Pediatric Transplantation

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Seraph 100 Microbind Affinity Blood Filter for Persistent Pediatric BK Virus Nephropathy

Meredith Harris[1,2] | Mahima Keswani[1,2] | Theresa Mottes[1,2] | Taylor Heald-Sargent[1,2] | Priya S. Verghese[1,2]

[1]Ann & Robert Lurie Childrens Hospital of Chicago, Chicago, Illinois, USA | [2]Northwestern Feinberg School of Medicine, Chicago, Illinois, USA

Correspondence: Meredith Harris (merharris@luriechildrens.org)

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ABSTRACT

Background: Resolution of BK viremia is almost universally required before kidney transplant. Unfortunately, proven anti-BK viral therapies are limited. The Seraph 100 mimics the action of the natural glycocalyx, which binds pathogens via heparin sulfate proteoglycans. In this case report, we describe the use of this filter to facilitate the clearance of BK viremia.

Methods: Our patient was a 14-year-old cardiac transplant recipient secondary to familial dilated cardiomyopathy. She developed BK nephropathy resulting in end stage kidney disease (ESKD). After failed medical management and immunoreduction over 4 years, the Seraph 100 Microbind Affinity Blood Filter was utilized extracorporeally in line with continuous renal replacement therapy (CRRT) for 48 h to eliminate detectable BK viral replication.

Results: The patient's BK titers initially increased negligibly but cleared within 2 months of Seraph 100 treatment, and she successfully underwent kidney transplantation without recurrence of BK viremia. There were no adverse events other than one episode of emesis at the initiation of CRRT.

Conclusion: Our case provides proof of concept and feasibility for studying the Seraph 100 as a potential therapeutic option for the clearance of BK viral titers, especially in ESKD patients who already have dialysis access.

1 | Introduction

BK virus, from the Papovaviridae family of viruses, is highly seroprevalent, with an affinity for the renal tubular and transitional epithelial cells of the genitourinary tract after initial infection where it remains latent [1–4]. In its active state, the virus causes BK nephropathy (BKN) in kidney recipients, which can cause graft loss [3]. Unfortunately, BKN is increasingly recognized as a source of renal dysfunction even in non-kidney transplant recipients [3, 5, 6]. Without standard treatment for BKN, initial approaches include decreasing immunosuppression medications, cidofovir, fluoroquinolones, intravenous immunoglobulin, and leflunomide [2, 4]. Viral-specific T cells have also been used to treat BKN in patients with hematopoietic stem cell transplantation and solid organ transplant in case studies [7, 8]. However, there remains no conclusive treatment for BK viremia/nephropathy.

The Seraph 100 Microbind Affinity Blood Filter (Seraph 100) (ExThera Medical Corporation, Martinez, CA) mimics the action of the natural glycocalyx, which binds pathogens via heparin sulfate proteoglycans. Via the heparin-coated microbead absorption media, the Seraph 100 is used pre-filter via continuous renal replacement therapy (CRRT) to bind both gram-positive and -negative bacteria as well as fungal and viral organisms [9–11]. In the United States, the Seraph 100 is currently FDA approved under an Emergency Use Authorization in adults for treatment of life-threatening COVID-19 infection with severe acute respiratory distress syndrome. The Seraph 100 has also been successfully used to treat disseminated adenovirus in an

adolescent kidney transplant recipient, disseminated Epstein–Barr Virus, herpes simplex virus 2, and cytomegalovirus with variable efficacy [9, 10, 12]. Based on the efficacy of previous viral load reduction with the Seraph 100, we hypothesized the Seraph 100 may decrease BK viral load and herein report our experience in a pediatric cardiac transplant recipient with persistent BK viremia, precluding renal transplant.

2 | Case

A 14-year-old female with familial dilated cardiomyopathy developed new onset BK viremia, 8 years post-cardiac transplant. Due to elevated BK PCR titers ranging from < 200 IU/mL to ~6600000 IU/mL for 48 months, a nephrology consultation was obtained. A kidney biopsy demonstrated globally and segmentally sclerotic glomeruli with patchy and focally marked interstitial fibrosis and tubular atrophy. Definite viral cytopathic effect was not identified, likely secondary to the delay in the nephrology consult as well as the focal nature of BK virus replication in the kidney. She was treated with leflunomide, IVIG, and immunoreduction with tacrolimus monotherapy with a reduced goal trough of 3–5 ng/mL. Despite these interventions over 4 years, BK virus continued to be detectable, albeit mostly with titers < 2000 IU/mL. Due to progressive decline in her glomerular filtration rate, she underwent a kidney transplant evaluation and was deemed ineligible due to ongoing detectable BK viremia. With her impending need for renal replacement therapy (RRT), the family opted for hemodialysis allowing for utilization the Seraph 100 filter. The Seraph 100 was approved via our Institutional Review Board, and parental consent and patient assent were obtained. The patient's estimated GFR at initiation of CRRT was 9 mL/min/1.73 m^2 using the U25 combined GFR equation [13]. A hemodialysis catheter was placed and CRRT was initiated using the Seraph 100 filter. The patient remained on continuous veno-venous hemodialfiltration with the Seraph 100 for 48 h with the filter changed at 24 h. She did have emesis at the initiation of RRT, but no other adverse effects were noted. Blood flow (Qb) was started at 100 mL/min and increased to 150 mL/min during the course of Seraph 100 treatment. The CRRT circuit was anticoagulated with regional citrate and calcium without any unplanned circuit stops or thrombotic events. The effluent dose delivered was deliberately lowered between 1000 and 1500 mL/1.73 m^2/h to prevent dialysis disequilibrium syndrome. BK virus level the day of initiation was 542 IU/mL. Figure 1 shows trends of BK level from the time of initiation of the Seraph 100 filter. The patient was then initiated on hemodialysis for ongoing chronic RRT. Two months post Seraph 100, her BK level was undetectable despite no additional medical treatments or immunoreduction. She underwent a living donor kidney transplant and is now 6 months post-transplant with no recurrence of BK viremia and an unremarkable 3-month surveillance kidney biopsy.

