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Single Case

First-Time Use of the Seraph® 100 Microbind® Affinity Blood Filter in an Adolescent Patient with Severe COVID-19 Disease: A Case Report

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Keywords
Pediatric patient · COVID-19 · Continuous renal replacement therapy · Acute kidney injury · Critical care

Abstract
The Seraph® 100 Microbind® Affinity Blood Filter (Seraph® 100) is a hemoperfusion device designed to adsorb bacteria, viruses, and toxins when added to extracorporeal circuits. The FDA granted emergency use authorization in adults, but this device had never been utilized in children. A 17-year-old patient with asthma presented with respiratory distress due to COVID-19. His course was complicated by respiratory failure, rhabdomyolysis, and stage 3 AKI requiring initiation of continuous kidney replacement therapy (CKRT) on ICU day 3. The Seraph® 100 filter was added on ICU day 4. He was treated with 3 filters from ICU day 4 to 8. On ICU day 8, he was extubated and CKRT discontinued. He required no further kidney replacement therapy but did not have laboratory work post-discharge. In conclusion, this adolescent patient with COVID-19 and AKI requiring CKRT tolerated treatment with the Seraph® 100 Microbind® Affinity Blood Filter without significant adverse events.

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Introduction

The Seraph® 100 Microbind® Affinity Blood Filter (ExThera Medical Corporation, Martinez, CA) is a sterile single-use device designed as an extracorporeal broad-spectrum sorbent hemoperfusion device. Within the device, ultra-high molecular weight polyethylene beads, surface-modified with nonleaching endpoint-attached heparin, reduce bacteria, viruses, and toxins in blood as it passes through the filter. As an extracorporeal therapy, it can be added in-line to both continuous kidney replacement therapy (CKRT) and hemodialysis or in a side loop during extracorporeal membrane oxygenation circuits.

The FDA has granted emergency use authorization for the use of the Seraph® 100 Microbind® Affinity Blood Filter (Seraph® 100) for patients who are 18 years of age or older and have at least one of the following as a result of a COVID-19 infection: (a) early acute lung injury or early acute respiratory distress syndrome (ARDS), (b) severe disease, or (c) life-threatening disease. Chitty et al. [1] described a cohort of adult patients that were treated with the Seraph® 100 and overall showed improved mortality and more ICU-free days, as well as lower need for kidney replacement therapy (KRT) after discharge. Both in vitro and in vivo studies show that use of the Seraph® 100 Blood Filter decreases SARS-CoV-2 RNA and nucleocapsid-protein (N-protein) levels [2, 3]. The filter has been used safely in adults with the potential to improve morbidity and mortality but has not yet been used in patients under 18 years of age.

Case Report

A 17-year-old 180 kg adolescent (BMI 63.3 kg/m^2) with asthma on maintenance mometasone furoate/formoterol fumarate inhaler presented to the emergency department (ED) after 2 weeks of cough and congestion with subsequent respiratory distress. He was found to be positive for COVID-19 infection in the ED and had not been vaccinated against COVID-19 prior to presentation. His respiratory status worsened in the ED and eventually required bi-level positive airway pressure and pediatric intensive care unit admission. His COVID-19 infection was treated with dexamethasone, remdesivir, and one dose of tocilizumab. On admission, he was found to have severe rhabdomyolysis and KDIGO stage 3 acute kidney injury (AKI), with serum creatinine 10.54 mg/dL and oliguria. UA showed >500 mg/dL protein and large blood (urine output trends shown in Table 1). CKRT using an HF1000 (surface area 1.4 m^2) with regional citrate anticoagulation was initiated on ICU day 2 due to rhabdomyolysis and AKI (serum creatinine 10.84 mg/dL). On ICU day 3, his respiratory status declined, and he developed ARDS needing intubation. From ICU day 3-4, he required escalation of ventilator settings and developed concerns for possible pulmonary hypertensive crisis. His clinical picture continued to worsen on ICU day 4, leading to a multidisciplinary discussion of extracorporeal membrane oxygenation and prone positioning. As he neared the end of treatment options, the team considered all potential remaining treatment options available.

Under FDA guidance for emergency use for expanded access for medical devices, the Seraph® 100 filter was added to his extracorporeal circuit on ICU day 4 with continued citrate anticoagulation to the CKRT circuit. He had transient hypotension starting approximately 5 min after initiation of CKRT with the Seraph® 100 filter which required an increase in vasoactive support that lasted about 5 min until blood pressure returned to baseline. He continued CKRT for 24 h with subsequent change in CKRT filter and the Seraph® 100 filter. During this filter change, he had a similar episode of transient hypotension lasting roughly 5 min after initiation and requiring increase in vasoactive support that returned to baseline in

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Table 1. Trend of cardiorespiratory support and laboratory markers during treatment course with the Seraph® 100 Microbind® Affinity Blood Filter

