JGH Open Open Access An open access journal of gastroenterology and hepatology JGHF

CASE REPORT OPEN ACCESS

Rapid Resolution of Anabolic Androgenic Steroid-Induced Refractory Pruritus and Bile Cast Nephropathy With Therapeutic Plasma Exchange

Samuel Wong[1] | Danny Con[1] | Avik Majumdar[1,2]

[1]Liver Transplant Unit, Department of Gastroenterology, Austin Health, Heidelberg, Victoria, Australia | [2]Department of Medicine, Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne, Melbourne, Victoria, Australia

Correspondence: Samuel Wong (samuelkangyouwong@gmail.com)

Received: 5 November 2024 | **Revised:** 3 February 2025 | **Accepted:** 25 February 2025

Keywords: anabolic steroids | bile cast nephropathy | bland cholestasis | drug-induced liver injury | plasma exchange

ABSTRACT

The proportion of non-paracetamol drug-induced liver injury (DILI) is increasing in Australia and other Western countries. Androgenic anabolic steroids (AAS) commonly cause a bland cholestasis that can persist for months despite withdrawal. A 35-year-old male presented with progressive painless jaundice associated with pruritus, nausea, loss of weight, dark urine, and pale stools. He had recently commenced AAS; DILI was suspected and confirmed on biopsy. His pruritus was refractory to medical therapy, and PLEX was commenced. He also developed renal failure from bile cast nephropathy (BCN) and required hemodialysis. At 10 weeks post-discharge, his pruritus and jaundice were significantly improved, and his renal function had completely recovered. The case adds to the growing evidence that PLEX can be used safely and effectively to treat cholestatic pruritus and BCN.

1 | Introduction

The proportion of non-paracetamol drug-induced liver injury (DILI) is increasing in Australia and other Western countries [1, 2]. Of these, AAS-DILI is becoming more prevalent, especially due to increasing use outside of the professional community [2]. AAS commonly cause an acute cholestatic syndrome (bland cholestasis) which can last several months despite withdrawal of the offending agent [3]. Most make a full recovery without needing transplantation. Therapeutic plasma exchange (PLEX) has been shown to be an effective treatment for hyperbilirubinaemia [4–6]. We present a case where PLEX was used in the treatment of anabolic steroid DILI complicated by debilitating pruritus and renal failure due to bile cast nephropathy (BCN).

2 | Clinical Record

A 35-year-old male was admitted with an 8-day history of progressive painless jaundice. This was associated with a 1-month history of worsening debilitating pruritus, nausea, loss of weight, dark urine, and pale stools. He was previously successfully treated for chronic hepatitis C and had no other medical or surgical history. He was a non-smoker and non-drinker. He had recently completed a 4-week course of amoxicillin for a dental abscess. He admitted to commencing daily anabolic steroids, human growth hormone, and anastrazole for bodybuilding 4 months prior.

Physical examination revealed deep jaundice but was otherwise unremarkable, with no stigmata of chronic liver disease. Laboratory investigations were as follows: bilirubin 728 μmol/L (conjugated bilirubin >170 μmol/L (maximum laboratory value), unconjugated bilirubin was undetectable), alkaline phosphatase (ALP) 173 IU/L, and gamma glutamyltransferase (GGT) 73 IU/L, with normal liver transaminases and coagulation studies. Hemolysis screen showed a low haptoglobin (<0.3 g/L) with marginally raised LDH 256 units/L and a negative DAT. He had normal G6PD testing. Viral serologies (Hepatitis A, Hepatitis B, hepatitis C, CMV, and EBV) were consistent with a past history

