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CASE REPORT

Immunoadsorption therapy for a meningococcemia patient with myocarditis, adrenal hemorrhage, and purpura fulminans: a case report

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Abstract *Neisseria meningitidis*, also known as meningococcus, is a relatively uncommon cause of invasive infection, but when it occurs, it is frequently severe and potentially life-threatening. A ten-year-old female patient developed a purpuric rash with fever. Upon arrival to the pediatric intensive care department, she was unconscious and in a poor general condition. We combined treatment with antibiotics, volume resuscitation, hydrocortisone, and CytoSorb® therapy resulted in a stabilization of hemodynamics, as well as control of hyperinflammation. We observed a significant decrease in vasopressor dosage in this patient.

Introduction

Neisseria meningitidis (meningococcus) infections are a particular threat since they may cause epidemics and pandemics, rather than sporadic or endemic transmission. Around 12 serological groups have been identified among *N. meningitidis* strains, but more than 90% of infections are caused by A, B, C, Y, and W group isolates. Identification of *N. meningitidis* serogroups that predominate in a given country is vital for the development of local vaccination strategies. The clinical presentation of *N. meningitidis* is similar to the case of other bacterial neuroinfections. A common, but not pathognomonic sign of meningococcal septicemia is purpuric rash. The rash and adrenal hemorrhage (Waterhouse-Friderichsen syndrome) can be observed in fulminant infections, especially in children.[1] CytoSorb® (CytoSorbents Europe, Berlin, Germany) is a promising new extracorporeal cytokine hemoadsorption therapy that can modulate the cytokine storm during sepsis. Here we present a case of severe meningococcemia that was successfully

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treated with CytoSorb® hemadsorption therapy in the pediatric intensive care unit.

Case description

A ten-year-old female patient was admitted to our emergency clinic with purpuric rash and confusion. Her immunization status was appropriate to her age, and her previous medical history was unremarkable. She had vomiting, rash, fever, and stomachache, all started two hours before admission. She was given fluid replacement therapy and ceftriaxone of 50 $mg.kg^{-1}$ IV (intravenous) in the emergency department with a pre-diagnosis of meningococcemia. She had an ecimotic lesion on her hand where she had a peripheral venous line and this lesion progressed through her arm after the antibiotic treatment. She was then transferred to our pediatric intensive care unit since she was hypotensive despite fluid replacement. When she was admitted, she was unconscious and in a poor general condition. Her Glasgow Coma Score was 7 (E: 2, V: 1, M: 4), blood pressure was 91/75 (82) mmHg, heart rate was 140/min, the body temperature was 37.5 °C, respiratory rate was 24/min, SpO_2 was 88, capillary refill time was 5 seconds, and the pupillary light reflex was positive in both eyes. She had many petechial and purpuric lesions on her trunk and legs as well as an ecimotic lesion beginning from her hand, leading towards her shoulder. She had signs of meningeal irritation in the form of neck stiffness, positive Kernig's, and Brudzinski's sign. Other physical exam findings did not show a pathologic sign. The patient was intubated due to her worsening clinical condition and put on invasive mechanical ventilation. PRISM score was 20, Predicted mortality was 22.2%; PELOD 9 and Predicted mortality were 66%. Laboratory test results showed: urea 46 $mg.dL^{-1}$, creatinine 0.74 $mg.dL^{-1}$, glucose 176 $mg.dL^{-1}$, proBNP 23,500 $ng.L^{-1}$, hemoglobin 10.2 $g.dL^{-1}$, leukocyte 16,990/mm^3, thrombocyte 120,000/uL, prothrombin time 19.4 seconds, INR 1.64, activated partial thromboplastin time 44.7 seconds. Blood gas analysis: pH 7.34, pCO_2 45.7 mmHg, lactate 4.5 $mmol.L^{-1}$, and bicarbonate 23.8 $mmol.L^{-1}$. The other laboratory parameters were in normal ranges. Adrenaline infusion was initiated because she was hypotensive and poor peripheral perfusion despite isotonic boluses (20 $mL.kg^{-1}$ twice). Vancomycin (60 $mg.kg^{-1}.day^{-1}$ divided into 4 doses) and ceftriaxone (100 $mg.kg^{-1}.day^{-1}$ divided into 2 doses) treatments were initiated. Control thrombocyte and INR levels were 42,000/uL and 2, respectively. After insertion of the central venous line and hemodialysis catheters, therapeutic plasma exchange was initiated. Her ejection fraction was 15% on echocardiography and therefore milrinone infusion of 0.5 $mcg.kg^{-1}.min^{-1}$ was added and PiCCO (Pulsion Medical Systems, Munich, Germany) (Pulse index Continuous Cardiac Output) monitorization was applied. Adrenaline and noradrenaline infusions were titrated up to 0.5 $mcg.kg^{-1}.min^{-1}$ according to blood pressure and PiCCO parameters. Hydrocortisone was added on as shock-dose treatment since the patient's inotropic agent needs to increase. Hemodialysis with coexisting use of CytoSorb® cytokine trapping filter was initiated since she was anuric. Inotropic agent need of the patient decreased after the use of CytoSorb® filter. Cytokine trapping filter was used twice in 24 hours and there was an absolute decrease in inotrope need. Therapeutic plasma exchange was continued daily. She was free of inotropes on the third day of her hospitalization and her ejection fraction rose to 40% on echocardiography. The abdominal ultrasonography showed adrenal hemorrhage (Fig. 1). Immediate laboratory and clinical response were achieved (Table 1) after 3 days of hemodialysis and CytoSorb® therapy. Meningococcal type B was isolated from the blood specimen of the patient. Therapeutic plasma exchange was performed for five days and then stopped since her thrombocyte levels reached 100,000/uL and the patient was extubated. Hydrocortisone was decreased to maintenance dose gradually. After the patient's need for intensive care was over, she was transferred to the ward on the 11th day of her treatment.