3 | Discussion

We present the first reported case of the Seraph 100 filter for a patient with 48 months of persistent BK viremia, with failure to respond to immunoreduction and medical management, precluding kidney transplantation. The patient tolerated 48 h on the Seraph 100 filter well with no adverse events other than emesis at the initiation of CRRT and no unplanned circuit terminations. While no significant change was noted in the BK viral load immediately after Seraph100 use, the BK viral load became negative within 2 months and has remained negative despite increased immunosuppression after kidney transplantation. Given the months of persistent BK viremia prior to the Seraph utilization, we do surmise that the filter was effective. We theorize that the outside capsid protein of the BK virus (VP1) binds to the negatively charged heparin sulfate on the Seraph 100 microbeads and sequesters the BK virus [14]. The delayed response

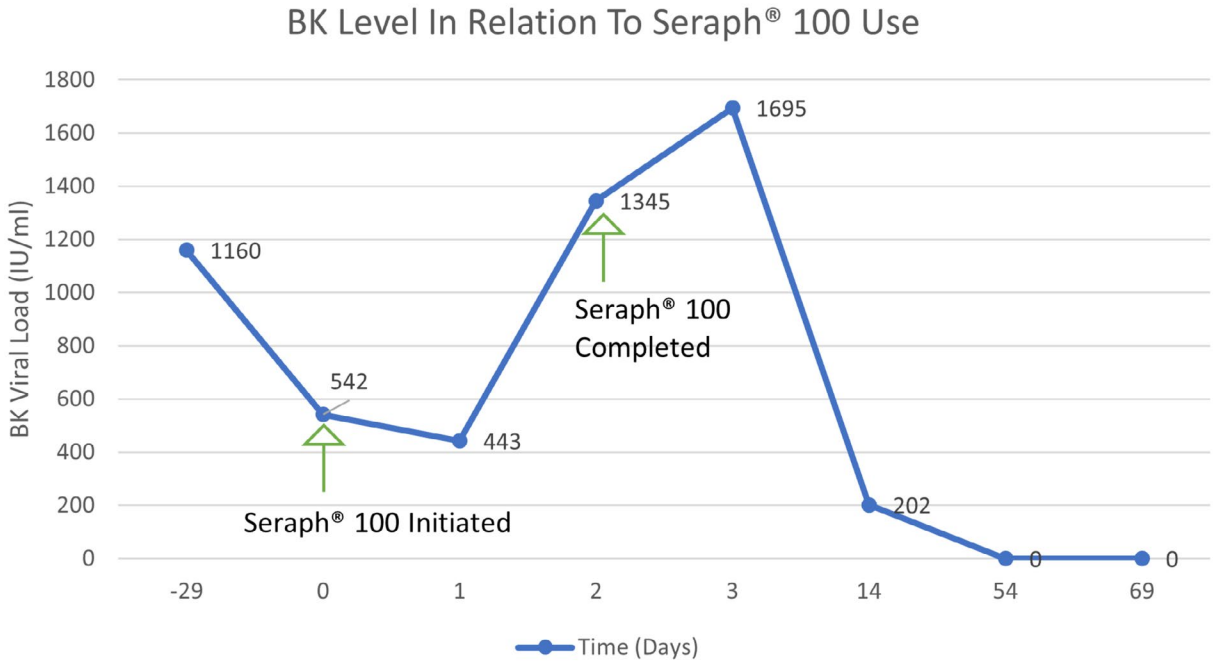

FIGURE 1 | BK viral load in relation to the time of initiation to Seraph 100 use. Time 0 is the time of initiation of the Seraph 100 filter.

could represent that the patient achieved viral load reduction by the Seraph 100 to a level that the patient had immunocompetency to eliminate. Additionally, the BK PCR measures DNA, not whole virus, and potentially was detecting DNA released from lysed virally infected cells or viral particles.

