

Pericarditis Caused by *Enterococcus faecium* with Acute Liver Failure Treated by a Multifaceted Approach including Antimicrobials and Hemoadsorption

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Case Reports in Critical Care 2021; epub

This case reports on a 29-year-old woman with a history of Crohn's disease and cachexia, who was hospitalized due to painful diarrhea and unintentional weight loss of 13 kilograms over the previous three weeks caused by a mechanical ileus.

Case presentation

- Transfer to the intensive care unit (ICU) occurred 2 weeks later because of increasing somnolence, impaired gas exchange and hemodynamic instability. She quickly required high dosage of norepinephrine (up to 1.56 µg/kg/min)
- Laboratory diagnostics revealed significantly altered hepatic (albumin 23.8g/l, gamma-GT 118U/l, alkaline phosphatase 142U/l, cholinesterase 1814 U/l) and elevated inflammatory parameters (C-Reactive Protein CRP 194.8mg/l, and procalcitonin PCT 59.80 µg/l)
- The Sequential Organ Failure Assessment (SOFA) score was 6
- The severity of the clinical picture demanded an exploratory laparotomy for source control. Intraoperatively, a perforation with local peritonitis was found in the lower abdomen. A right hemicolectomy, partial resection of the small bowel, and side-to-side anastomosis were performed. Histology revealed massive chronic inflammation of the terminal ileum, typical of Crohn's disease
- Preoperatively started antibiotic therapy with piperacillin/tazobactam was continued for four days according to the resistogram (*Providencia stuartii*, *Escherichia coli*, and anaerobic bacteria)
- Blood cultures taken on ICU admission were negative
- The patient was treated with differentiated volume and catecholamine therapy
- As she still required high doses of norepinephrine, a combination of continuous renal replacement therapy (CRRT) and adjunctive CytoSorb hemoadsorption therapy was initiated (1st treatment cycle with 3 consecutive CytoSorb treatments) resulting in rapid hemodynamic stabilization and reductions in inflammatory parameters and bilirubin (see results section)
- Four days after the operation and after CytoSorb discontinuation, the patient's condition started to worsen rapidly again with tachycardia, hypotension, and fever up to 39.0°C, as well as diminishing oxygen saturation levels
- The patient had to be reintubated and norepinephrine administration had to be re-initiated for hemodynamic stabilization (1.09 µg/kg/min)
- In the next hours, hemodynamics stabilized while diuresis resumed spontaneously and renal replacement therapy could be stopped shortly after
- A chest X-ray performed the same day revealed a pleural effusion

- In search of an infectious source, samples (pleural fluid, two sets of blood cultures and bronchoalveolar fluid) were sent to microbiology but all proved negative
- Abdominal and chest CT scan revealed an intact anastomosis but showed multiple dense foci inside the lungs
- Despite the negative microbiology, the decision was made to intensify antibiotic therapy by escalation to meropenem
- Liver function testing indicated severe liver insufficiency
- In addition, a subsequent CT scan confirmed severe, previously unknown, changes consistent with emphysema (bullae) in the lungs which further compromised gas exchange
- Over the next 9 days, both chest X-ray and CT scans indicated morphological improvements
- However, the patient's condition rapidly deteriorated once more, now presenting as a multiple organ dysfunction syndrome (SOFA score 12)
- Inflammatory marker levels were clearly increased and the patient became anuric, while FiO₂ levels required an increase up to 100% and liver function was still severely impaired
- The hypothesis was septic shock syndrome, and blood culture samples were taken; however, these showed no bacterial or fungal growth
- As the patient required CRRT at this time point, the decision was made to re-apply the CytoSorb system in order to attenuate the hyperinflammatory response and to eliminate liver metabolites, such as bilirubin, ammonia, and bile acids in the context of sepsis-associated acute liver failure (2nd treatment cycle with 13 consecutive CytoSorb treatments)
- While under CytoSorb treatment, an emergency re-laparotomy was performed excluding any intra-abdominal source of sepsis. However, echocardiography revealed a significant increase in pericardial effusion and pericardial tamponade was diagnosed. The patient underwent a pericardial tap, and a drain was inserted. Enterococcus faecium was identified in the pericardial fluid and also in all blood cultures, intra-abdominal, urine and tracheal fluids.
- All strains proved to have equal resistance patterns suggesting a common origin that was most likely the ruptured ileum
- Based on these findings, an antimicrobial chemotherapy supplemented by tigecycline and the antifungal caspofungin was considered appropriate

