olmayan hastalarda görülmüştür. Burada hepatit B sirozu olan bir hastada toksik adenoma bağlı hipertiroidizmin eşlik ettiği belirgin kolestatik sarılık vakasını sunuyoruz. Hipertiroidizmin radyoaktif iyot tedavisi ile düzeltilmesi sonrasında hastanın serum bilirubin seviyesi bazal değere dönmüştür. Kronik karaciğer hastalığı ile beraber görülen kolestazın ayırıcı tanısında hipertiroidizm gözönüne alınmalıdır. *Turk Jem 2008; 12: 99-100*

Anahtar kelimeler: Kolestaz, siroz, hipertiroidizm, hepatit B

Introduction

Abnormalities of liver function tests (LFT) are frequently reported with hyperthyroidism (1). These include transaminase elevations and intrahepatic cholestasis (1-4). In the case of cholestasis, exclusion of biliary tree obstruction, among other causes of hepatic injury is essential before attributing it to concomitant hyperthyroidism (2). Features indicative of a role of the endocrine disease in the pathogenesis of the cholestatic syndrome are the appearance of jaundice in temporal relation with the clinical onset of thyroid hyperfunction and its disappearance with the amelioration of the hyperthyroidism (1,2). We report a case of marked intrahepatic cholestasis associated with hepatitis B cirrhosis in association with hyperthyroidism caused by toxic adenoma. Cholestatic jaundice responded well to control of hyperthyroidism. Hyperthyroidism may cause deterioration of LFT in patients with no previous liver disease, as well as in patients with chronic liver disease. The return of LFT to baseline values supports the causal relationship.

Case Report

A 43-year-old man presented with progressive jaundice and itching for the previous 3 weeks. There was no history of fever, anorexia, nausea, or abdominal pain. He had lost 6 kg of body weight during the previous 2 months. One year previously, he had been diagnosed with hepatitis B cirrhosis; his current medications were oral lactulose and a β-blocker. Clinically there was deep jaundice, splenomegaly, gynecomastia, and a few spider angiomata over the right arm. The liver was not palpable;

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there was no ascites clinically; and he did not show any manifestations of hepatic encephalopathy. He was observed to have a goiter with a more prominent right lobe, fine hand tremors, sinus tachycardia with a pounding pulse, and an ejection systolic murmur over the precordium. Chest radiograph showed clear lungs and no cardiomegaly.

Laboratory investigations showed serum total bilirubin=320 µmol/L (normal range 3-17); direct bilirubin=197 µmol/L; aspartate aminotransferase (AST)=120 IU/L (0-37); alanine aminotransferase (ALT)=60 U/L (0-45); alkaline phosphatase (ALP)=366 U/L (40-129); γ-glutamyl transpeptidase=96 U/L (15-73), and INR=1.3. Values obtained from his records dated 3 months previously showed total bilirubin=54 µmol/L, direct bilirubin=28 µmol/L, AST=60 IU/L, ALT= 64 U/L, and ALP=120 U/L; these values had been stable for the previous year.

Abdominal ultrasonography showed a normal sized liver with coarse hepatic echotexture and no focal lesions, mild ascites, and splenomegaly with normal gall bladder, common bile duct, and pancreas. Computed tomography showed nodular outline of the liver with no focal lesions, enlarged spleen, minimal ascites, and no evidence of intra- or extra-hepatic biliary dilatation. Endoscopic retrograde cholangiopancreatography was normal. Antibodies to hepatitis A, C, D, and E virus antigens were negative. He tested positive for hepatitis B surface antigen, hepatitis B e-antigen, hepatitis B e-antibody, and hepatitis B surface antibody, but negative for both IgG and IgM hepatitis B core antibodies. HIV antibody was negative. Antinuclear and antimitochondrial antibodies were negative. Alpha-fetoprotein was 36 mcg/L (10-20 mcg/L). The patient declined liver biopsy. Echocardiography showed a hyperdynamic left ventricle with increased flow velocity across the aortic valve, an ejection fraction of 65%, and a normal pulmonary artery pressure. Thyroid function tests showed TSH of 0.005 µIU/mL (0.3-5.0) and T4 of 55 pmol/L (7-21). Thyroid ultrasound showed a large nodule in the right lobe of the thyroid gland, and thyroid scan showed a hot nodule. After excluding right ventricular failure, biliary obstruction, superin fection, and hepatocellular carcinoma, the marked cholestatic jaundice was thought to be caused by thyrotoxicosis. Treatment with radioiodine and with propranolol 20 mg three times daily was started. After two months of therapy, manifestations of hyperthyroidism were controlled. Marked improvement in jaundice and hyperbilirubinemia were seen in conjunction with improved control of hyperthyroidism (Table 1). Serum bilirubin returned to baseline value and remained steady for the following year.

Discussion

Deterioration of previously stable LFTs in a patient with chronic hepatitis B viral infection could be related to viral reactivation (5), superinfection (6), or HIV co-infection (7). Hepatocellular carcinoma may present with hepatic decompensation or obstructive jaundice (8). Hepatitis B reactivation usually presents with elevation in transaminase levels, particularly ALT, and is commonly precipitated by immunosuppression (5). Superinfection on top of hepatitis B may be with hepatitis A, C, D, or E viruses. The development of hepatocellular carcinoma can be excluded by lack of rise of alpha-fetoprotein and absence of hepatic focal lesions (9). Hyperthyroidism is reported to be associated with deterioration of liver function tests as either elevated transaminase levels (1) or findings suggestive of cholestatic jaundice (1,2). Raviolo et al reported 3 cases of cholestasis related to hyperthyroidism with disappearance of cholestasis upon amelioration of hyperthyroidism (2). Hassan et al reported a case of severe cholestatic jaundice that improved after treating hyperthyroidism with radioiodine (3). Gürlek et al reported that at least one LFT abnormality was found in 60% of patients with hyperthyroidism (4). Bellassoued et al reported a case of thyrotoxicosis hepatitis with transaminase elevations and cholestasis that improved with radioiodine therapy (10). Malik et al reported that elevated levels of γ-glutamyl transpeptidase were found in 17% of cases of hyperthyroidism, while hyperbilirubinemia was found in 5% (1). The mechanism of injury appears to be relative hypoxia in the perivenular regions, caused by an increase in hepatic oxygen demand without an appropriate increase in hepatic blood flow. Histologically, there are nonspecific changes of mild lobular inflammatory cellular infiltrate in addition to centrilobular intrahepatic cholestasis (1).

Correction of hyperthyroidism is usually associated with improvement in liver function tests (1,2,10). Malik et al stated that in the vast majority of cases, the hepatic abnormalities associated with hyperthyroidism are reversible following treatment of hyperthyroidism (1). Radioiodine therapy seems to be the best treatment for toxic thyroid nodule (11).

Our case may represent the first report of thyrotoxicosis cholestasis associated with hepatitis B cirrhosis. Hyperthyroidism should be considered in the differential diagnosis of intrahepatic cholestasis occurring in a patient with chronic liver disease.

Table 1. Values of liver function tests and thyroid hormones before and after treatment of hyperthyroidism

		Baseline	Hyperthyroid	Euthyroid*
Bilirubin	(µmol/L)	54 (3-17)	320	63
ALP	(U/L)	120 (40-129)	366	128
AST	(IU/L)	60 (0-37)	120	68
ALT	(U/L)	64 (0-45)	60	40
TSH	(µ IU/L)		0.005 (0.3-5.0)	4.2
T_4	(p mol/L)		55 (11-24)	15.9

*After treatment with radioiodine

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