International Journal of Research in Medical Sciences
Singh N et al. Int J Res Med Sci. 2023 Oct;11(10):3906-3908
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20233060

Case Report

Acute pancreatitis and severe hyperbilirubinemia as initial presentation of Gilbert syndrome

Navtej Singh[1], Tarun[1], Jyotsna Singh[2], Arvind[1]*, Laxman Vir Yadav[1], Ashutosh Pandey[1], Vinod Tarfe[1]

[1]Department of General Medicine, Bhagat Phool Singh government medical college for women, Khanpur Kalan, Sonepat, Haryana, India
[2]Department of Anotomy, Government Medical College and hospital, Sector 32, Chandigarh, India

Received: 18 August 2023
Accepted: 14 September 2023

***Correspondence:**
Dr. Arvind,
E-mail: sheoransahab123@gmail.com

ABSTRACT

Gilbert syndrome (GS) is benign, often familial condition characterized by recurrent but asymptomatic mild unconjugated hyperbilirubinemia in the absence of hemolysis or underlying liver disease. The coexistence of GS with other more clinically significant conditions could interfere with their diagnoses. The genetic variation described as GS may affect drug glucuronidation and could potentially precipitate. Gallstones are the commonest ailment affecting the hepato-biliary system. Associated jaundice is usually direct, commonly due to biliary obstructive lesions. Unconjugated hyperbilirubinemia with cholelithiasis is commonly seen with hemolytic disease. In the absence of hemolysis or systemic causes, congenital causes prevail, commonest of which is Gilbert' Syndrome. Here we report a case of 21-year old male who presented to our hospital with complaint of pain abdomen and was diagnosed as gall stone induced pancreatitis which was further diagnosed as GS after genetic testing for UGT1A1 gene polymorphism.

Keywords: GS, Acute pancreatitis, Severe hyperbilirubinemia, UGT1A1 gene polymorphism

INTRODUCTION

Augustine Gilbert and Pierre Lereboullet first described GS, the most common inherited cause of unconjugated hyperbilirubinemia, in 1901. Both autosomal recessive and autosomal dominant patterns have been described. The syndrome is characterized by intermittent jaundice in the absence of haemolysis or underlying liver disease. The hyperbilirubinemia is mild and by definition <6 mg/dl. However, most patients exhibit levels of 3 mg/dl. Considerable daily and seasonal variations are observed and bilirubin level occasionally may be normal in as many as one-third of patients. GS may be precipitated by dehydration, fasting, menstrual periods or stress, such as an intercurrent illness or vigorous exercise. Patients may complain of vague abdominal discomfort and general fatigue for which no cause is found. These episodes resolve spontaneously and no treatment is required except for supportive care.[1] More elevated values are associated with stress, fatigue, alcohol use, reduced caloric intake and concomitant illness.[3] Here we report a case of GS who first time presented to our hospital with complaint of pain abdomen and was diagnosed as gall stone induced pancreatitis.

CASE REPORT

A 21-year old male presented to emergency department of our hospital with chief complaint of pain abdomen, yellowish discoloration of eyes and generalized weakness from 1 week. Pain in abdomen was in epigastric region and right hypochondrium which was radiating to back. Patient was having history of slight yellowish discoloration of eyes from childhood for which he was never evaluated and was told that it is natural by a quack.

Yellowish discoloration started increasing from previous 1 week. Patient was not having any history of any chronic disease like hypertension, diabetes mellitus, thyroid disorder, asthma, tuberculosis etc. On presentation patient blood pressure was 128/84 mmHg, pulse rate was 98 beats/minute, temperature was 98.6^0 F, SpO_2 was 99% on room air, RBS was 122 mg/dl. Patient was not having any history of drug intake. Patient was non-alcoholic, non-smoker, vegetarian by diet. Patient was not having any history of allergy. Patient was not having any family history of similar disease. On examination patient was having tenderness in epigastric region and patient spleen was palpable 3 cm below subcostal margin. Patient was getting relief on bending forward. Abdomen was normal in structure and shape and there was no other visible abnormality found. Patient was icteric on examination. Patient higher mental function were intact. There was no abnormality found in respiratory system, central nervous system and cardiovascular system. Patient was having negative tests for hepatitis (A, B, C, D, E), HIV, Epstein Barr virus, cytomegalovirus. Patient hemoglobin-12.3 gm%, total leukocyte count-9000/mm^3, platlet count-1.98 lakh/mm^3, retic count-0.6%. Total bilirubin was 33.9 mg/dl out of which conjugated bilirubin was 9.0 mg/dl and unconjugated bilirubin was 24.9 mg/dl. Patients SGOT-78 IU/l (normal value <50 IU/L), SGPT-56 IU/L (normal value <50 IU/L), alkaline phosphatase-113 IU/l (normal value 39-117 IU/L), prothrombin time-12.1 sec, INR- 1.06, serum amylase-570.2 IU/L (normal value <120 IU/l), serum lipase- 642.7 IU/l (normal value <160 IU/l), Renal function test and total protein level were within normal limit. Patient's lipid profile was within normal range. All tests done for hemolytic anemia were within normal range.

