

Dubin-Johnson syndrome coexisting with glucose-6-phosphate dehydrogenase deficiency presenting after acute viral hepatitis

Laima Alam¹, Jehangir Ahmed², Asma Asghar³, Mafaza Alam⁴

Abstract

Dubin-Johnson syndrome presents as asymptomatic recurrent hyperbilirubinemia, while Glucose-6-Phosphate-Dehydrogenase-deficiency as acute haemolytic anaemia. We present a case with coexisting Dubin-Johnson syndrome and Glucose-6-Phosphate Dehydrogenase deficiency unmasked by acute viral hepatitis E.

Keywords: Dubin Johnson syndrome, Glucose-6-Phosphate Dehydrogenase Deficiency, haemolytic anaemia, hyperbilirubinemia

<https://doi.org/10.5455/JPMA.45538>

Introduction

Dubin-Johnson-syndrome is a rare autosomal-recessive condition, characterised by recurrent, benign conjugated hyperbilirubinaemia secondary to defective bilirubin secretion with accumulation of dark pigment in hepatocytes,¹ manifesting in early adulthood usually during inter-current illness, oral contraceptive pills and pregnancy,² with most of the patients being asymptomatic and having normal life spans. G6PD deficiency is an X-linked-recessive disorder with acute haemolysis in response to oxidative stresses such as infections and drugs like primaquine, salicylates, sulfonamides, etc. and fava beans.³ A case of Dubin-Johnson syndrome with Hereditary Spherocytosis⁴ and another with G6PD deficiency⁵ has been reported. To the best of our knowledge, no case with co-existing Dubin-Johnson syndrome and G6PD-deficiency has been reported from Pakistan.

Case Report

A 28-year-old male, with no history of drugs or alcohol intake, presented with malaise, lethargy and yellowing of sclera on August 23, 2017 at the Gastroenterology outpatient department of Military Hospital, Rawalpindi.

.....
¹⁻³Department of Gastroenterology, Pak Emirates Military Hospital Rawalpindi, Pakistan; ⁴Department of Operative Dentistry, Armed Forces Institute of Dentistry, Pakistan.

Correspondence: Laima Alam. e-mail: laima_alam@yahoo.com

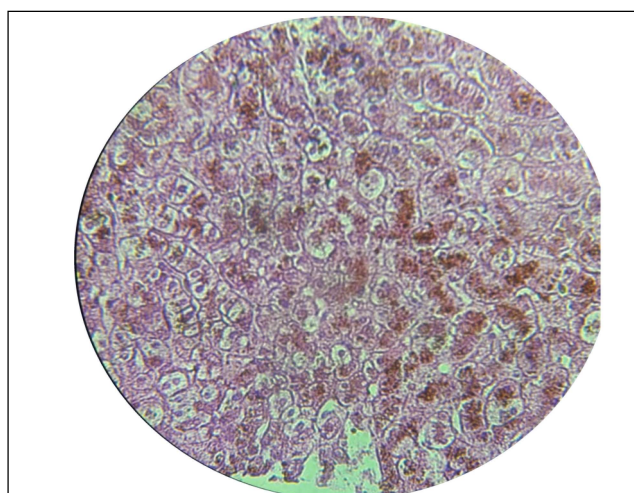


Figure: Microscopic examination of liver biopsy specimen. Liver biopsy showing intact portal and lobular architecture, dense hepatocellular pigment deposition specially concentrated in centrilobular area with no necrosis or ductular inflammation.

Laboratory tests showed a picture of mixed hyperbilirubinemia (Total bilirubin 148umol/L, direct 90umol/L, indirect 58umol/L), mildly raised transaminases (AST 56-IU/L, ALT 70-IU/L), normal Alkaline Phosphatase, Gama Glutamyl Transpeptidase (GGT), International Normalisation ratio (INR) 1, Albumin (40g/L), Haemoglobin at 11 and a reticulocyte count of 4.5% with a negative Direct Coomb's test. Further, investigations confirmed G6PD deficiency with quantitative G6PD levels of only 3.3g/units (explaining the high retic count) and acute viral hepatitis secondary to Hepatitis E Virus (anti HEV IgM positive). The patient was given symptomatic care and was discharged after detailed counselling. On regular follow up, he showed little change in his bilirubin over a period of six months, though transaminases (AST 32-IU/L, ALT 44-IU/L) and retic count (2.5%) normalised, and he lost IgM for HEV. Autoimmune profile (ANA, ASMA, ALKM, AMA), iron and copper studies (Ceruloplasmin, Transferrin saturation, Ferritin) were normal. Viral serologies, using HBsAg, Anti HCV, anti-HAV IgM, HIV were negative and so was the PCR for CMV, EBV and HSV. Abdominal ultrasonograph was normal. A liver biopsy showed intact portal and lobular architecture,

dense hepatocellular pigment deposition specially concentrated in centrilobular area with no necrosis or ductular inflammation suggesting DJS (Figure) that was unmasked by acute viral hepatitis.

