Symptomatic Case of Gilbert’s Syndrome

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ABSTRACT

**Introduction**: Gilbert’s syndrome is a common cause of unconjugated hyperbilirubinemia, but these patients are generally asymptomatic. Herein we are presenting a case of Gilbert’s syndrome.

**Case report**: Patient came with the complaints of intermittent fever, generalised weakness and easy fatigability. He had a family history of similar complaints and was found to have unconjugated hyperbilirubinemia. Complete work up was done to rule out the causes of unconjugated hyperbilirubinemia and was found to be negative and the diagnosis of Gilbert’s Syndrome was made.

**Conclusion**: Reports of Gilbert’s syndrome show associations of disorders like Elliptocytosis and Spherocytosis. But in this rare symptomatic case with a strong family history and presence of unconjugated hyperbilirubinemia, no other associated conditions were found.

**Keywords**: Gilbert’s syndrome, unconjugated hyperbilirubinemia, asymptomatic.

INTRODUCTION

Gilbert syndrome, the most common inherited disorder of bilirubin glucuronidation, is a benign condition that has also been called “Meulengracht disease”, “constitutional hepatic dysfunction” and “familial nonhemolytic jaundice”. It is characterized by recurrent episodes of jaundice and can be triggered by dehydration, fasting, intercurrent diseases and overexertion. The prevalence of Gilbert syndrome has been reported to be between 4 to 16 % in different populations. The hyperbilirubinemia in patients with Gilbert syndrome is typically unconjugated.

CASE REPORT

A 20 year old boy from West Bengal presented with complaints of reduced appetite and generalized weakness since 1 year. He also gave history of intermittent fever for the past 1 year, of mild degree and would reduce on taking antipyretics. Weakness and fatigue was continuously present hindering his normal day to day activities and studies. He also gave history suggestive of postural hypotension. There was no history of alcoholism, hepatitis, drug ingestion or drug abuse. He was born to a non consanguinous parents and his siblings had similar complaints of fatigue with decreased work efficiency. History of his father having similar complaints was also noted.

**Laboratory investigations**

Biochemical findings showed Indirect hyperbilirubinemia (Total Bilirubin - 3.68 mg/dl, Direct Bilirubin - 0.31mg/dl). Liver function tests revealed elevation of serum bilirubin with normal serum Alanine transaminase(ALT), serum alkaline phosphatase(ALP), serum albumin and prothrombin time. Serum bilirubin was predominantly unconjugated.

Urine biochemistry did not detect any bilirubin. This is suggestive of unconjugated bilirubinemia.

Vitamin B12 levels was found to be greater than 2000 pg/ml. Common viral markers which included tests for HIV, HBsAg and HCV were negative. Ultrasonography of abdomen showed features of Splenomegaly. A normal hemoglobin level, peripheral blood film, reticulocyte count and Serum LDH levels (169 IU/L) excluded the possibility of a haemolytic disorder. Coombs Test (Direct and Indirect) were negative. Quantitative estimation of G6PD performed also was found to be normal. Hemoglobin electrophoresis was done to rule out variants of Hemoglobin like HBC which would also present with unconjugated hyperbilirubinemia and was found to be normal.

**DISCUSSION**

In this case, the boy had presented with history of intermittent fever, fatigue and generalised weakness. Laboratory investigations are indicative of high indirect hyperbilirubinemia. Hemolytic disorders, causes for pyrexia of unknown origin which could have also presented with similar clinical picture were excluded by laboratory tests. Hemoglobin electrophoresis was done to rule out variants of Hemoglobin which can also present with features of unconjugated hyperbilirubinemia, and were found to be normal. The only positive finding was unconjugated hyperbilirubinemia, thus confirming the diagnosis of Gilberts Syndrome.

Gilbert syndrome is the result of a defect in the promoter of the gene that encodes the enzyme uridine diphosphoglucuronate - glucuronosyl transferase 1A1 (UGT1A1), which is responsible for the conjugation of bilirubin with glucuronic acid. Unconjugated bilirubin is a lipid-soluble substance. Uridine diphosphate glucuronosyl transferase (UGT) is the enzyme that converts unconjugated bilirubin to conjugated bilirubin monoglucuronide and diglucuronide, thus making it water soluble and facilitates its excretion into the bile. The gene expressing Uridine diphosphate glucuronosyl transferase (UGT) is on chromosome 2, having 5 exons and the promoter region (TATAA box).

Gilbert syndrome manifests only in people who are homozygous for the variant promoter. As a result, its inheritance is more consistent with an autosomal recessive trait. The
mutation responsible for Gilbert syndrome is in the promoter region, upstream to exon 1 of UGT1A1.1,2 The normal sequence of the TATAA element within the promoter is A[TAA]6TAA. Caucasian and black patients with Gilbert syndrome are homozygous for a longer version of the TATAA sequence, A[TAA]7TAA, which causes reduced production of bilirubin-UGT1A1.3

With the exception of intermittent episode of jaundice, most patients with Gilbert syndrome are asymptomatic and have normal physical examination findings. Symptoms of Gilberts syndrome is usually seen when there is associated disorders like Elliptocytosis, Spherocytosis.4,5 In this case though the presence of spherocytosis is not confirmed by classical tests, the normal glucose 6 phosphate dehydrogenase (G6PDH) levels and absence of spherocytes in peripheral smear rules out the above mentioned conditions.

CONCLUSION

Gilberts Syndrome is usually diagnosed by excluding the other causes for elevation in unconjugated bilirubin. Deficiency of the UGT enzyme will decrease the conjugating capacity of the liver and hence the concentration of unconjugated bilirubin increases in the blood. The manifestations usually appear first during adolescence, when alterations in sex steroid concentrations change bilirubin metabolism, leading to increased plasma bilirubin concentrations.5 The Biochemical findings reveals unconjugated hyperbilirubinemia, with total bilirubin levels usually less than 3 mg/dL, however in the conditions when there is predisposition towards increased bilirubin production, the levels may be higher. Nevertheless Gilberts Syndrome is a benign condition, rare in occurrence and has an excellent prognosis. Though they have hyperbilirubinemia life long but are not associated with increased morbidity.

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REFERENCES


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