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Case of the week 17/2021

Treatment of a patient with pronounced cytokine storm in severe COVID-19 pneumonia using hemoadsorption in combination with the administration of tocilizumab. A case report

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This case reports on a 58-year-old male patient with a medical history of ulcerative colitis, who was admitted to the Emergency Department with a body temperature up to 40°C, dry cough, fatigue for 3 days and a respiratory rate of >40/min.

Case presentation

- One day before, the patient had already had an external test which showed positive for SARS-CoV-2 with a Ct (cycle-threshold) value of >30
- Computed tomographic imaging (low-dose CT) on the day of admission showed the typical picture of COVID-19 pneumonia with bilateral, multifocal, ground-glass opacity consolidations without recess of the subpleural space
- Laboratory diagnostics revealed a C-reactive protein (CRP) of 64.44 mg/l, a lactate dehydrogenase (LDH) of 490 U/l, a serum ferritin of 618 µg/l and an interleukin (IL)-6 level of 294.1 pg/ml
- In addition, there was a thrombocytopenia of 112 x 10^3/µl, a D-dimer value of 1.2 mg/l and lymphopenia (5.9 %), which in the overall constellation suggested the second phase of a COVID-19 disease with bilateral pneumonia
- After transfer to the intensive care unit, non-invasive ventilation methods were initially used, including high-flow oxygen therapy with FiO_2 (inspired oxygen fraction) values of 50-60% and flow rates of up to 60 l/min alternating with BiPAP (Bilevel Positive Airway Pressure) therapy with an average PEEP (positive end-expiratory pressure) of 10 cmH_2O, resulting in the initial stabilization of the patient's condition
- On the first day after admission, a virus-specific therapy with remdesivir was started, which was supplemented by dexamethasone (6 mg 1x/day) on the following day. Prophylactic administration of an antibiotic was omitted; an extensive smears collection had already been done on admission
- In the course of the fourth day, progressing respiratory insufficiency was noted with a Horovitz index down to a minimum of 61 mmHg, necessitating endotracheal intubation; in addition, the patient was placed in the prone position
- After an increasing amount of putrid tracheal secretion was obtained around the third day of treatment, antimicrobial therapy with ampicillin/sulbactam (3 x 3 g/day i.v.) was started
- Proof of other viral causes of the disease were negative
- On the 6th day of ventilation, the patient's respiratory situation deteriorated rapidly again despite constant prone positioning for 16 hours
- Laboratory tests showed a sharp rise in IL-6 plasma concentrations (> 5,000 pg/ml) accompanied by an increase in the CRP levels and body temperature up to 39.8°C, suggesting a hyperinflammatory syndrome

- In addition, a PVPI of >4 (pulmonary vascular permeability index) in the context of an advanced hemodynamic monitoring was indicative of increasing capillary leakage syndrome
- In view of this clinical course, the decision was made towards an individualized therapy attempt, administering a monoclonal antibody against IL-6, tocilizumab (i.v. with 8 mg/kg bw once daily)
- Given the hyperinflammatory syndrome, and even in the absence of renal failure, but in order to ensure the blood pump-driven usage of hemoadsorption therapy, continuous renal replacement therapy (CRRT) was established and a CytoSorb adsorber was additionally integrated into the circuit

Treatment

- A total of 6 consecutive CytoSorb therapy sessions were performed. Adsorbers were changed every 12 hours in the first 24 hours, from the third adsorber use onwards, adsorbers were changed every 24 hours
- CytoSorb was performed in conjunction with CRRT run in continuous veno-venous hemodialysis (CVVHD) mode

Measurements

- Hemodynamics and vasopressor requirements
- Inflammation
- Lung function

Results

- The combined treatment consisting of standard therapeutic measures, hemoadsorption, CRRT and tocilizumab was associated with significant hemodynamic stabilization accompanied by a reduction in vasopressor doses
- Already on the 2nd day of the new treatment regimen, control of the hyperinflammatory situation was noted with significantly decreased IL-6 plasma concentrations (440 pg/ml). After a brief rise in IL-6 levels (1,921.9 pg/ml) on the 3rd day of treatment, a sustained stabilization of the hyperinflammatory response (in combination with renewed administration of tocilizumab) was achieved
- Furthermore, there was a clear improvement in lung function under combined therapy. In the context of rapidly improving Horovitz indices, prone positioning could be stopped

Patient Follow-Up

- Already one day after discontinuation of CytoSorb therapy on ventilation day 11, invasive ventilation could be clearly de-escalated and the patient was successfully ventilated with assisted spontaneous ventilation in CPAP (Continuous Positive Airway Pressure) mode
- On ventilation day 13, the patient could be successfully extubated after a successful spontaneous breathing test (SBT)
- Subsequently, the patient stabilized under non-invasive BiPAP therapy with an average IPAP (Inspiratory Pressure Above PEEP) of 10 cmH_2O and an EPAP (Expiratory Pressure Above PEEP) of 5 cmH_2O

- Over the following days, there were repeated but small increases in IL-6, LDH and D-dimers, however, there was no clinical correlation in the sense of deterioration
- Finally, on treatment day 23, the patient could be transferred to the normal ward, although he still had a positive nasopharyngeal smear for SARS-CoV-2

Conclusion

- In this case of a patient with a pronounced cytokine storm in the context of severe COVID-19 pneumonia, the combined treatment consisting of standard therapeutic measures, hemoadsorption, CRRT and tocilizumab was associated with significant hemodynamic stabilization with consecutive reductions in vasopressor doses, while hyperinflammation could be well controlled and lung function significantly improved
- The combination of CytoSorb therapy and IL-6 blockade by tocilizumab appeared, at least in this case, to be an effective measure for modulating an overshooting immune response in COVID-19 with a concomitant clinical improvement in both respiratory and hemodynamic function, and thus could be used as a potential therapeutic option in this clinical picture
- The incorporation of the hemoadsorber into the therapeutic regimen proved to be safe and straightforward. Removal of tocilizumab was not expected due to a molecular weight of about 145 kD