Patient's ultrasonography of abdomen showed multiple gall bladder stones and splenomegaly. Liver size was normal, grade 1 fatty changes were present. Patients CECT abdomen showed Hepatic steatosis, cholelithiasis, acute pancreatitis, splenomegaly and mesenteric lymphadenopathy as shown in Figure 1-3. Patient MRCP was not suggestive of any obstruction.

UGT1A1 gene polymorphism test (nucleotide TA repeat PCR fragment analysis).

Table 1: UGT1A1 gene polymorphism test.

TA repeats	UGT1A1 genotype
7/7	UGT1A1*28/*28

Remarks-patient with 2 alleles each with 7 TA repeat (7/7 homozygous) demonstrate severely reduced glucuronidation activity, with about 50% risk of severe toxicity and significant risk for grade 4 neutropenia or severe diarrhea following irinotecan treatment.

After all necessary investigations patient was diagnosed as a case of GS with gall stone induced acute pancreatitis. All necessary investigations were done to rule out hemolytic anemias. Patient was kept nill per oral for 24 hours then was started on liquid diet and then to semisolid and solid diet gradually. Patient was started on ursodeoxycholic acid and phenobarbitone. Total bilirubin levels decreased to 5 mg/dl within 1 week. Patient relieved symptomatically and was discharged after telling future drug precautions and necessary counselling was done. Surgery consultation was advised for cholecystectomy.

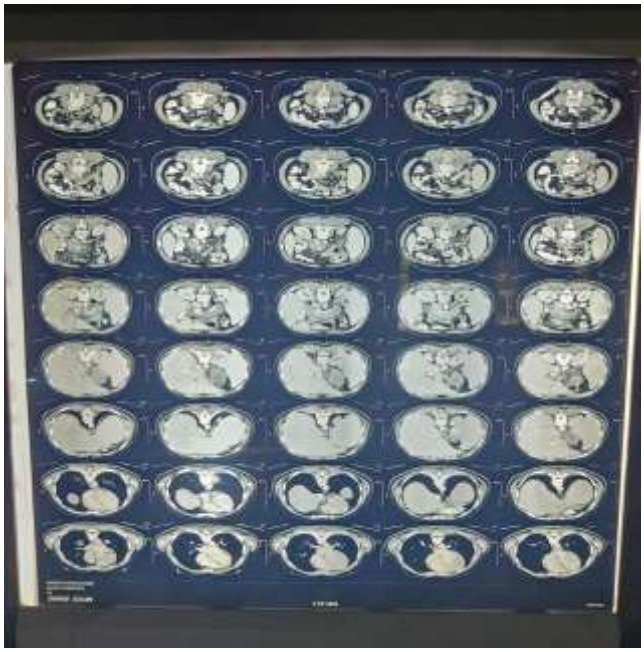

Figure 1: Patients CECT abdomen showed hepatic steatosis, cholelithiasis, acute pancreatitis, splenomegaly and mesenteric lymphadenopathy.

Figure 2: Patients CECT abdomen showed hepatic steatosis, cholelithiasis, acute pancreatitis, splenomegaly and mesenteric lymphadenopathy.

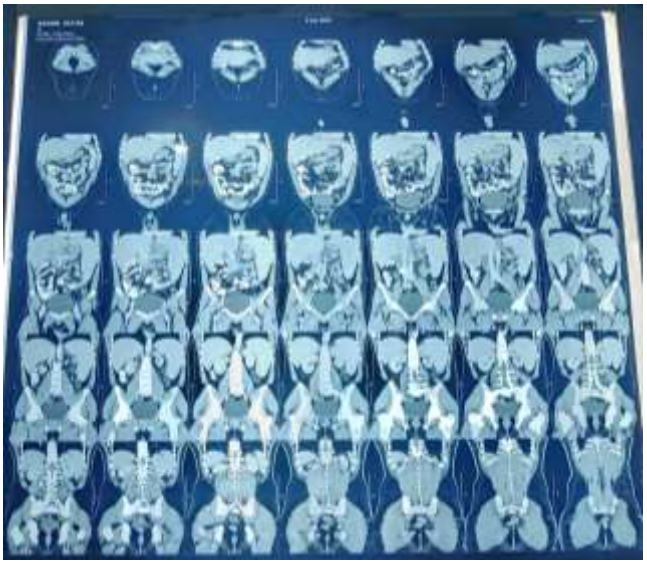

Figure 3: Patients CECT abdomen showed hepatic steatosis, cholelithiasis, acute pancreatitis, splenomegaly and mesenteric lymphadenopathy.

