

## Use of CytoSorb during a cytokine storm following fulminant tumor lysis syndrome in a patient with diffuse large splenic B-cell lymphoma

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*This case reports on a 40-year-old female patient with no significant pre-existing medical conditions, who was transferred from a peripheral hospital to University Hospital Essen in a significantly reduced general condition including renal and liver failure.*

### Case presentation:

- Laboratory analyses showed severe hemolytic anemia requiring transfusion (HB 5.4 g/dl, lactate dehydrogenase (LDH) 2018 U/L, bilirubin 12.7 mg/dl) as well as pronounced thrombocytopenia (20/nL)
- During the physical examination on the day of admission, she additionally presented as icteric, hypotonic (100/60mmHg) and tachycardic (90/min) with severe fatigue. Morphological imaging revealed a hepatosplenomegaly. Abdominal findings were otherwise unremarkable and there was no neurological deficit. Only axillary lymphadenopathy was found
- Overall, the suspected diagnosis was thrombotic microangiopathy despite a Coombs-positive test of hitherto unclear origin. After sampling of the corresponding diagnostic markers (TTP/ HUS/hepatitis/HIV diagnosis), plasmapheresis therapy was started (initially 6 plasma separations). Furthermore, a skin biopsy was performed to exclude cutaneous lymphoma
- Infection diagnostics showed significantly increased infection parameters (CRP 33.3 mg/dl, leukocytes 22,000/ $\mu$ L) along with with a fever
- Change of antibiotic therapy to meropenem shortly after admission
- The patient had to be transferred to the intensive care unit on day 6 after admission with global respiratory insufficiency, and intubation and mechanical ventilation was started
- She had severe acute respiratory distress syndrome (ARDS) with CT-morphologically confirmed extensive bilateral pulmonary infiltrates
- Escalation of antibiotic therapy into the atypical range, including viral and antifungal coverage
- Due to hydropic decompensation in the context of her septic state, continuous renal replacement therapy (CRRT) was initiated for acute renal failure grade III
- Despite optimal ARDS/sepsis therapy, lactate dehydrogenase (LDH) continued to increase, and there was a further decrease in thrombocytes requiring additional transfusions
- As a result, tumor diagnostics was accelerated by means of bone marrow biopsy. There was no reliable evidence of a suspected secondary hemophagocytosis syndrome or other pathologies
- In the context of progressive liver failure and initial hemodynamic improvement under plasmapheresis, plasma separation was performed 3 more times
- ADAMTS-13 diagnostic findings confirmed only slightly decreased activity and thus TTP was excluded, followed by discontinuation of plasmapheresis therapy
- Due to further deterioration of her clinical situation with continued hemolysis, a splenectomy with simultaneous intraoperative liver biopsy was performed after optimization of the coagulation regimen

- Histological findings confirmed infiltration of the spleen by a diffuse large B-cell lymphoma. An attempt at lymphoma detection in the liver was unsuccessful
- Initiation of causal chemotherapy according to the R-CHOP-LIGHT protocol
- The initial administration of rituximab (CD20 antibody, first component of the R-CHOP-LIGHT protocol, 750 mg) resulted in a rapid and dramatic increase in catecholamine requirements (from 0.3 to 1.3 µg/kg/min norepinephrine) with acutely unstable hemodynamics so administration of Rituximab was stopped. This was interpreted as a massive tumor lysis syndrome
- In this acute situation, the decision was made to install a CytoSorb adsorber into the already running renal replacement therapy (CRRT) circuit

### Treatment

- Treatment with three CytoSorb adsorbers for a total of 72 hours
- CytoSorb was used in conjunction with CRRT (Multifiltrate, Fresenius Medical Care) in continuous veno-venous hemodiafiltration mode (CVVHDF)
- Blood flow rate: 100 ml/min
- Anticoagulation: citrate
- CytoSorb adsorber position: pre-hemofilter

### Measurements

- Hemodynamics and need for vasopressors
- Inflammatory parameters
- LDH

### Results

- Already during the first hours of treatment, norepinephrine requirements could be reduced from 1.3 to 0.1 µg/kg/min. Vasopressor support could be stopped on day 3 while CytoSorb therapy was still ongoing
- Treatment was also associated with a significant reduction in CRP levels (from 30 mg/dl to 10 mg/dl)
- During the first 24 hours of treatment LDH plasma concentrations were halved and thus reduced to 1016 U/l

### Patient Follow-Up

- After successful CytoSorb treatment, further chemotherapy and in particular the additional rituximab doses were tolerated without complications which led to an overall improvement in the clinical condition of the patient
- After clinical stabilization and causal chemotherapy, weaning could be initiated
- The patient was transferred to the normal ward after an intensive care stay of 5 weeks and further chemotherapy was continued there

## Conclusions

- In this patient with cytokine storm after fulminant tumor lysis syndrome as part of chemotherapeutic treatment of a diffuse large B-cell lymphoma, the combined treatment of standard therapy, CRRT and CytoSorb hemoadsorption was associated with rapid hemodynamic stabilization and control of the inflammatory situation
- In the case of high tumor load and subsequent start of chemotherapy with consecutive cytokine storm syndrome, early application of CytoSorb resulted in a positive clinical course
- A clinically relevant adsorption of rituximab was considered unlikely due to the high molecular weight of the antibody, therefore no dose adjustment was performed
- The application of CytoSorb was safe, simple, and the patient was hemodynamically stable during treatment even after re-initiation of chemotherapy