First Successful Therapeutic Plasma Exchange in a 3-Year-5-Month Old Bangladeshi Paediatric Patient: A Case Report

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indications, frequent technical problems regarding vascular access and lower blood volume, higher incidence of adverse events during the procedure and poor cooperation of the patient.³ Among paediatric nephrological diseases, aHUS is a leading clinical indication for TPE.⁴

ABSTRACT

Therapeutic plasma exchange (TPE) has evolved to an accepted therapy for selected indications. The aim is to remove putative disease mediators from the body. It is technically challenging in children but has become increasingly common practices for last several decades. We report a successful case of TPE along with renal replacement therapy in a 3-year-5-month old boy, weighing 15kg, diagnosed as atypical haemolytic uremic syndrome (aHUS). To the best of our knowledge TPE and Haemodialysis for such age and weight was for the first time in Bangladesh.

Key words: Therapeutic Plasma Exchange (TPE), Atypical Haemolytic Uremic Syndrome (aHUS), Haemodialysis

Introduction

TPE consists of drawing venous blood into the extracorporeal circuit, separating and removal of plasma from cellular component and return of all cellular components with appropriate replacement fluid (Albumin or FFP) to the patient. In clinical practice two rationales for TPE are to remove a circulating pathogenic molecule (antibody, immune complex, toxin) and to replace a deficient factor. One plasma volume (PV) exchange will remove around 65% of the initial component from intravascular space, 1.5 PV exchange around 75% and 2 PV around 83%.¹ The American Society for Apheresis (ASFA) guideline is most widely followed and it provides evidence-based indications for TPE particularly for adults and automated apheresis machines are mostly used in adults.² Therefore, application of TPE in paediatric patients is more challenging for multiple factors: lack of universally accepted

Case Report

A three-year- five-month old boy weighing 15kg diagnosed as aHUS at Dhaka Shishu Hospital who initially presented with diarrhoea with pneumonia. He had low complement (C3) level and underwent renal biopsy but formal report was missing. He received

peritoneal dialysis but with rapid deterioration of his condition, the boy was referred to Apollo Hospitals Dhaka (now Evercare hospital Dhaka). He was found severely pale, lethargic and drowsy, with non-recordable BP, SPO2 80% at room air; hepatomegaly, oozing from peritoneal dialysis catheter site, thrombophlebitis over right forearm and in septic shock at emergency. He was immediately transferred to ICU. CV line was placed, started nor-adrenaline and optimized antibiotics with Polymyxin B, Teicoplanin, Anidulafungin according to blood and urine culture report (Candida in blood and urine; Klebsiella in blood). His laboratory evaluation revealed very critical HB 2.4 gm/L, platelet 10000/micro litre, WBC 12000/micro litre, features of micro-angiopathic haemolytic anaemia in peripheral blood smear, a negative Coomb's test, LDH 2042 U/L, S. Haptoglobin <29mg/dl, INR 1.84, APTT 38 sec, Fibrinogen 181 mg/dl, Creatinine 2.9 mg/dl, Urea 174, Bilirubin 0.5 mg/dl, ADAMTS13 was not done. His procalcitonin was > 200 ng/ml. Patient was managed by PRBC and one aphaeretic unit platelet was transfused before the insertion of Femoral catheter. On next day urgent decision of TPE was taken.

One session of TPE was initiated in ICU using Optia Apheresis (Terumo BCT, Lakewood, CO, USA) machine. His total blood volume (TBV) was 1275ml with plasma volume (PV) of 730ml. His extra corporeal volume (ECV) was exceeding 10% from his TBV and intra procedural haematocrit below 24% during the session. So, we performed custom prime with PRBC before connecting the circuit to the patient. Throughout the session his vitals were monitored carefully. To avoid systemic hypocalcaemia, calcium gluconate injection was given accordingly. Fluid balance was kept at 90% to keep the patient at negative balance for renal impairment. Fresh frozen plasma (FFP) and normal saline were used as replacement fluids. One volume of plasma exchange was done successfully without any complications.