The written informed consent to publication was obtained from the parents on behalf of the patient.

Discussion

We, herein, described a 10-year-old girl who presented with severe septic shock associated with Neisseria meningitidis type B. Neisseria meningitidis is one of the most important bacterial infections that shows off as meningitis and/or septicemia. The predominant feature in some children is cardiovascular collapse leading to septic shock with Neisseria meningitidis. High concentrations of IL-6, IL-8, TNF, IL-1, and endotoxins are seen in meningococcal shock. Overproduction of nitric oxide lowers arterial blood pressure due to vasodilation and impairs cardiac contractility. A most severe form of meningococcemic septic shock is named purpura fulminans and it is associated with a large number of bacteria in the bloodstream.[2] Hemodynamic stabilization is the mainstay of therapy in pediatric septic shock. Resuscitation in septic shock can be rapidly achieved by restoration of perfusion by administration of intravenous fluid, inotropic support, and vasopressor drugs. It is of utmost importance to maintain the appropriate mean arterial pressure level.[2–4]

We used norepinephrine and epinephrine to stabilize mean arterial pressure as our patient had myocardial dysfunction and avoided fast fluid resuscitation. Milrinone was added to support cardiac contractility. We initiated early antibiotic treatment.

Hemadsorption is an adjunctive therapy to reduce elevated cytokine levels. CytoSorb® has been designed to remove multiple inflammatory mediators from the bloodstream in a size range of approximately 10–55 kD. Moreover, CytoSorb® results in rapid hemodynamic stabilization and increased survival, particularly if initiated within 24 hours.[5] We used hemadsorption in our patient with an indication of a severe septic shock.

We observed a significant decrease in vasopressor dosage in this patient. Notably, this patient who was given CytoSorb® therapy < 48 hours after onset of septic shock, survived and we obtained a reduction in all biomarker levels (procalcitonin, C-reactive protein, and serum lactate) after CytoSorb® therapy.

In this patient with meningococcemia, the combined treatment with antibiotic therapy, volume resuscitation, hydrocortisone, and CytoSorb® therapy resulted in a stabilization of hemodynamics, as well as a well-controlled