The Seraph 100 has shown efficacy in the reduction of adenovirus viral load in a pediatric solid organ transplant (kidney) patient in a prior study; we hypothesized that there could be similar efficacy for the BK virus. Ongoing studies are needed to evaluate the success of the Seraph 100 in dialysis-dependent patients with BKN. We also acknowledge that the patient had a relatively low BK viral load at the initiation of Seraph 100; it is unclear how effective the Seraph 100 will be in patients with a viral load in multiples of our patient. There is potential that the patient may have tolerated renal transplantation without complications from BKN as her titers were low, although increased immunosuppression at the time of renal transplantation may have exacerbated BKN.

4 | Conclusion

In our patient, the Seraph 100 filter appears to be safe and potentially effective for the removal of BK viral burden. Additional data is required to assess the efficacy of the Seraph 100 in other patients with BKN. As BKN is notoriously difficult to treat, the Seraph 100 may serve as an adjunct in patients who have failed medical management.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

References

1. T. Ahlenstiel-Grunow, M. Wilhelm, S. Wilk, and H. H. Hirsch, "BK Polyomavirus-Specific T Cells as a Diagnostic and Prognostic Marker for BK Polyomavirus Infections After Pediatric Kidney Transplantation," *Transplantation* 104, no. 11 (2020): 2393–2402.

2. M. Borriello, D. Ingrosso, A. F. Perna, et al., "BK Virus Infection and BK-Virus-Associated Nephropathy in Renal Transplant Recipients," *Genes (Basel)* 13, no. 7 (2022): 1290.

3. J. F. Nieto-Rios, D. A. Benavides-Henao, A. Aristizabal-Alzate, et al., "BK Virus Nephropathy in a Heart Transplant Recipient," *Jornal Brasileiro de Nefrologia* 43, no. 3 (2021): 434–439.

4. H. H. Hirsch, P. S. Randhawa, and AST Infectious Diseases Community of Practice, "BK Polyomavirus in Solid Organ Transplantation-Guidelines From the American Society of Transplantation Infectious Diseases Community of Practice," *Clinical Transplantation* 33, no. 9 (2019): e13528.

5. Z. M. Thompson, G. Ajene, P. A. Kulkarni, N. Aggarwal, S. Fedson, and M. K. Shah, "Native BK Polyomavirus Nephropathy in an Orthotopic Heart Transplant Patient," *Journal of Investigative Medicine High Impact Case Reports* 11 (2023): 84770.

6. P. S. Verghese, L. S. Finn, J. A. Englund, J. E. Sanders, and S. R. Hingorani, "BK Nephropathy in Pediatric Hematopoietic Stem Cell Transplant Recipients," *Pediatric Transplantation* 13, no. 7 (2009): 913–918.

7. I. Tzannou, A. Papadopoulou, S. Naik, et al., "Off-The-Shelf Virus-Specific T Cells to Treat BK Virus, Human Herpesvirus 6, Cytomegalovirus, Epstein-Barr Virus, and Adenovirus Infections After Allogeneic Hematopoietic Stem-Cell Transplantation," *Journal of Clinical Oncology* 35, no. 31 (2017): 3547–3557.

8. R. Khoury, M. S. Grimley, A. S. Nelson, et al., "Third-Party Virus-Specific T Cells for the Treatment of Double-Stranded DNA Viral Reactivation and Posttransplant Lymphoproliferative Disease After Solid Organ Transplant," *American Journal of Transplantation* 24, no. 9 (2024): 1634–1643.

9. V. Votrico, M. Grilli, U. Gerini, and G. Berlot, "Hemoperfusion With High-Affinity Polyethylene Microbeads (Seraph-100((R))) for the Removal of Pathogens in Chronic Critically Ill Patients: Clinical Experience," *International Journal of Artificial Organs* 47, no. 2 (2024): 115–117.

10. D. S. Li, T. M. Burke, J. M. Smith, R. C. Reed, D. M. Okamura, and S. Menon, "Use of the Seraph(R) 100 Microbind(R) Affinity Blood Filter in an Adolescent Patient With Disseminated Adenoviral Disease," *Pediatric Nephrology* 39, no. 1 (2024): 331–335.

11. V. Premuzic, I. Situm, D. Lovric, et al., "Sequential Extracorporeal Blood Purification Is Associated With Prolonged Survival Among ICU Patients With COVID-19 and Confirmed Bacterial Superinfection," *Blood Purification* 52, no. 7–8 (2023): 642–651.

12. R. Andermatt, G. V. Bloemberg, C. C. Ganter, et al., "Elimination of Herpes Simplex Virus-2 and Epstein-Barr Virus With Seraph 100 Microbind Affinity Blood Filter and Therapeutic Plasma Exchange: An Explorative Study in a Patient With Acute Liver Failure," *Critical Care Explorations* 4, no. 8 (2022): e0745.

13. C. B. Pierce, "Age- and Sex-Dependent Clinical Equations to Estimate Glomerular Filtration Rates in Children and Young Adults With Chronic Kidney Disease," *Kidney International* 99, no. 4 (2021): 948–956.

14. E. M. Geoghegan, D. V. Pastrana, R. M. Schowalter, et al., "Infectious Entry and Neutralization of Pathogenic JC Polyomaviruses," *Cell Reports* 21, no. 5 (2017): 1169–1179.