EJCRIM
European Journal
of Case Reports
in Internal Medicine

BILE CAST NEPHROPATHY (CHOLEMIC NEPHROPATHY) ASSOCIATED WITH HEPATITIS A-INDUCED ACUTE LIVER FAILURE AND HAEMOLYSIS IN A PATIENT WITH GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY

Ali Hamdan[1] Johny Salem[2], Karam Karam[2], Maria Ziadeh[1], Pierre Hani[2]

[1] Department of Internal Medicine, Faculty of Medicine, University of Balamand, Dekwaneh-Beirut, Lebanon
[2] Department of Gastroenterology, Faculty of Medicine, University of Balamand, Dekwaneh-Beirut, Lebanon

Corresponding author's e-mail: Drpierrehani@gmail.com

Received: 25/11/2024
Accepted: 24/12/2024
Published: 27/01/2025

Conflicts of Interests: The Authors declare that there are no competing interests.
Patient Consent: The authors certify that they have obtained the appropriate patient consent form. On the form the patient has given their consent for their images and other clinical information to be reported in the case.
This article is licensed under a Commons Attribution Non-Commercial 4.0 License

How to cite this article: Hamdan A, Salem J, Karam K, Ziadeh M, Hani P. Bile cast nephropathy (cholemic nephropathy) associated with hepatitis A-induced acute liver failure and haemolysis in a patient with glucose-6-phosphate dehydrogenase deficiency. *EJCRIM* 2025;**12**:doi:10.12890/2025_005064

ABSTRACT

Introduction: The hepatitis A virus (HAV) is a common cause of acute hepatitis, while glucose-6-phosphate dehydrogenase (G6PD) deficiency is a widespread enzyme disorder that predisposes individuals to haemolysis and hyperbilirubinemia. We report a case of a G6PD-deficient patient with hepatitis A-induced acute renal failure (ARF), highlighting the role of plasmapheresis and haemodialysis in management.

Case description: A 40-year-old male with G6PD deficiency and hypertension was transferred for further care after presenting with fever, diarrhoea and jaundice. Laboratory results showed severe haemolysis and elevated bilirubin (70 µmol/l); hepatitis A serology was positive. The patient developed acute liver failure and ARF, with creatinine reaching 7.3 mg/dl. Plasmapheresis and haemodialysis were initiated, leading to stabilisation of renal function and a significant decrease in bilirubin by six weeks post-discharge.

Discussion: G6PD deficiency increases the risk of haemolysis, especially during infections such as hepatitis A. This can lead to severe hyperbilirubinemia and complications including bile cast nephropathy. In this case, plasmapheresis effectively reduced bilirubin and inflammatory mediators, while haemodialysis addressed renal dysfunction. Together, these therapies were crucial in stabilising renal function.

Conclusion: Bile cast nephropathy is an important cause of kidney injury in severe hyperbilirubinemia. This case highlights the effectiveness of plasmapheresis and haemodialysis in managing the condition and supporting renal recovery, especially in the absence of established treatment guidelines.

KEYWORDS

Haemolysis, renal failure, hepatitis A, glucose-6-phosphate dehydrogenase deficiency, bile cast nephropathy

EFIM
European Federation of Internal Medicine

Publisher
smc media srl

LEARNING POINTS

- Bile cast nephropathy is a significant yet underrecognised cause of acute kidney injury, often associated with severe hyperbilirubinemia in the setting of acute liver failure.
- In this case, glucose-6-phosphate dehydrogenase (G6PD) deficiency combined with hepatitis A-induced haemolysis led to elevated bilirubin levels, contributing to kidney injury.
- This case highlights the importance of extracorporeal therapies in managing bile cast nephropathy and promoting renal function recovery, particularly in the absence of standard treatment guidelines.