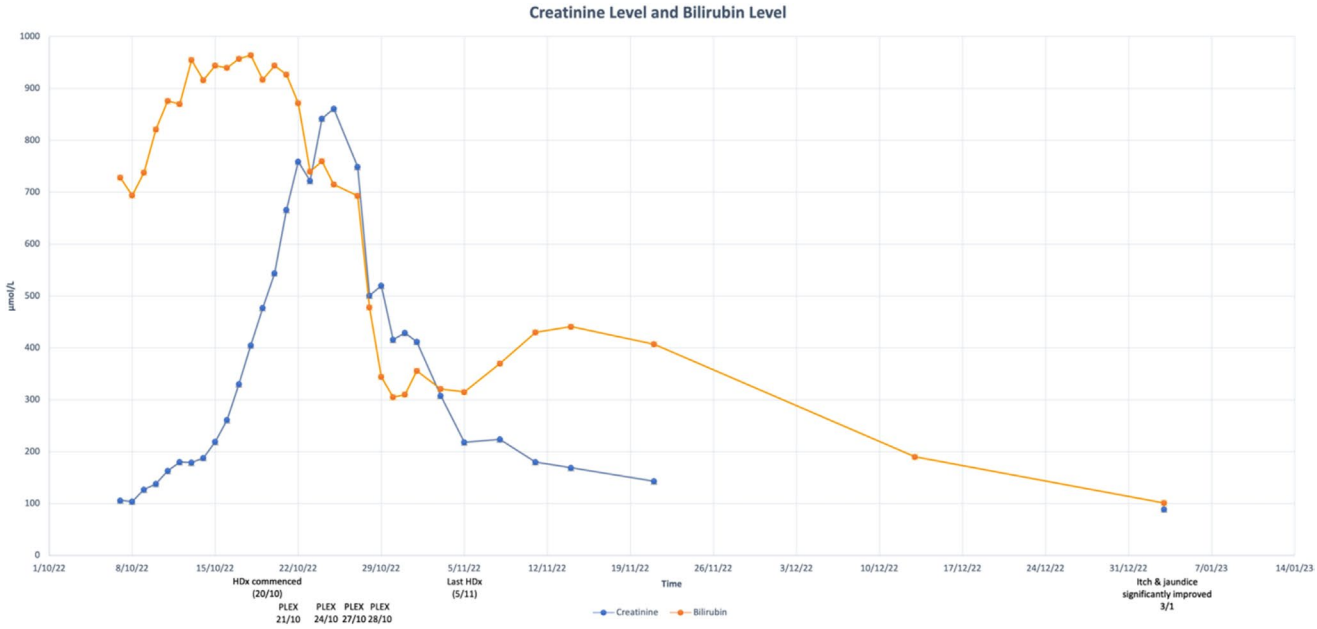

FIGURE 1 | Creatinine and bilirubin levels over time.

of hepatitis C. An autoimmune screen including smooth muscle Ab, mitochondrial Ab, liver-kidney microsomal Ab, anti-dsDNA, ANCA, ANA, and serum IgG was negative. Copper and ceruloplasmin were slightly raised. Computerized tomography of his abdomen was normal. His RUCAM score was 7, indicating probable DILI. MRCP was performed, and PSC was excluded. A liver biopsy was performed to exclude an autoimmune etiology. Histology revealed marked "bland" hepatocanalicular cholestasis with mild lobular/venular inflammation, mild duct injury, with mild duct loss in 6 of 26 examined portal tracts, typical of anabolic steroid-induced cholestasis.

He was initially treated with a combination of ursodeoxycholic acid, colestyramine, rifampicin, sorbolene, and pregabalin for refractory pruritus with minimal relief. Simultaneously, his bilirubin steadily increased to a peak of 964 µmol/L on day 12 and was associated with oliguric renal failure that persisted despite intravenous fluid therapy. He had no hematuria or proteinuria, an unremarkable glomerulonephritis screen, and a negative renal tract doppler ultrasound. Urine microscopy was positive for bilirubin. Bile cast nephropathy was assumed given the prolonged hyperbilirubinaemia. He was commenced on hemodialysis via permacath with no improvement in his pruritus. The decision to perform PLEX as treatment for pruritus was made. The patient had four cycles of PLEX using the membrane filter technique (TPE2000) with PRISMAFLEX. This was performed against albumin on alternate days to hemodialysis with 4 L exchanged per session. PLEX was well tolerated with no adverse effects. His bilirubin decreased to 478 µmol/L. His symptoms were partially alleviated, although jaundice and pruritus would only be significantly improved at 2 months.

He was discharged with a plan for hemodialysis three times a week. His renal function showed signs of recovery 1 month post discharge, with eGFR 52, creatinine 143 µmol/L, and dialysis was ceased. Repeat blood tests 10 weeks post discharge revealed complete recovery of renal function and improving liver function tests, with a bilirubin of 101 µmol/L. Jaundice and pruritus were significantly improved.

3 | Discussion

Non-paracetamol DILI, especially herbal and dietary supplement-related DILI, has been increasing in Australia and is associated with poorer outcomes compared to DILI caused by paracetamol and prescription medicines [1]. Of particular concern is the increasing use of AAS mostly by young males outside of athletic and weightlifting circles [2].

