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Case of the week 27/2019

Use of CytoSorb in a pediatric patient with complex Shigatoxin-induced thrombotic microangiopathy and severe multiple organ failure

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This case reports on a 2-year-old male patient (weight 12 kg), who was admitted to the children's outpatient department with anuria, bloody diarrhea, anemia and severe edema (anasarca).

Case presentation

- A microbiological quick test from stool confirmed the presence of Shigatoxin-producing Escherichia coli (STEC) and the patient showed the typical initial symptoms of hemorrhagic colitis with bloody diarrhea
- Hematological diagnostics also revealed thrombocytopenia, fragmentocytes and pronounced hemolysis, followed by the diagnosis of infection-mediated thrombotic microangiopathy (previously known as: hemolytic-uremic syndrome or HUS)
- Initiation of antibiotic therapy with azithromycin (mitochondrial RNA synthesis inhibitor, which intervenes in cell metabolism and unlike other common antibiotics, does not lead to an additional release of shigatoxin through disruption of the bacterial cell wall)
- Subsequently, the patient presented with pronounced symptoms of STEC-associated thrombotic microangiopathy including thrombocytopenia, acute renal failure, hemolytic anemia (however without convulsions or neurological symptoms (Neuro-STEC))
- Due to acute anuric renal failure, the patient was transferred to the pediatric intensive care unit within one hour after initial admission and continuous renal replacement therapy (CRRT) was started
- As a result, diuresis and renal function parameters stabilized and renal replacement therapy could be discontinued after a total of 5 weeks
- In the context of evident hyperbilirubinemia, administration of ursodesoxycholic acid was started early (20 mg/kg/day at 3 individual doses per probe)
- 10 days later hemorrhagic shock occurred due to complete intestinal necrosis (with concomitantly persisting hemorrhagic colitis) with perforation in the ileocecal region, resulting in emergency laparotomy and resection of the necrotic intestinal section as well as formation of an ileostomy and colostomy
- A significant increase in cholestasis parameters was already observed preoperatively (presumably an accompanying ischemic cholangiopathy)
- Over the postoperative course, hepatobiliary dysfunction with hepatic encephalopathy, hyperammonemia (max. 125 µmol/L) and hyperbilirubinemia (present since the onset of the disease, 13.9 mg/dL) increased, followed by initiation of plasma exchange therapy as an hepatic detoxification procedure (5 treatments, 1.5-fold plasma exchange, under octaplas substitution) and normalization of NH3 and bilirubin levels over time

- Within one week after cessation of plasma exchange therapy, there was a rebound in cholestasis parameters and ammonia plasma levels (hepatic synthesis parameters were only slightly affected)
- The patient was hemodynamically stable at all times and only required transient low-dose support with vasoactive substances (norepinephrine)
- Tracheotomy was performed and steroid therapy started due to suspected cholangitis and enteritis (methylprednisolone 10 mg/kg/day IV)
- To support hepatic detoxification function with the hyperammonemia (125 µmol/L), hyperbilirubinemia (15.6 mg/dL), elevated cholestasis parameters (gamma GT 13422 U/L, alkaline phospatase (AP) 1437 U/L) and presumably simultaneously elevated bile acids (not measured), as well as increasing renal retention parameters (urea 80 mg/dL, creatinine 0.9 mg/dL), combined treatment with high-flux continuous veno-venous hemodiafiltration (CVVHDF, 2. CRRT episode)) and CytoSorb hemoadsorption was commenced

Treatment

- Four treatment cycles with CytoSorb for a total treatment period of 10 days (treatments over 24 hours each with corresponding pause intervals)
- CytoSorb was used in combination with CRRT (Prismaflex, Gambro) run in CVVHDF mode
- Blood flow rate: 100 mL/min
- Anticoagulation: Citrate only during the first treatment cycle, followed by a change to heparin due to a profound metabolic alkalosis under citrate anticoagulation
- CytoSorb adsorber position: post-hemofilter

Measurements

- Hepatic detoxification function (ammonia, bilirubin)
- Cholestasis parameters (gamma GT, AP)
- Renal function (urea, creatinine)
- Hepatic encephalopathy

Results

- Within the 4 treatments, ammonia and bilirubin levels could be significantly reduced (ammonia from 125 to 58 µmol/L, bilirubin from 15.6 to 3.3 mg/dL)
- Additionally, cholestasis parameters also clearly decreased during CytoSorb therapy (gammaGT from 13422 to 3151 U/L, AP from 1437 to 851 U/L)
- The combined treatment of high flux-CVVHDF and CytoSorb hemoadsorption also resulted in a reduction in renal retention parameters (urea from 80 to 12 mg/dL, creatinine from 0.9 to 0.2 mg/dL), diuresis was adequate throughout all treatment sessions
- The patient became more awake under CytoSorb and was more alert, indicative of declining hepatic encephalopathy

Patient Follow-Up

- Discontinuation of CVVHDF (2. CRRT episode) together with CytoSorb therapy after 10 days
- Abdominal sonography showed typical pathological alterations of the intra- and extrahepatic bile ducts in the sense of a secondary sclerosing cholangitis (radiological findings using magnetic resonance cholangiopancreaticography had meanwhile been performed and confirmed the suspicion of secondary sclerosing cholangitis)
- Over time, serum ammonia levels could be controlled and hepatic synthesis function was sufficient, cholestasis parameters however remained persistently elevated (gamma GT 728 U/L, AP 1319 U/L)
- Notwithstanding the confirmed brain atrophy via cMRT, there was clinical improvement noted neurologically (follow-up examination still pending)
- Transfer of the patient after approx. 3 months of intensive therapy to the normal ward in an adequate general condition with continuing hepato-biliary dysfunction due to the now confirmed secondary sclerosing cholangitis, with sufficient hepatocellular function and without cirrhotic remodeling of liver tissue confirmed by liver biopsy and sonography

Conclusions

- In this pediatric patient with complex Shigatoxin-induced thrombotic microangiopathy and severe multiple organ failure with intestinal necrosis and secondary sclerosing cholangitis, the combined treatment of high flux-CVVHDF and CytoSorb hemoadsorption resulted in the preservation of liver integrity as well as a significant improvement in excretory liver function and renal function
- According to the medical team, CytoSorb was technically much easier to use than the plasma exchange therapy and also showed higher efficiency in eliminating liver-associated toxins
- Given the very early application of CytoSorb within the 10-day total treatment period with ammonia levels below 130 µmol/L together with its efficient reduction, the development of brain swelling or edema (development at values of 150-200 µmol/l) could be prevented in this very young patient
- CytoSorb was safe and easy to use in combination with CRRT despite the body weight of only 10 kg