CytoSorb®

Case of the week 16/2019

Hemoadsorption in isolated conjugated hyperbilirubinemia after extracorporeal membrane oxygenation support. Cholestasis of sepsis: A case report and review of the literature on differential causes of jaundice in ICU patient

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This report describes the case of a 58-year-old woman who was referred to a tertiary hospital with the primary diagnosis of severe ARDS caused by sepsis originating from unspecified pneumonia.

Case presentation

- Prior to transfer to the Medical University of Lublin, the patient was sedated and ventilated for 4 days at the tertiary hospital, with elevated positive end-expiratory pressure (PEEP) (15 cm H_2O) and a low PaO_2/FiO_2 ratio of approximately 75 mmHg at an $ETCO_2$ of 8.8 vol % (approximately 65 mmHg)
- Due to respiratory failure (RESP score 3), she was accepted for extracorporeal respiratory support and directly transferred to the ICU of the Medical University of Lublin
- Upon arrival the patient required considerable norepinephrine support (0.62 µg/kg/min) and her sequential organ failure assessment (SOFA) score on admission was 14
- Inflammatory markers were highly elevated (leucocytes 27.8×10³/µl, C-reactive protein 473.5 mg/l, procalcitonin 28.7 ng/ml)
- Subsequent lung ultrasound revealed bilateral C profile in midclavicular lines and B-line artefacts. A hyperdynamic condition was observed during echocardiography with left ventricular ejection fraction of 75%–80%
- Chest X-ray on the first day of her ICU stay showed massive, merging, bilateral opacities corresponding with consolidations, which was followed by initiation of VV-ECMO therapy (ILA; NovaLung GmbH, Talheim, Germany)
- Continuous veno-venous hemodialysis with regional citrate anticoagulation (CVVHD Ci-Ca) (Multifiltrate; Fresenius, Bad Homburg, Germany) was started simultaneously with ECMO
- Three units of blood and platelets were transfused during ECMO support while a subcutaneous nadroparin dose of 0.8 ml/day was used as anticoagulant prophylaxis
- The patient required continuous infusions of norepinephrine (0.12–0.36 µg/kg/min) and dobutamine (3.7–7.8 µg/kg/min) throughout the treatment and dosages as well as fluid therapy were adjusted according to echocardiographic imaging
- Empiric broadspectrum antibiotic therapy (meropenem, linezolid, sulfamethoxazole/trimethoprim) were administered until blood and bronchoalveolar lavage (BAL) cultures results were available. After identification of Acinetobacter baumannii from BAL, antibiotic treatment was adapted accordingly to amikacin and tigecycline

- Enteral and parenteral nutrition was initiated
- Eight days after admission to the ICU, the patient's respiratory condition improved allowing discontinuation of the ECMO support
- Mechanical ventilation was continued with a PEEP set to 6–8 cm H_2O accompanied by a reduction of norepinephrine infusion to 0.02–0.07 µg/kg/min and discontinuation of dobutamine
- CVVHD was discontinued on day 11 due to stable urine output, however, after cessation of renal replacement therapy, serum levels of creatinine and urea were increasing necessitating continuation of CVVHD on day 14
- Despite withdrawal of sedation with propofol and fentanyl after 5 days, the patient remained unconscious (–4 Richmond Agitation-Sedation Scale score)
- While the patient's primary problem i.e. severe respiratory failure was diminishing, bilirubin levels increased progressively and the patient developed jaundice with a noticeable change in total bilirubin serum levels (0.81 mg/dl at admission; 3.88 mg/dl after 3 days of ECMO therapy; 7.1 mg/dl at day of ECMO discontinuation) reaching a peak of 18.41 mg/dl of total bilirubin (2.74 mg/dl of unconjugated bilirubin and 15.67 mg/dl of direct bilirubin) on day 13. Gamma-glutamyltransferase (157 IU/mL) and alkaline phosphatase (228 IU/ml) were increased, while coagulation markers were stable
- Abdominal computed tomography (CT) performed on day 11 showed an enlarged liver, however homogeneous in structure, with non-dilated bile ducts and lack of evidence of focal lesions
- Viral hepatitis was excluded, CIOMS/RUCAM score was 0
- As bilirubin serum levels remained high, the decision was made to install CytoSorb into the renal replacement therapy circuit as a last resort therapy in cholestasis

Treatment

- Two treatments with CytoSorb for 48 hours (24 hours per treatment)
- Cytosorb was used in combination with CRRT run in CVVHD mode
- Blood flow rate: 100 ml/min
- Anticoagulation: citrate
- CytoSorb adsorber position: post-hemofilter

Measurements

- Bilirubin levels
- SOFA Score
- Albumin levels

Results

- The treatment resulted in a reduction of total bilirubin concentration from 18 mg/dl before to 2.4 mg/dl after the two consecutive treatments
- Significant improvement in SOFA from 16 before start to 10 after discontinuation of CytoSorb therapy
- Albumin levels were not affected during CytoSorb treatment

Patient Follow-Up

- After improvement of her medical condition, the patient regained partial consciousness to the point of spontaneous eye opening and was transferred to the regional hospital for continuation of the treatment
- Hyperbilirubinemia did not return during the 3-month follow-up period

Conclusion

- This is the first published clinical case report of sepsis-induced cholestasis in a patient supported with respiratory ECMO successfully treated with CytoSorb hemoadsorption resulting in a marked reduction in bilirubin levels and the SOFA score
- Therefore, CytoSorb was a useful therapeutic option in prolonged cholestasis
- Sepsis-related cholestasis is a result of a decrease in hepatic canalicular transport of cholephilic substances resulting in intrahepatic cholestasis. This dysfunction is mainly promoted by cytokines, endotoxins and other pathogen-associated molecular patterns (PAMPs). Therefore CytoSorb might have had multiple effects in the treatment of this patient including the elimination of bilirubin per se, but also a re-establishment of hepatic canalicular transport by eliminating excess inflammatory mediators
- Invasive diagnostic procedures (i.e. liver biopsy) to rule out the underlying cause of hyperbilirubinemia could be omitted as hemoadsorption therapy led to its quick reduction with concomitant clinical improvement making testing redundant
- Hyperbilirubinemia did not return during the 3-month follow-up period suggesting that adsorption therapy could facilitate a re-balancing between the inflammatory process, cytokine production and bilirubin turnover