INTRODUCTION

The hepatitis A virus is one of the most common causes of acute hepatitis infection worldwide, estimated by the WHO to infect approximately 1.5 million people each year[1]. Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most common human enzyme defect, affecting over 400 million people worldwide. In adults, common symptoms and examination findings of G6PD deficiency include those of haemolytic anaemia or possibly red blood cell sequestration by the spleen[2]. Because hepatitis A infection in a patient with G6PD deficiency presents much more severe clinical symptoms, G6PD enzyme should be examined in patients with triggering factors of haemolysis such as hepatitis A infection, culminating to possible acute liver failure and concomitant acute renal failure (ARF)[3]. We report a case highlighting the role of plasmapheresis and haemodialysis in a G6PD deficient patient presenting with hepatitis A related ARF.

CASE DESCRIPTION

This is a case of a 40-year-old male known to have G6PD deficiency and hypertension, who was transferred from another institution to our emergency room for the continuation of care. He was known to have G6PD deficiency and was diagnosed with hepatitis A-induced haemolysis and secondary acute liver and kidney failure.

The history started six days prior to presentation, when the patient was admitted to another hospital with symptoms of fever, diarrhoea and jaundice. Initial laboratory tests revealed a white blood cell count of 33,000/µl, haemoglobin level of 7 g/dl and creatinine level of 2.35 mg/dl. Liver function tests showed total bilirubin 70 µmol/l, direct bilirubin 7 µmol/l, serum glutamate-pyruvate transaminase 1467 U/l, serum glutamic-oxaloacetic transaminase 316 U/l, alkaline phosphatase 149 U/l and gamma-glutamyl transferase 119 U/l. International normalised ratio (INR) was 8.2, and urinalysis showed bilirubin 4+. Hepatitis A virus serology was positive. During his stay at the other institution, the patient received multiple units of fresh frozen plasma.

On day six of his hospitalisation, the patient was transferred to our facility for ongoing care. On arrival, his laboratory results were as follows: white blood cell count 17,000/µl, haemoglobin 4.5 g/dl, platelet count of 378, INR 1.3, creatinine 7.3 mg/dl, C-reactive protein 41 mg/l, total bilirubin 25 µmol/l, direct bilirubin 15 µmol/l, amylase 1,100 U/l, lipase 689 U/l, serum glutamate-pyruvate transaminase 92 U/l, serum glutamic-oxaloacetic transaminase 60 U/l and gamma-glutamyl transferase 190 U/l. Hepatitis A IgM was positive at 9.47.

A CT scan of the chest, abdomen and pelvis, performed without contrast, revealed bilateral lung fields with scattered ground glass opacities and nodular infiltrates, consistent with an infectious process. Mild bilateral pleural effusion and partial consolidation of the lower lobes were also noted. The liver was enlarged, measuring around 18 cm with mild perihepatic and perisplenic ascites and moderate free intraperitoneal fluid. The fluid was surrounding the gallbladder which was noted as collapsed with reactive wall

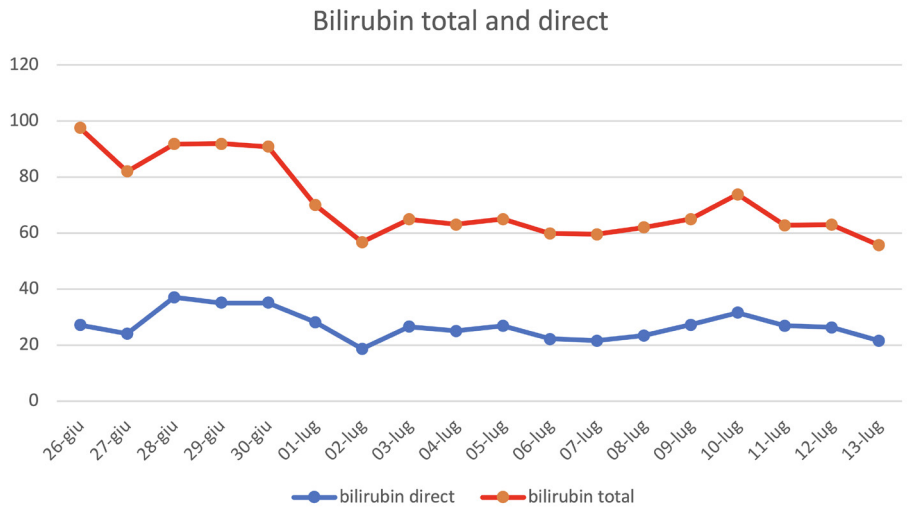


Figure 1. Variation in creatinine levels with time.

