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Letter to the Editor

Hemoadsorption in Infection-Associated Rhabdomyolysis

Dear Editor,

We herein report on a 55-year-old patient with history of arterial hypertension who was admitted to a peripheral hospital with complaints of dyspnea and symptoms of respiratory infection. In the further course, the patient developed a fulminant septic shock with massive requirements for fluids and catecholamines for hemodynamic stabilization. Due to increasing levels of creatine kinase as a sign of rhabdomyolysis and for further diagnosis, the patient was transferred to our hospital with manifest pneumogenic sepsis and acute respiratory distress syndrome (ARDS). Chest X-ray confirmed pneumonia and lung edema. Antibiotic therapy was started instantly. At this stage, the patient also showed drastically increased plasma concentrations of myoglobin and creatine kinase on top of his inflammatory response, indicative of massive infection-associated rhabdomyolysis. Furthermore, he exhibited a generalized compartment syndrome concomitant with pronounced fluid overloading (+30 L), elevated creatinine levels and acute liver injury as evidenced by hyperbilirubinemia. For treatment of his acute kidney injury grade III (crush kidney) and for negative fluid balancing, renal replacement therapy was initiated using a Genius device with an AV600S filter (both Fresenius Medical Care, Bad Homburg, Germany). In order to lower inflammatory mediator and myoglobin levels, an additional CytoSorb hemoadsorption device (CytoSorbents Inc., Monmouth Junction, NJ, USA) was installed into the continuous veno-venous hemofiltration (CVVH) circuit in a pre-dialyzer position. In total, four consecutive sessions were run over periods of 20 h each, separated from one another by a pause interval of 4 h. Blood flow rates were 150 mL/min, and anticoagulation was achieved using citrate. During the course of the treatment, plasma concentrations of IL-6, procalcitonin, myoglobin and creatine kinase decreased significantly (Table 1). Furthermore, levels of leukocytes, thrombocytes, alanine aminotransferase, and aspartate aminotransferase normalized over the four consecutive treatments. The clinical situation improved considerably including improvement of the patient's respiratory situation and liver function. Kidney function remained impaired after a total of 5 days on CytoSorb and the patient was discharged at day 13 with ongoing renal failure and need for renal replacement therapy. Two days after the last treatment with CytoSorb the patient could be

TABLE 1. *Markers of inflammation, myoglobinemia, organ (dys)function and blood composition throughout the treatment period. In total, four CytoSorb treatments were performed from day 1 to day 5 in this patient. Samples for data presented in the table were collected immediately after each treatment.*

	Reference	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 9	Day 12
Myoglobin (µg/L)	23–72	30000	16982	7095	4055	N/A	1384	921	758
Creatine kinase (U/L)	<190	22000	22000	9652	6064	4201	3102	2200	1950
C-reactive protein (mg/L)	<7	87.5	87.5	83.1	93.1	61.6	39.6	29	21
IL-6 (ng/L)	<5.0	N/A	226,9	173,2	116,6	53,2	32,2	N/A	N/A
Procalcitonin (µg/L)	<0.05	100	100	56.51	24.74	12.18	5.54	N/A	N/A
Creatinine (µmol/L)	59–104	229	155	128	130	140	150	N/A	145
Urine output (mL/day)	>1500	<500	<500	<500	<500	<500	<500	<500	<500
ALT (U/L)	<50	646	649	587	508	410	347	216	129
AST (U/L)	<50	1990	1905	1236	821	538	404	294	228
Bilirubin (µmol/L)	2.0–21.0	85.1	50.1	35.6	N/A	N/A	12.8	N/A	N/A
Leukocytes ($x10^9$/L)	3.9–10.2	19.89	22	33.4	29	29	20	13.9	10.1
Thrombocytes ($x10^9$/L)	150–370	66	84	126	160	184	223	321	299
Hct (%)	39.5–50.5	25.5	26.6	24	21.8	22.1	24.1	23.2	25.3
Hb (g/dL)	13.5 – 17.2	8.6	8.9	8.8	8.3	8.1	7.3	7.4	7.9
Albumin (g/L)	35–53	19.9	N/A	N/A	25,3	N/A	26.4	N/A	29.5
Glucose (mg/dL)	74–106	76	88	102	96	88	87	92	102
Na / K		norm	norm	norm	norm	norm	norm	norm	norm

ALT, alanine aminotransferase; AST, aspartate aminotransferase; Hct, hematocrit; Hb, hemoglobin.

extubated without further complications. Antibiotic dosages did not have to be adjusted at any time. Treatments appeared as safe with no adverse device-related events reported. The course of hematocrit, Hb and platelet count provided no evidence for a potential lack of hemo- or biocompatibility of the CytoSorb treatment. However, although we did not experience adverse clinical events, possible undesired effects of this hemoadsorbent technology cannot be ruled out based on the currently available, published data.

Approximately 7–10% of all cases of acute renal failure are attributable to rhabdomyolysis. Of these, approximately 10% have an underlying infectious origin (1). However, the impact of myoglobin removal on the course of rhabdomyolysis-associated AKI remains under discussion (2). In this patient, the application of CytoSorb resulted in a significant reduction of cytokines (i.e. IL-6) but also had an important additive effect on myglobin removal. These observations are in line with published data on cytokine removal (3) and a recently published report of *Legionella*-pneumonia associated rhabdomyolysis, where the adjunctive therapy with CytoSorb had similar effects on myoglobin levels (4). Of note, the effects seen are a sum of both adsorption techniques used (i.e. CVVH and CytoSorb). The root cause for the massive rhabdomyolysis in this patient could not be sorted out satisfactorily until the end of the treatment. However, taking into account the clinical course of the patient we assume the most probable reason is of infection-associated etiology. It remains speculative to what extent the effects seen can be ascribed to the application of the Cytosorb adsorber and therefore needs to be investigated in future randomized controlled trials.

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