Case Reports

Persistent Hyperbilirubinaemia with Absence of Urinary Bile Salts and Bile Pigments

Vishrutha S Poojari*, Ira Shah**

Abstract

Gilbert Syndrome is a rare benign condition of abnormal bilirubin conjugation. Patients with Gilbert syndrome are usually asymptomatic except for intermittent episode of unconjugated hyperbilirubinaemia, needing no treatment. We report a case of 14 year old boy with persistent hyperbilirubinaemia otherwise asymptomatic, diagnosed clinically as Gilbert syndrome.

Introduction

Gilbert syndrome is a benign condition of abnormal bilirubin conjugation affecting 4-16% in different population requiring no immediate treatment.[1] Patients usually present with jaundice and no other complaints. Frequency of Gilbert syndrome in African and Indian subcontinent ranges from 10-25%.[2] We present a case of 14 year old boy who presented with isolated hyperbilirubinaemia which was subsequently diagnosed clinically to be Gilbert syndrome.

Case Report

A 14 year old boy presented in October 2015 with jaundice without high coloured urine since July 2015. There was no clay coloured stools or itching. He was investigated for the same and serial liver function tests (LFT) are depicted in Table 1. HBsAg was negative. His urine was negative for bile salts and bile pigments. He had dengue with dengue NS1 antigen positive on serum in August 2015 when his urine bile salts and bile pigments became positive and then again subsequently became negative. On presentation to us, he had jaundice. Systemic examination was normal. Liver function tests (LFT) revealed slightly elevated bilirubin with normal serum transaminases and normal albumin. Ultrasound abdomen showed hepatomegaly with normal echotexture of the liver. Fibroscan was normal. Genetic test could not be done due to non-affordability. He was advised yearly liver function tests.

Table 1: Serial liver function tests of the patient

	July 2015	August 2015	August 2015 with dengue illness	Sept-ember 2015	October 2015	Nove-mber 2015
Total bilirubin (mg/dl)	1.2	1.2	2	1.1	1.6	1.5
Direct bilirubin (mg/dl)	0.6	0.6	0.8	0.6	0.7	0.9
SGOT (IU/L)	26	-	-	-	-	23
SGPT (IU/L)	21	16	13	32	24	17
Total proteins (gm/dl)	-	-	-	-	-	6.8
Albumin (gm/dl)	-	-	-	-	-	4.3
Alkaline phosphatase (IU/L)	-	-	-	-	-	348
GGPT (IU/L)	-	-	-	-	-	18

Discussion

Among the inherited disorder of bilirubin metabolism, Gilbert syndrome (GS) is common.[1] It most commonly affects males due to higher daily bilirubin

*Pediatric Gastroenterology, Hepatology and Nutrition Fellow, **Professor and Head, Pediatric Gastroenterology, Hepatology and Nutrition Fellow, Dept. of Pediatrics, B J Wadia Hospital for Children, Mumbai, India

production and during puberty. The change in sex steroid concentration during adolescence influences bilirubin metabolism, thus increasing the bilirubin levels.[1] Precipitating factors associated with an episode of jaundice are fasting, febrile episode, dehydration, stress, menstruation, haemolysis.[1] Our patient was also an adolescent boy presenting with jaundice with persistent mild hyperbilirubinaemia which got aggravated during dengue fever. His other liver functions were normal. Enzyme responsible for conjugation of glucuronic acid with bilirubin is uridine 5'diphosphoglucuronyl transferase (UGT1A1) enzyme and which converts bilirubin into water-soluble substance. GS can have variable inheritance pattern. When there is change in the promoter region of UGT1A1 gene, homozygous polymorphism A(TA)7TAA which is a TA insertion into promoter designated UGT1A1*28, then it is inherited as autosomal recessive pattern. When caused by a missense mutation UGT1A1 gene, it is inherited as autosomal recessive pattern.[3,4] There are over 100 mutations which are implicated in the causation of this disease resulting in reduction of UGT1A1 enzyme activity to 30% of normal.[1,3] We could not do genetic test in our patient due to non-affordability.

Patients with Gilbert syndrome are usually asymptomatic except for intermittent episode of unconjugated hyperbilirubinaemia usually below 3 mg/dl, with less than 20% conjugated bilirubin level.[1] In combination with haemolytic disease there is significant increase in bilirubin levels noted and thus increased risk for gall stones. Our patient also had bilirubin < 3 mg/dl with absence of bile salts and bile pigments in urine suggestive of indirect hyperbilirubinaemia. There is no specific treatment required for Gilbert syndrome. It is important to avoid unnecessary testing and be cautious towards drug associated toxicity and in co-existing disorder with high bilirubin level wherein phenobarbital can be used as enzyme inducer.[1] Bilirubin is known to have anti-oxidant effect. Individuals with Gilbert syndrome are noted to have low prevalence of ischaemic heart disease compared to general population.[5] Studies have shown that mortality rates observed for the people with Gilberts syndrome are almost half when compared to those without Gilbert syndrome.[6]

Conclusion

Gilbert syndrome should be suspected in any individual with high bilirubin usually < 3 mg/dl with absence of urine bile salts and bile pigments. It is necessary to avoid unnecessary investigation for this benign condition.

References

1. Thoguluva Chandrasekar V, John S. Gilbert Syndrome. [Updated 2017 Nov 29]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2017 Jun. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470200/.
2. Premawardhena A, Fisher CA, Liu YT, et al. The global distribution of length polymorphisms of the promoters of the glucuronosyltransferase 1 gene (UGT1A1): Hematologic and evolutionary implications. Blood Cells Mol Dis. 2003; 31 :98-101.
3. Fretzayas A, Moustaki M, Liapi O, Karpathios T. Gilbert syndrome. *Eur J Pediatr.*

2012; 171: 11-15.
4. Genetics Home Reference. Gilbert syndrome. Available at URL: https://ghr.nlm.nih.gov/condition/gilbert-syndrome. Accessed on 19th Jan 2018
5. Vítek L, Jirsa M, Brodanová M, et al. Gilbert syndrome and ischemic heart disease: a protective effect of elevated bilirubin levels. *Atherosclerosis*. 2002; 160: 449-56.
6. Horsfall LJ, Nazareth I, Pereira SP, Petersen I. Gilbert's syndrome and the risk of death: a population-based cohort study. *J Gastroenterol Hepatol*. 2013; 28:1643-7.