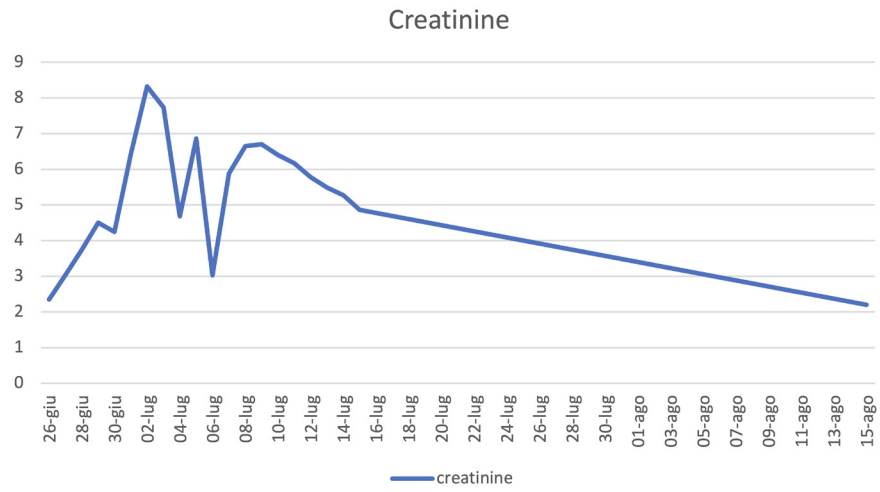


Figure 2. Variation in bilirubin levels with time.

thickening due to ascites. The kidneys were normal in size and show bilateral fatty stranding.

The patient was initiated on piperacillin/tazobactam 2.25 g every 8 hours, albumin 1 vial three times daily and received two units of packed red blood cells. On day two, a Kimal® catheter was placed, and first session of plasmapheresis was done. The patient underwent haemodialysis and a second session of plasmapheresis by day three of admission. Due to the high bleeding risk, a renal biopsy was deferred. On days four and six, the patient received additional haemodialysis. As seen in *Fig. 1*, by day eleven his creatinine levels had stabilised and began to trend downward. He was transferred to the regular floor, with antibiotics discontinued.

The patient was discharged on day 16, with follow-up laboratory tests planned post-discharge. As seen in *Fig. 2*, after discharge, his bilirubin had decreased to 3 µmol/l by six weeks post-discharge.

DISCUSSION

G6PD deficiency, a common hereditary disorder, impairs the antioxidant defence in red blood cells (RBCs). G6PD catalyses the first step of the pentose phosphate pathway, producing nicotinamide adenine dinucleotide phosphate (NADPH), which is essential for regenerating reduced glutathione. This protects RBCs from oxidative damage caused by free radicals. Without sufficient G6PD glutathione is depleted, leaving RBCs vulnerable to oxidative stress and resulting in haemolysis[2,4].

Patients with G6PD deficiency are typically asymptomatic unless exposed to certain medications, infections or foods. While severe haemolysis is uncommon, it is more frequently observed when acute hepatitis A infection occurs simultaneously. Viral infections themselves may trigger significant haemolysis in G6PD-deficient individuals. Additionally, G6PD deficiency can limit the repair of damaged hepatocytes in viral hepatitis, leading to a more severe clinical course[3,5,6].

Acute kidney injury in the context of acute liver failure can arise from various aetiologies, with bile cast nephropathy being an underdiagnosed cause. This condition typically occurs when bilirubin levels exceed 20 mg/dl, driven by a multifactorial pathophysiology with most case reports showing a correlation between rising bilirubin levels and worsening kidney function[7,8].