He had single session of haemodialysis on the following day. He was also started prednisolone and mycophenolate mofetil. His renal function started to improve gradually. Patient's clinical, haematological and renal conditions responded dramatically well after TPE with haemodialysis and more TPE sessions were planned but patient couldn't continue due to financial ground. His hospital stay was complicated with hypertension requiring antihypertensive. With other supportive treatments patient was improved and was discharged on 17th day.

Discussion

Atypical HUS is a rare clinical condition which is associated with significant morbidity and mortality.^{5,6} Classical

presentation of aHUS is the triad of thrombocytopenia, microangiopathic haemolytic anaemia, and acute renal failure.⁷ Our patient presented in this manner. Atypical HUS is a multigenic complement-mediated disorder.⁷ It is often associated with a genetic or acquired defect, resulting in host cell dysregulation of complement. In many patients, a gastrointestinal or a urogenital infection pave the way for the clinical triad and leads to aHUS.⁸ In complement-mediated HUS mutations in the complement factor H (CFH) gene that encodes regulatory proteins are commonly found genetic abnormalities.^{9,10} This condition often most commonly inflicts females and children. Current therapeutic options for aHUS are plasma exchange and eculizumab (anti C5 antibody). Empirically, TPE is considered as the first-line treatment. Although TPE is associated with a reduction of mortality from 50% to 25%, in a 3-year follow-up, 48% of paediatric patients and 67% of adult patients died or progressed to ESRF.^{6,11,12} TPE in combination with immunosuppressive drugs such as corticosteroids and azathioprine or mycophenolate mofetil and an anti-CD20 antibody (rituximab) has shown long-term dialysis-free survival in 60–70% of patients.^{13,14}

Eculizumab is recommended as the first-line therapy for children.¹⁵ However, when eculizumab is unavailable in resource-poor settings such as Bangladesh, TPE may be the first treatment of choice. In our patient, TPE was a successful treatment, because he completely recovered following TPE with prednisolone. ASFA assigns TPE in aHUS in category I.

Since last few decades TPE has been successfully used in various paediatric neurologic, immunologic, renal and haematological conditions. First plasma exchange was reported in patient of Waldenström's Macroglobulinemia in 1960.¹⁶ Modern Apheresis instruments are fully auto-mated and separation can be done on basis of density, size or differential adsorptions.

Paediatric patients are considered special and attention should be given to access, anticoagulation, volume shifts and replacement fluid. Continuous centrifugation is generally considered preferable to intermittent centrifugation for children. The large ECV, which is fixed in automated apheresis instrument and blood loss in the circuit, increase the risk of hypotension and anaemia.¹⁷ At the beginning of the procedure the blood volume removed acutely from the patient is the equivalent to the volume of the circuit including tubing and centrifuge. Also, an obligatory red cell mass is retained in the channel throughout the procedure to allow separation of blood component.¹⁸ This obligatory ECV can represent a significant percentage of patient's TBV and it ranges

from 200-400ml in different apheresis instruments.¹⁹ If ECV exceeds 10-15% (In paediatric patient usually 8-10%) of patient's TBV it can cause hypotension and impaired oxygen delivery.²⁰ To avoid this complication the circuit can be primed with PRBC or albumin. Successful TPE can be done safely in children weighing as little as 3.2kg after blood priming.²¹ Another challenge for paediatric population is the vascular access. Under standard draw negative pressure, the catheters should be stiff and should not collapse. Carter et al reported catheter related complications were common in paediatric population.²² Large bore, dual lumen catheters which are used for haemodialysis can be used and proper care should be taken to prevent infections and clotting.²³ Michon et al found complications are relatively less (<6%) and minor in adults, where as it is up to 55% procedures in children.²⁴ The most common complication was hypotension (14%) but only <5% required fluid bolus.²⁴ ECV was exceeding >15% of TBV in our patient. So, we needed to prime the circuit with PRBC. Patient responded well after one session.

Conclusion

TPE is safe and highly effective therapy in paediatric patients when volume shifts, calcium supplementation, venous access, anticoagulation, and psychological aspects are taken care of properly.

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