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Selected Abstracts

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Extracorporeal blood purification therapy with Cytosorb (™) for severe hyperbilirubinemia and jaundice in drug-induced liver injury

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Background: Drug-induced liver injuries (DILI) are a group of multiform hepatic injuries related to a specific drug assumption. Among DILIs, pattern of cholestatic injury is characterized by disproportionate elevation of alkaline phosphatase compared with the serum aminotransferases and elevation of serum bilirubin, sometimes to very high levels (1). Anabolic steroids are a known cause of DILI. More importantly, anabolic steroids are linked to a distinctive form of acute cholestasis that generally arises within 1 to 4 months of starting therapy (2).

Methods: A previously healthy man, 46 years old, developed clinically evident jaundice with mild increase in liver enzymes (1.5 x upper normal limit), more marked increase of alkaline phosphatase (3 x upper normal limit) and severe mixed hyperbilirubinemia (12.5 mg/dl).

Haemocromocitometric and coagulative parameters, haemolysis markers, haptoglobin and lactate dehydrogenase, were normal. Viral, infectious and immunologic causes were excluded as well as presence of biliopancreatic pathology. CT and MR scan showed a liver with slightly increased dimension in the absence of focal lesions or other parenchymal abnormalities, excluding neoplastic diseases. Subsequently a liver biopsy was performed with evidence of focal-sever cytoplasmic and intracanalicular cholestasis with limited focal hepatocyte necrosis. In complex, the histopathological characteristics suggested the hypothesis of a toxic hepatitis. A careful pharmacological anamnesis highlighted patient's assumption of anabolic drugs in the previous weeks for weight training and muscle bulk. In the following days after admission, there was a progressive increase in total bilirubin levels up to 40 mg/dl. The patient was in good clinical conditions with no other organ damage and in particular no signs of renal dysfunction, electrolyte abnormalities or urinary abnormalities.

Results: Bilirubin values continued to rise despite forced diuresis and urine alkalinisation so that we indicated extracorporeal blood purification therapy (EBPT) with regional citrate anticoagulation in association with a sorbent cartridge (CytoSorb™). A first cycle of 72 hours with cartridge change every 24 hours showed a 50% reduction of bilirubin values. For a subsequent rebound of bilirubin values another cycle of treatment of 24 hours was performed. We observed no circuits clotting or other complications related to extracorporeal therapy. Thereafter bilirubin values began to decrease slowly below 10 mg/dl and the patient was discharged. The evolution of bilirubin levels in correlation with EBPT was showed in figure 1. Five month later the patient was in good clinical conditions and showed normal hepatic enzymes and bilirubin values without clinical jaundice signs.

Conclusions: Severe hyperbilirubinemia with jaundice, although isolated, represents a potential life-threatening situation that, in the absence of acute liver insufficiency, does not have indication to liver transplant. CytoSorb is a relatively new extracorporeal blood purification device with a large sorbent surface of about 45 m² capable to adsorb a wide spectrum of molecules up to 55 kDa. For its characteristics, it is largely used in septic shock or other forms of vasoplegic shock to contrast the effects of cytokine storm. Some case series and *in vivo* and *in vitro* data demonstrated the effective removal of bilirubin by CytoSorb despite lacking of large prospective or randomized trials results (3). A recent analysis on 109 patients from CytoSorb international registry that underwent hemoadsorption therapy for liver indication confirmed a significant bilirubin removal (mean value of -4.6 mg/dl with median treatment duration of 46 hours) with vast majority of patients alive at the discontinuation of therapy (4). To date there are no established bilirubin cut-off that indicate EBPT. The use of EBPT in patients without renal dysfunction as an adjunctive treatment to provide support for other organs is highly debated due to cost, potential complications and logistic problems related to intensive care needed. Start of extracorporeal support, in this field, should be carefully evaluated by a multidisciplinary assessment. In the present case, EBPT was considered as a feasible bridge therapy due to the lacking of direct liver indication (e.g. Liver transplantation) and due to the intrinsic characteristic of DILI that generally includes improvement of the liver injury following to drug discontinuation.

Bibliography

1. Lee WM. Drug-induced hepatotoxicity. *N Engl J Med.* 2003 Jul 31;349(5):474–85.
2. LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012-. Androgenic Steroids. [Updated 2020 May 30].
3. Tomescu D, Popescu M, David C, Sima R, Dima S. Haemoadsorption by CytoSorb® in patients with acute liver failure: A case series. *Int J Artif Organs.* 2021 Aug;44(8):560–4.
4. Ocskay K, Tomescu D, Faltlhauser A, Jacob D, Friesecke S, Malbrain M, et al. Hemoadsorption in “Liver Indication”-Analysis of 109 Patients” Data from the CytoSorb International Registry. *J Clin Med.* 2021 Nov 5;10(21):5182.

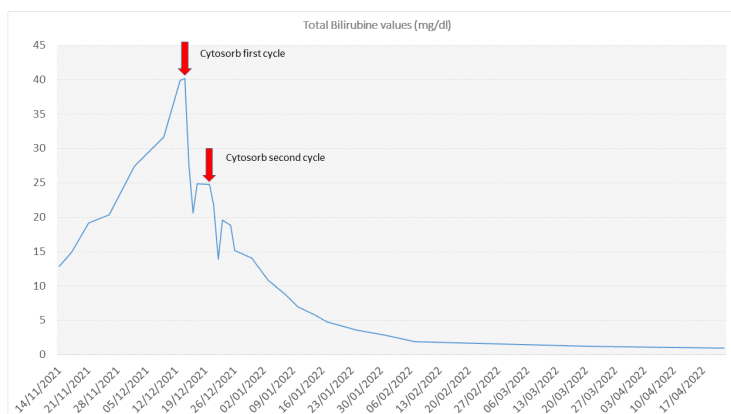


Fig. 1