DISCUSSION

Gilbert's syndrome is an inherited disorder of hepatic bilirubin metabolism occurring in the population with a frequency range from 2-13%. It causes a mild chronic unconjugated hyperbilirubinemia in otherwise healthy people. Screening for liver disease or hemolysis reveals no pathological finding, but the hepatic glucuronidation capacity is reduced by 70%. It is caused by a mutation of the specific UDP glucuronyl transferase conjugating bilirubin with glucuronic acid resulting in a reduced activity of this enzyme. It is crucial to establish a correct diagnosis and differentiate this syndrome from serious disorders of the liver tissue.[3] It is important to be aware of GS in patients presenting as gallstones with unconjugated hyperbilirubinemia. A prudent approach can avoid unnecessary and repeated investigations. Additionally, an informed consent should be obtained for persistent and fluctuating jaundice despite uneventful surgery owing to GS, as it can avoid future confusion. We recommend performing genetic testing for GS on "high-risk" patients suspected to harbor the condition; namely the middle-aged male patient with persistent unconjugated hyperbilirubinemia in whom all other contributory factors have been ruled out. This will not only improve the quality of practice and patient care, but reduce health care costs by avoiding unnecessary and invasive investigations.[4] Any stress can aggravate the symptoms of Gilbert's syndrome e.g. prolonged fasting, surgery, infection, exercise, fatigue, alcohol intake and menstruation.[3] Individuals with the 7TA/7TA genotype have been reported to undergo cholecystectomy for pigment gallstones much more frequently than those with the 6TA/6TA or 6TA/7TA genotypes.[5] Therapy of symptomatic cholelithiasis is surgical and in uncomplicated cases the laparoscopic approach is preferred and widely adopted. Symptoms and signs of cholelithiasis in our patient were quite characteristic.[6]

CONCLUSION

Gilbert's syndrome should be considered as a cause of recurrent and persistent unconjugated hyperbilirubinemia in the middle-aged male patient presenting with cholelithiasis. Genetic testing with PCR is diagnostic and allows patient counselling. In the light of above case, if a patient comes with severe hyperbilirubinemia and cholelithiasis in the absence of hemolysis or underlying liver disease; Gilbert syndrome should be entertained in differential diagnosis of unconjugated hyper-bilirubinemia, being the most common inherited cause. It has no deleterious associations and excellent prognosis, and those who have it can lead normal lifestyle.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Manandhar SR, Gurubacharya RL, Baral MR, Manandhar DS. A case report of Gilbert Syndrome. Kathmandu University Med J. 2003;1(3):187-9.
2. Radu P, Atsmon J. Gilbert's Syndrome-Clinical and Pharmacological Implications. IMAJ. 2001;3:593-8.
3. Chandra A, Banavaliker JN, Dixit RM. Gilbert's syndrome. Anaesth Pain Intensive Care. 2012;16(2):195-9.
4. Kumar S, Jha S, Pandey A, Madhavan S, Kumar D, Chauhan S et al. Gallstone Disease with Unconjugated Hyperbilirubinemia: Clinical Approach to Gilbert's Syndrome. J Surgical Sci. 2019;6(2):19.
5. Radoi V, Ursu R, Poenaru E, Arsene C, Bohiltea C, Bohiltea R. Frequency of the UGT1A1*28 Polymorphism in a Romanian Cohort of Gilbert Syndrome Individuals. J Gastrointestin Liver Dis. 2017;26(1):25-8.
6. Radlović V, Golubović Z, Leković Z, Dučić1 S, Radlović N, Jovanović B et al. Gilbert syndrome as a risk factor for the development of cholelithiasis in children. Srp Arh Celok Lek. 2023;151(3-4):186-9.

Cite this article as: Singh N, Tarun, Singh J, Arvind, Yadav LV, Pandey A, Tarfe V. Acute pancreatitis and severe hyperbilirubinemia as initial presentation of Gilbert syndrome. Int J Res Med Sci 2023;11:3906-8.