In our case, the patient with a history of G6PD deficiency presented with acute hepatitis A infection, resulting in severe liver failure, profound haemolytic anaemia and marked hyperbilirubinemia (total bilirubin reached 70 µmol/l). The patient's elevated bilirubin levels were accompanied by a concurrent rise in creatinine, raising suspicion of bile cast nephropathy. This diagnosis was considered in the absence of nephrotoxic drug exposure, hypovolaemia or evidence of structural kidney disease. Kidney biopsy remains the gold standard test for the diagnosis of bile cast nephropathy; however, it is often challenging in the context of ongoing liver failure and coagulopathy[7]. In our case this limitation, coupled with the high risk of bleeding (INR 8.2 before fresh frozen plasma transfusions), prevented us from performing the biopsy.

The management of bile cast nephropathy remains challenging, with no established protocol. Treatment is primarily focused on addressing the underlying cause of hyperbilirubinemia to prevent further kidney damage[7]. In cases of liver failure with non-obstructive jaundice, such as in our patient, some studies have demonstrated the effectiveness of extracorporeal therapies such as plasmapheresis and haemodialysis[9,10].

Plasmapheresis was initiated early to our patient after presentation to our institution on day two, and repeated on day three, as a targeted measure to reduce the circulating levels of bilirubin and haemolysis-related inflammatory mediators. That was complemented by haemodialysis, which addressed metabolic derangements and fluid overload. This combination of intervention was critical in creating a favourable environment for renal recovery, as evidenced by the subsequent stabilisation and gradual decline in the patient's creatinine levels by day 11 and later in the follow-up period.

CONCLUSION

Bile cast nephropathy is a significant yet underrecognised cause of acute kidney injury, often associated with severe

hyperbilirubinemia in the setting of acute liver failure. In this case, G6PD deficiency combined with hepatitis A-induced haemolysis led to elevated bilirubin levels, contributing to kidney injury. This case highlighted the importance of extracorporeal therapies in managing bile cast nephropathy and promoting renal function recovery, particularly in the absence of standard treatment guidelines.

REFERENCES

1. Girish V, Grant LM, John S.Hepatitis A. StatPearls. 4 July 2023. Accessed 9 September 2024. https://www.ncbi.nlm.nih.gov/books/NBK459290/
2. Richardson SR, O'Malley GF. Glucose-6-phosphate dehydrogenase deficiency. StatPearls. 26 September 2022. Accessed September 9, 2024. https://www.ncbi.nlm.nih.gov/books/NBK470315/
3. Bajpai M, Kakkar B, Patale D. Role of high-volume plasma exchange in a case of a G6PD deficient patient presenting with HAV related acute liver failure and concomitant acute renal failure. *Transfus Apher Sci* 2019;**58**:102677.
4. Eren Durmuş M, Yalçın İŞ, Şahintürk Y. G6PD deficiency resulting in massive hemolysis and acute renal failure: a case report. *DAHUDER MJ* 2021;**1**:25–29.
5. Bajpai M, Kakkar B, Patale D. Role of high-volume plasma exchange in a case of a G6PD deficient patient presenting with HAV related acute liver failure and concomitant acute renal failure. *Transfus Apher Sci* 2019;**58**:102677.
6. Chau TN, Lai ST, Lai JY, Yuen H. Haemolysis complicating acute viral hepatitis in patients with normal or deficient glucose-6-phosphate dehydrogenase activity. *Scand J Infect Dis* 1997;**29**:551–553.
7. Somagutta MR, Jain MS, Pormento MKL, Pendyala SK, Bathula NR, Jarapala N, et al. Bile cast nephropathy: a comprehensive review. *Cureus* 2022;**14**:e23606.
8. Patel J, Walayat S, Kalva N, Palmer-Hill S, Dhillon S. Bile cast nephropathy: a case report and review of the literature. *World J Gastroenterol* 2016;**22**:6328–6334.
9. Ravi R, Suthar K, Murlidharan P, Lakshmi K, Balan S, Safeer M. Bile cast nephropathy causing acute kidney injury in a patient with nonfulminant acute hepatitis A. *Saudi J Kidney Dis Transpl* 2018;**29**:1498–1501.
10. Luciano RL, Castano E, Moeckel G, Perazella MA. Bile acid nephropathy in a bodybuilder abusing an anabolic androgenic steroid. *Am J Kidney Dis* 2014;**64**:473–476.