Variable	ICU day 3	ICU day 4	ICU day 5	ICU day 6	ICU day 7	ICU day 8	ICU day 9
Seraph® filter		| --- Filter #1 --- |	| --- Filter #2 --- |	| --- Filter #3 --- |			
Lowest PaO_2:FiO_2 ratio	101	124.6	136.7	141.7	191.4	171.4	
Highest oxygenation index	19.3	14.4	13.2	12.7	6.2	6.4	
Mean oxygenation index	16.2	12.1	10.7	8.7	5.3	5.8	
Highest norepinephrine dose, μg/min	7.5	4	8	2	1	0	0
Cumulative daily dose, μg	1,432	5,124	3,119	2,435	657	0	0
Mean norepinephrine dose, μg/min (μg/kg/min)	2.4 (0.133)	3.6 (0.020)	2.2 (0.122)	1.7 (0.009)	0.7 (0.004)	0	0
pSOFA score	10	10	9	8	8	6	4
Urine output, mL/day	115	116	140	141	86	167	529
Troponin, pg/mL		257.74	164.57	89.52	49.86		19.74
CRP, mg/dL		7.9	4.6	3	1.9		0.6
Procalcitonin, ng/mL		5.05	3.46	1.54	0.87		0.38
Ferritin, ng/mL		775	643.7	890.5	936.7		505.6
CPK, u/L		1,300	1,099	721	782		490
COVID-19 N-protein, mean (CV %), pg/mL		2.45 (10)	2.06 (18)	1.02 (20)	0.57 (21)		
Anti-spike IgG, mean (CV %), ug/mL		71.7 (4)	79.4 (8)	120 (11)	130 (1)		

less than 5 min. He continued the second Seraph® 100 for a total of 48 h as he was tolerating it well and a third filter was unavailable until ICU day 7. On ICU day 7, the last Seraph® 100 was placed in his CKRT circuit for a planned 24-h treatment. Total treatment time was approximately 96 h from ICU day 4 to 8 with 3 separate Seraph® 100 filters. His CKRT was prescribed with an effluent dose of 40 mL/kg/h and a blood flow of 200 mL/min for the duration of the Seraph® 100 treatment course. During this course, his respiratory status improved to the point of extubating on ICU day 8 and CKRT was discontinued. Vasoactive medication requirement and inflammatory markers decreased over this interval (Table 1). Serum was tested for COVID-19 N-protein levels as well as anti-spike IgG before, during, and after treatment with the Seraph® 100. As shown in Figure 1, this patient had decreasing serum levels of COVID-19 N-protein as well as rising levels of anti-spike IgG during the duration of his Seraph® 100 filter treatment course. He did not require further kidney replacement therapy during his hospitalization. He was discharged on hospital day 23 with a creatinine of 1.65 mg/dL. He was not followed up with nephrology since his discharge nor had any laboratory testing.

Discussion

This patient was the first pediatric patient to be treated with the Seraph® 100 Microbind® Affinity Blood Filter for ARDS and AKI due to COVID-19 infection. He received approximately 96 h of exposure to the filter in conjunction with his CKRT treatments via a total

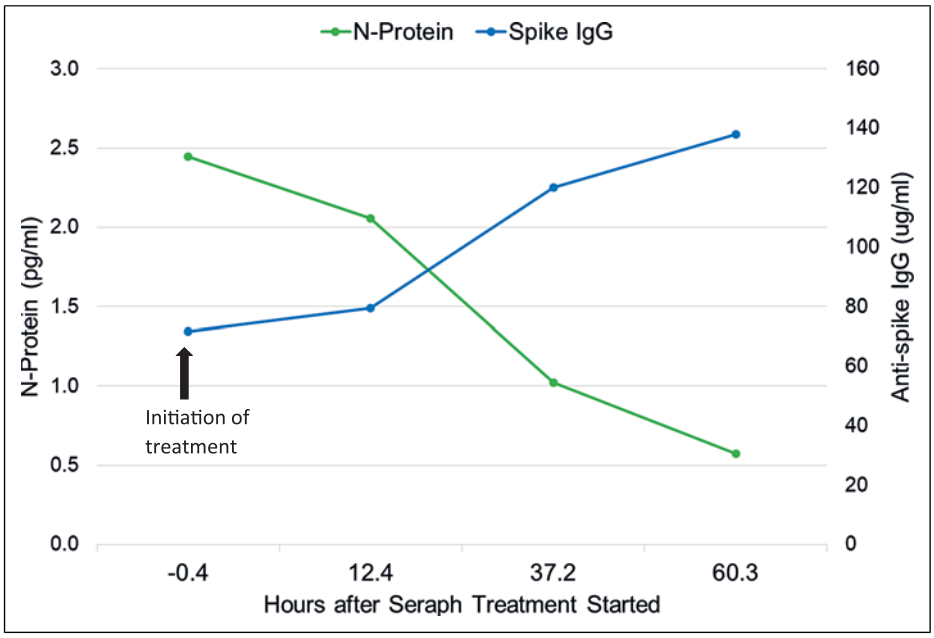

Fig. 1. COVID-19 N-protein and anti-spike IgG levels during treatment course with Seraph® 100 Microbind® Affinity Blood Filter.