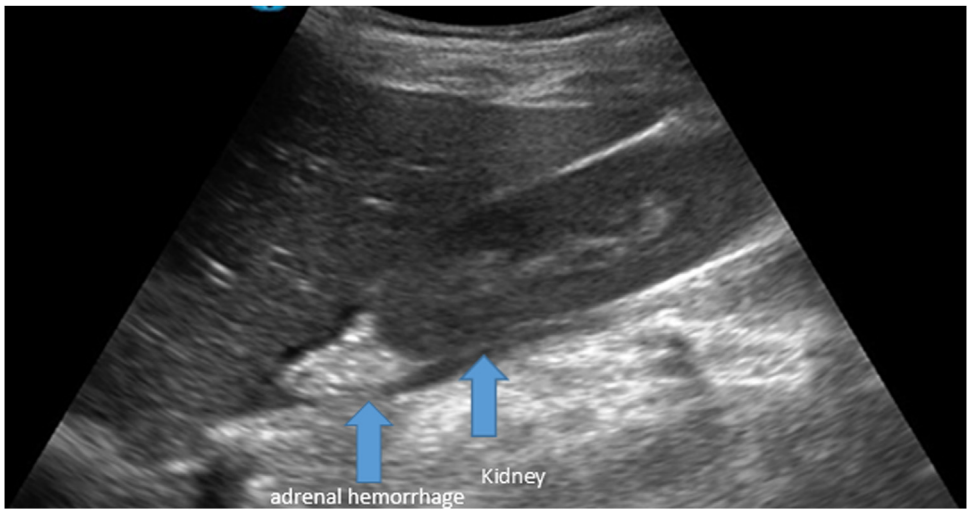

Figure 1 The image of the adrenal hemorrhage that was detected on the abdominal ultrasonography.

Table 1 Changes in biochemical, hematological, and hemodynamic parameters after the CytoSorb®.

CytoSorb® hemadsorption	Before CytoSorb® administration	12th hour	24th hour	72nd hour
WBC (per μL)	16,990	16,920	26,010	32,990
Platelet (per μL)	120	126	72	59
CRP ($mg.L^{-1}$)	136.8	99.2	32.3	14.7
Procalcitonin ($ng.mL^{-1}$)	52.73	17.9	8.76	1.02
Urea ($mg.dL^{-1}$)	46	31	23	43
Creatinine ($mg.dL^{-1}$)	0.74	0.52	0.49	0.25
AST ($U.L^{-1}$)	35	28	25	23
ALT ($U.L^{-1}$)	14	17	15	29
Fibrinogen ($mg.dL^{-1}$)	352	305	364	258
INR	1.64	1.28	1.59	1.09
APTT (s)	44.7	49.1	38.9	31.4
PT (s)	19.4	15.2	18.9	13
D, dimer ($\mu g\ FEU.mL^{-1}$)	7.17	2.85	1.23	0.46
PELOD	7	3	2	2
$ScvO_2$ (%)	58	75	78	76
Lactate ($mmol.L^{-1}$)	8.1	2.2	1.3	1.1
EF (%)	15	22	28	42
VIS	77.5	9.5	9.5	2.5
Adrenaline dose ($\mu g.kg^{-1}.min^{-1}$)	0.50	0.07	0.07	–
Noradrenaline dose ($\mu g.kg^{-1}.min^{-1}$)	0.20	–	–	–
Milrinone dose ($\mu g.kg^{-1}.min^{-1}$)	0.75	0.25	0.25	0.25
BP (mmHg)	93/46	115/74	103/63	104/74
CVP (mmHg)	10	11	9	11
CI ($L.min^{-1}.m^{-2}$)	3,57	3,82	3,88	3,99
GEDVI ($mL.kg^{-1}$)	357	302	395	516
EVLWI ($mL.kg^{-1}$)	15	9	13	10
SVRI ($dyne.sec.m^2/cm^5$)	820	1140	1316	1744

CRP, C-reactive protein; PCT, procalcitonin; WBC, white blood cell; ALT, alanine aminotransferase; AST, aspartate aminotransferase; APTT, activated partial thromboplastin time; PT, prothrombin time; PELOD, pediatric logistic organ dysfunction; EF, ejection fraction; VIS, vasoactive-inotropic score; BP, blood pressure; CVP, central venous pressure; CI, cardiac index; GEDVI, global end-diastolic volume index; ELWI, extravascular lung water index; SVRI, systemic vascular resistance index.
(VIS [vasoactive inotropic score]: dopamine dose ($\mu g.kg^{-1}.min^{-1}$) + dobutamine dose ($\mu g.kg^{-1}.min^{-1}$) + 100 x adrenaline dose ($\mu g.kg^{-1}.min^{-1}$) + 100 x noradrenaline dose ($\mu g.kg^{-1}.min^{-1}$) + 10 x milrinone dose ($\mu g.kg^{-1}.min^{-1}$) + 10.000 x vasopressin dose ($U.kg^{-1}.min^{-1}$).

hyperinflammation. In our opinion, the use of CytoSorb® helped to take the severe hyper inflammation in septic shock under control and presumably, helped the patient to overcome the acute phase by early intervention. We can also predict that CytoSorb® was safe and easy to use in combination with hemodialysis.

Conclusion

To our knowledge, this is the first report on the successful use of hemoadsorption for cytokine removal therapy in a pediatric patient with meningococcal septic shock and Waterhouse-Friderichsen Syndrome. It enables a rapid and clear stabilization in hemodynamics as well as a reduction in catecholamine need and a decrease in lactate.

Conflicts of interest

The authors declare no conflicts of interest.

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