Treatment

- 1st treatment cycle: 3 consecutive CytoSorb treatments were performed for a total of 73 hours
- 2nd treatment cycle: 13 consecutive CytoSorb treatments were run for a total duration of 346 hours (14 days)
- CytoSorb was performed in conjunction with CRRT run in continuous veno-venous hemodialysis (CVVHD) mode
- Anticoagulation: citrate

Measurements

- Hemodynamics and norepinephrine requirements
- Inflammatory parameters (interleukin - IL-6)
- Parameters of liver dysfunction including bilirubin, ammonia, severity of hepatic dysfunction score (Model for End-stage Liver Disease [MELD]-Score)
- Ventilation
- Renal function

Results

- 1st treatment cycle (3 treatments)
 - CytoSorb therapy was associated with a rapid stabilization in her hemodynamic situation (norepinephrine down to 8.3% of the maximum initial dose)
 - IL-6 levels decreased from ~850 pg/ml to ~140 pg/ml during the 3 CytoSorb treatments
 - Treatment was also associated with a reduction in bilirubin (from 1.2 to 0.3 mg/dl) as well as an improvement in MELD score from ~27 to ~11 points
 - Extubation was possible on the day of CytoSorb cessation
- 2nd treatment cycle (13 treatments)
 - Throughout the 2nd treatment cycle, there was a reduction in vasopressor requirements down to 16.9% of the maximum initial dose
 - The hyperinflammatory response declined as evidenced by a decrease in IL-6 plasma concentrations from ~550 pg/ml to ~150 pg/ml and a consistent improvement over the course of the following days
 - Furthermore, treatment resulted in a normalization in bilirubin levels accompanied by an improvement in MELD score from ~26 to ~10 points
 - Invasive ventilation could be switched to assisted ventilation
 - Onset of spontaneous diuresis occurred at the end of the 2nd treatment cycle

Patient Follow-Up

- As norepinephrine requirements were minimal, CytoSorb therapy was discontinued
- Following discontinuation of CytoSorb treatment, the sedation rate could be gradually reduced and the patient regained consciousness with continuous improvement in her mental state
- To facilitate weaning, a tracheotomy was performed
- In the meantime, the patient's overall clinical condition improved accompanied by a reduction in SOFA score to 6
- Five days later, *E. faecium* was cultivated from the tip of the central venous catheter under continued antimicrobial therapy with tigecycline. The catheter was removed and tigecycline was changed to linezolid (600mg twice daily)
- Liver function testing 8 days after CytoSorb discontinuation showed a stable, but still medium-gross restricted hepatic function
- After further improvement, the patient was discharged in a stable clinical condition from the ICU to the normal ward 53 days after her initial admission

Conclusion

- This is the first detailed description of an *E. faecium* pericarditis in a patient with complex pathophysiological changes caused by a multitude of different chronic (Crohn's disease, cachexia) and acute diseases (septic shock with multiorgan failure in bacterial pericarditis), requiring multilayered interdisciplinary intervention including anti-infective therapy, hemoadsorption with the CytoSorb cartridge, and dynamic liver function testing
- This interdisciplinary intensive care therapy approach in combination with CytoSorb as an individual adjuvant treatment concept allowed control of the hyperinflammation and clear decreases in the vasopressor requirements
- The combination of the adsorption and elimination of bilirubin and bile acids, the modulation of involved cytokines, and the reduction of excess ammonia levels via parallel renal replacement procedure allow a bridge in time until functional recovery or orthotopic liver transplantation. CytoSorb therefore represents a promising, easy to perform method for liver support