of 3 separate Seraph® 100 filters. The use of the filter in this patient was tolerated well with only transient hypotension at filter initiation that resolved with transient (less than 5 min) increase in vasoactive medications. The additional 160 mL volume of the filter was primed with saline. It is possible that this played a role in his brief hypotension, but given his size and estimated blood volume, this is unlikely to play a significant role in hemodynamic change. Similar hypotension events have been shown as common adverse events in adult patients during initiation of CKRT without the use of the Seraph® 100 filter, who are of similar size and body habitus to this patient. In one study from 2015, 97% of the 595 patients had new-onset hypotension within the first hour of CKRT [4]. Therefore, it is not unexpected that this patient had transient hypotension with the initiation of the CKRT treatments. Additionally, there have been multiple case reports, case series, and even one recent multicenter study that showed that overall, the Seraph® 100 filter has been used without serious adverse events in adults [1, 3, 5–7]. The Seraph filter does not contain acrylonitrile-sodium methallyl sulfonate (AN-69) dialyzer and was not at higher risk for bradykinin reaction with his history of asthma. The filter is sterilized with ethylene oxide, but the patient had no known allergy to this component. Over the course of treatment with the Seraph® 100 filter, this patient showed clinical improvement through decreased ventilator support, decreased vasoactive support, and decreased levels of inflammatory markers.

Fajnzylber described in a recent study that COVID-19 plasma viral load was higher in patients with greater disease severity and higher inflammatory markers such as C-reactive protein (CRP) [8]. Additionally, the cohort showed that higher plasma viral load was associated with higher mortality. It is possible that the Seraph® 100 Microbind® Affinity Blood Filter contributed to the clinical improvement of the patient through attenuation of the cytokine storm, but at this time this is still speculative. Measuring viral load can be performed via nucleic acid amplification test (NAAT), but recently Wang et al. [9] described the use of nucleocapsid antigen (N-protein) in place of NAAT in patients with known COVID-19 infection and found that N-protein was comparable to NAAT, particularly within 2 weeks of initial

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infection. The patient's improvement in clinical status may correlate with clearance of the COVID-19 virus by the Seraph® 100 filter as the COVID-19 N-protein level decreased as treatment time progressed, as seen in Figure 1. While the N-protein level decreased, the anti-spike antibody increased, suggesting that the Seraph® 100 filter does not remove unit-spike antibodies. This finding was recently supported by Eden et al. [10] demonstrating immunoglobulins were not removed using the Seraph® 100 filter with hemodialysis. Belogiannis described a case report of patients with COVID-19 infection in which seroconversion was delayed in patients with a high viral antigen load, suggesting that seroconversion may not occur with a high viral load due to saturating the antibody by the viral load and limiting the detection of produced antibodies until viral load is decreased [11]. Although we did not compare N-protein levels and anti-spike IgG levels in patients who were not treated with the Seraph® 100 filter, it is of interest that this patient clearly demonstrated increasing levels of anti-spike IgG with decreasing levels of N-protein during treatment with the Seraph® 100 filter. However, the question remains as to whether this was due to the use of the Seraph® 100 filter or the immunologic phenomenon of the neutralizing antibody and additional studies are necessary to further investigate this hypothesis.

Conclusion

This pediatric patient with severe COVID-19 ARDS and stage 3 AKI requiring CKRT tolerated treatment with the Seraph® 100 Microbind® Affinity Blood Filter without device-related adverse events.

Acknowledgment

The authors would like to thank ExThera Medical Corporation for providing the Seraph® 100 Microbind® Affinity Blood Filters for use with this patient under FDA guidance for emergency use for expanded access for medical devices and for their expeditious support to provide this therapy to this patient under emergency use. It should be noted that ExThera Medical Corporation did not have a role in development of the manuscript or laboratory testing on COVID-19 N-protein and anti-spike IgG levels, nor the treatment of the patient.

Statement of Ethics

Written informed consent was obtained from the patient's mother for publication of the details of their medical case and any accompanying images. The study protocol was reviewed and the need for approval was waived by the Institutional Review Board at Cincinnati Children's Hospital Medical Center.

Conflict of Interest Statement

Stuart Goldstein serves on the Scientific Advisory Board for ExThera Medical Corporation who developed the Seraph® 100 Microbind® Affinity Blood Filter. Dawn Mattoon and Dandan Shan work for Quanterix Corporation who provided laboratory testing for COVID-19 N-protein and anti-spike IgG levels for authorship in this case report. Quanterix provided testing of patient serum for COVID 19 N-protein levels and COVID anti-spike IgG levels.

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Author Contributions

Kyle Merrill wrote the draft and final version of this manuscript. Kelli Krallman, Daniel Loeb, Steve Standage, Dawn Mattoon, Dandan Shan, and Stuart Goldstein contributed to reviewing, editing, and revisions of the manuscript. Dawn Mattoon and Dandan Shan performed the testing for COVID-19 N-protein and anti-spike IgG levels. Meredith Schuh was the senior supervising author to the case report including writing the report and revisions. All authors read and approved the final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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