Four distinct forms of AAS DILI have been recognized: transient liver enzyme elevations, acute cholestasis (bland cholestasis), chronic hepatic vascular injury (peliosis hepatis) and tumors including adenomas and HCC [2, 3]. In this case, the clinical presentation and investigations, particularly the bland cholestasis, were pathognomonic of AAS liver injury. Patients usually present with an insidious onset of symptoms such as nausea, pruritus, and painless jaundice. Most make a full recovery without needing transplantation, though mortality due to secondary causes such as renal failure, malnutrition, and infection has been reported [3].

Cholestatic pruritus can be extremely debilitating. Furthermore, treatments are limited, and only bile acid resins (e.g., colestyramine) have been shown to be efficacious. Prolonged cholestasis can also lead to complications, including BCN. BCN is a collective term that encompasses tubular and interstitial inflammation, direct bile salt tubular injury, obstruction due to the deposition of bile casts, as well as altered renal hemodynamics. Biopsy is usually diagnostic. While AKI is not uncommon in liver injury, BCN is still underdiagnosed due to the diverse etiology of renal injury in liver disease. Several case reports have shown marked improvement in the empirical treatment of BCN,

though there are no clear guidelines due to the multifactorial mechanism of injury [6].

PLEX aims to remove pathological substances including antibodies, immune complexes, and toxins from the body by removing a large volume of plasma and exchanging it against fluid. PLEX has been suggested to be effective in treating severe hyperbilirubinaemia [5]. More specifically, PLEX has been used to treat patients with AAS cholestatic DILI complicated by BCN [6, 7]. The main indication for PLEX in this case was intractable cholestatic pruritus. The patient demonstrated a dramatic biochemical and clinical improvement with PLEX. Although dialysis was temporarily required, his renal function made a complete recovery, with marked improvement in liver function.

The case adds to the growing evidence that PLEX can be used safely and effectively to treat cholestatic pruritus and bile cast nephropathy. To our knowledge, this is the first use of PLEX in this context in Australia. This is pertinent in the context of the rising incidence of non-prescription DILI (Figure 1).

Acknowledgments

Open access publishing facilitated by The University of Melbourne, as part of the Wiley - The University of Melbourne agreement via the Council of Australian University Librarians.

Ethics Statement

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

References

1. E. Nash, A. H. Sabih, J. Chetwood, et al., "Drug-Induced Liver Injury in Australia, 2009–2020: The Increasing Proportion of Non-Paracetamol Cases Linked With Herbal and Dietary Supplements," *Medical Journal of Australia* 215, no. 6 (2021): 261–268, https://doi.org/10.5694/mja2.51173.

2. E. Nash, A. Nicoll, N. Batt, et al., "Drug-Induced Liver Injury From Selective Androgen Receptor Modulators, Anabolic-Androgenic Steroids and Bodybuilding Supplements in Australia," *Alimentary Pharmacology & Therapeutics* 59, no. 8 (2024): 953–961, https://doi.org/10.1111/apt.17906.

3. A. Petrovic, S. Vukadin, R. Sikora, et al., "Anabolic Androgenic Steroid-Induced Liver Injury: An Update," *World Journal of Gastroenterology* 28, no. 26 (2022): 3071–3080, https://doi.org/10.3748/wjg.v28.i26.3071.

4. M. R. Somagutta, M. S. Jain, M. K. L. Pormento, et al., "Bile Cast Nephropathy: A Comprehensive Review," *Cureus* 14, no. 3 (2022): 23606, https://doi.org/10.7759/cureus.23606.

5. M. Keklik, S. Sivgin, L. Kaynar, et al., "Treatment With Plasma Exchange May Serve Benefical Effect in Patients With Severe Hyperbilirubinemia: A Single Center Experience," *Transfusion and Apheresis Science* 48, no. 3 (2013): 323–326, https://doi.org/10.1016/j.transci.2013.04.009.

6. A. Flores, R. Nustas, H.-L. Nguyen, and R. S. Rahimi, "Severe Cholestasis and Bile Acid Nephropathy From Anabolic Steroids Successfully Treated With Plasmapheresis," *Acg Case Reports Journal* 3, no. 2 (2016): 133–135, https://doi.org/10.14309/crj.2016.24.

7. C. El Khoury, T. Sabbouh, H. Farhat, and A. Ferzli, "Severe Cholestasis and Bile Cast Nephropathy Induced by Anabolic Steroids Successfully Treated With Plasma Exchange," *Case Reports in Medicine* 2017 (2017): 4296474, https://doi.org/10.1155/2017/4296474.