Concomitant Gilbert’s Syndrome and Thalassemia Trait

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Abstract

A 23 years old male presented with fluctuating jaundice since age of five years. He was diagnosed to have thalassemia trait along with Gilbert’s syndrome. He had disproportionately higher bilirubin concentration for either disorder alone. The importance of the concomitance of these disorders is highlighted.

INTRODUCTION

Gilbert’s syndrome (GS) is a benign, familial disorder due to defect in bilirubin uptake and conjugation. It is characterized by mild unconjugated hyperbilirubinemia, normal values for standard hepatic biochemical tests and normal hepatic histology.1 Rarely, the disorder occurs with some primary haematological disorder such as β-thalassemia minor (thalassemia trait), glucose-6-phosphate dehydrogenase (G-6 PD) deficiency and hereditary spherocytosis.2 These patients can have considerably high serum bilirubin concentration. Here, we describe one such patient having GS and thalassemia trait.

CASE REPORT

A 23 years old male with history of fluctuating jaundice since the age of five years was admitted to the hospital. On questioning, he denied any history suggestive of liver disease. He never received blood transfusion. On examination he was found to have mild pallor, icterus and 4 cms non-tender splenomegaly. No other abnormality was detected on physical examination. He had haemoglobin (Hb) 10.8 g/dl, normal total and differential leucocyte count (TLC/DLC) and normal platelet count. On examination of peripheral blood smear red blood cells (RBC’s) were markedly microcytic and hypochromic. Few target cells were also seen. Mean corpuscular volume (MCV) was 70 fl. On Hb electrophoresis HbA₂ was 4.5%. Hbf was normal. So were serum iron and total iron binding capacity (TIBC). Liver function tests revealed total serum bilirubin 42 µmol/L (2.5 mg/dl) with 31 µmol/L (1.8 mg/dl) as unconjugated type, serum alkaline phosphatase 1.7 µ kat/L (110 U/L) and serum aminotransferases AST and ALT 36 µ kat/L (22 U/L), and 25 µ kat/L (15 U/L), respectively.

The patient was subjected to fasting test by placing on 1255 kj (300 kcl)/day for 48 hours. After which serum bilirubin concentration increased to 105 µmol/L (6.2 mg/dl) with 17 µmol/L (1.0 mg/dl) as conjugated type (major increase in unconjugated bilirubin of 88 µmol/L i.e. 5.2 mg/dl). The rifampicin test was done after one week. Baseline total serum bilirubin was found to be 37 µmol/L (2.2 g/dl) of which 7 µmol/L (0.4 g/dl) was conjugated and 31 µmol/L (1.8 g/dl) unconjugated type. After six hours of rifampicin administration total serum bilirubin increased to 71 µmol/L (4.2 mg/dl) of which 10 µmol/L (0.6 g/dl) was conjugated and 61 µmol/L (3.6 mg/dl) unconjugated (major increase in unconjugated bilirubin).

DISCUSSION

The patient was diagnosed to have thalassemia trait based on profound microcytosis, hypochromia with target cells, mild anaemia, raised HbA₂ and unconjugated hyperbilirubinemia. GS was diagnosed on basis of unconjugated hyperbilirubinemia, normal values of liver function tests and normal hepatic histology. Diagnosis of GS was further confirmed on subjecting the patient to fasting test and rifampicin test.4 These tests are said to be positive if after 48 hours of fasting (caloric restriction to 1255 kj i.e. 300 kcal/day) or six hours after administration of 900 mg rifampicin bilirubin rises by 25 µmol/L (1.5 mg/dl) or more. The major increase should be in unconjugated fraction.

The enzyme uridine diphosphate (UDP) glucuronosyltransferase catalyzes the conjugation of unconjugated bilirubin to its soluble (conjugated) form. The UDP-glucuronosyltransferases have been classified into gene families based on degree of homology between the various protein isoforms. Those that conjugate bilirubin have been designated the UGT-1 family. The molecular bases of GS have been elucidated and found to result from molecular lesions in one of the isoforms of the UDP-glucuronosyltransferase (UGT-1A) gene. Missense mutations of UGT-1A or polymorphic variations in the A (TA)n TATAA motif...
within promoter of the UGT-1A gene have been considered molecular mechanisms those lead to GS. The variations in expression of UGT-1A in patients with GS have been found to be major modifying factors of bilirubin levels in thalassemia trait. Here, we wish to highlight the patients with both GS and thalassemia trait have higher bilirubin concentrations and are more likely to be jaundiced than either defect alone. In a patient, with either disorder, if unconjugated bilirubin is disproportionately high and factors such as fatigue, stress alcohol use and intercurrent illnesses have been ruled out, then investigations should be directed to look for other disorder.

REFERENCES

Announcement

CME on Divices and Interventions in Internal Medicine is organised by Department of Internal Medicine, Sri Ramachandra Medical College and Research Institute, Chennai. Association of Physicians of India, Chennai Chapter, Chennai and Indian Medical Association - Chennai (Course content - Demonstration of practical procedures in Medicine) on March 23, 2003 at Dhanvantri Hall, Above Archana Annexe, SRMC and RI, Chennai.

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