Since no active management is required for both the disorders, he was followed up for a year with his bilirubin slowly settling (66 μ mol/L) and was provided with reinforcement of preventive measures.

Discussion

DJS is categorised as a rare disease by the Office of Rare Disease (ORD) of National Institute of Health (NIH).⁶ There is complete absence of the canalicular multispecific organic anion transporter (CMOAT), the gene for which is localised to chromosome 10q 24.⁷ In DJS urinary coproporphyrin excretion is abnormal; though total urinary coproporphyrin is normal, coproporphyrin isomer I is over 80%, while in normal individuals 75% is coproporphyrin isomer III.⁸

In this case, G6PD deficiency and Dubin-Johnson syndrome co-existed, both of which were unmasked by acute viral hepatitis secondary to HEV. Since the patient had deranged Liver Function Tests and a high retic count, the diagnosis of both G6PD deficiency and acute viral hepatitis was readily established but the prolonged asymptomatic hyperbilirubinaemia couldn't be explained by the aforementioned diseases. As autoimmune profile, iron and copper studies, other viral serologies and ultrasound were normal, liver biopsy was performed and the final diagnosis of co-existing DJS was established.

Our patient had no previous medical record of hyperbilirubinaemia and, therefore, the time duration of asymptomatic recurrent hyperbilirubinemia could not be extrapolated in retrospect as the jaundice was only noticed after an inter-currant illness. Both G6PD deficiency and DJS require no therapy and only reassurance and preventive measures.⁹

Conclusion

To the best of our knowledge, no such case with co-existing Dubin-Johnson syndrome and G6PD deficiency has been reported from Pakistan. Patients whose biopsy findings support the diagnosis of DJS should be offered urinary coproporphyrin I and III, but since our set-up lacked the availability of the test, biopsy was considered as a diagnostic tool.

Disclaimer: None.

Conflict of interest: None.

Funding disclosure: None.

Consent: The patient signed a written informed consent for using any data for research and educational purposes. Also, ethical committee letter was duly taken for this case report.

References

1. Erlinger S, Arias I, Dhumeaux D. Inherited Disorders of Bilirubin Transport and Conjugation: New Insights Into Molecular Mechanisms and Consequences. *Gastroenterology*. 2014; 146:1625-38.
2. Javitt N. History of hepatic bile formation: old problems, new approaches. *Adv Physiol Educ*. 2014; 38:279-85.
3. Stincone A, Prigione A, Cramer T, Wamelink M, Campbell K, Cheung E et al. The return of metabolism: biochemistry and physiology of the pentose phosphate pathway. *Biol Rev*. 2014; 90:927-63.
4. Robert D. Christensen, Hassan M. Yaish, Patrick G. Gallagher. A Paediatrician's Practical Guide to Diagnosing and Treating Hereditary Spherocytosis in Neonates. *Pediatrics*. 2015; 135: 1107-14.
5. Zamir D, Groisman G, Zamir C, Sternberg E, Luchtman M, Alfisi R, et al. Severe jaundice in a gunshot casualty due to the coexistence of Dubin-Johnson and glucose-6-phosphate dehydrogenase deficiency. *J Clin Gastroenterol*. 1999; 28:383-5.
6. Wu L, Zhang W, Jia S, Zhao X, Zhou D, Xu A, et al. Mutation analysis of the ABCC2 gene in Chinese patients with Dubin Johnson syndrome. *Exp Ther Med*. 2018; 4201-6.
7. Gupta A, Tiwari P, Sachdeva P. A Case of Dubin-Johnson Syndrome in Pregnancy. [Online] [Cited 20 April 2019]. Available from: URL: <https://www.cureus.com/articles/17643-a-case-of-dubin-johnson-syndrome-in-pregnancy>.
8. Kularatnam GAM, Warawitige D, Vidanapathirana DM, Jayasena S, Jasinge E, de Silva N, et al. Dubin-Johnson syndrome and intrahepatic cholestasis of pregnancy in a Sri Lankan family: a case report. *BMC Res Notes*. 2017; 10:487.
9. Memon N, Weinberger BI, Hegyi T, Aleksunes LM. Inherited disorders of bilirubin clearance. *Pediatr Res*. 2016; 79:378-86.