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Therapeutic Plasma Exchange does not Improve Renal Function in Hematopoietic Stem Cell Transplantation–Associated Thrombotic Microangiopathy: An Institutional Experience

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A B S T R A C T

Transplantation-associated thrombotic microangiopathy (TA-TMA) is a complication of hematopoietic stem cell transplant (HSCT) that causes severe multiorgan injury. The kidneys are almost universally affected. There is no proven therapy, but therapeutic plasma exchange (TPE) is commonly used to treat TA-TMA at Texas Children's Hospital (TCH). To date, there have been no studies assessing the long-term efficacy of TPE in preventing the development of chronic kidney disease (CKD) in TA-TMA patients. In this study we retrospectively analyzed the incidence of CKD in TA-TMA pediatric patients treated with TPE to determine if this treatment modality improves renal morbidity. We reviewed records between January 2007 and June 2017 of pediatric HSCT patients diagnosed with TA-TMA, identified through an internal database maintained at TCH. To be included patients must have completed a course of TPE per the "TPE in TA-TMA" institutional protocol at TCH. CKD was defined as kidney damage for at least 3 months and stratified into stages 1 through 5 according to estimated glomerular filtration rate. Stages 4 and 5 were considered "severe CKD." In the 10-year timeframe 15 patients with TA-TMA completed a course of TPE per our institutional protocol and were subsequently followed for a median of 963 days. Fourteen patients developed CKD, and 5 of these 14 patients developed severe CKD. The cumulative incidence of severe CKD development was 33% (95% confidence interval. 11% to 57%). 6 patients required dialysis, and 2 patients received a renal transplant. 5 patients received eculizumab in addition to TPE. In our patients a TPE course of at least 7 weeks (and up to 25 weeks) was not effective in the prevention of CKD. Our data indicate a need for alternative therapeutic measures to prevent the development of CKD in TA-TMA patients.

INTRODUCTION

Transplantation-associated thrombotic microangiopathy (TA-TMA) is a complication of hematopoietic stem cell transplant (HSCT) characterized by microangiopathic hemolytic anemia, thrombocytopenia, and microvascular thrombosis, which can lead to severe end-organ injury. The reported incidence of TA-TMA ranges from 12% to 39% [1-3], and mortality can be as high as 90% in severe or untreated cases [3-5]. The pathogenesis of TA-TMA is not entirely understood but is believed to be multifactorial, leading to microvascular endothelial cell injury and formation of microthrombi predominantly in the kidneys, lungs, gastrointestinal tract, and central nervous system [6]. Immunosuppressive drugs, radiation therapy, high-dose chemotherapy, certain HSCT conditioning regimens, graft-versus-host disease (GVHD), and infection are just some of risk factors associated with development of TA-TMA [1–3,7–11]. More recently, the alternative complement pathway has been implicated in the pathogenesis [5,6,12–14].

The kidney is the most universally affected organ in TA-TMA [11,15–17], and biopsy or autopsy of kidney tissue in TA-TMA patients reveals glomerular microthrombi, swelling of glomerular endothelial cells suggestive of endothelial cell damage, mesangiolysis, and often complement deposition in the renal arterioles [6,18–20]. At the time of TA-TMA diagnosis patients present with impaired renal function manifested by decreased glomerular filtration rate (GFR), proteinuria, and/or

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hypertension [13,17,19]. This acute kidney injury will often progress to chronic kidney disease (CKD) over time, leading to additional significant complications [6,7,17].

Therapeutic plasma exchange (TPE) is a commonly used therapy for TA-TMA at Texas Children's Hospital. Although reports on its efficacy vary in the literature, several studies show response rates to TPE ranging from 60% to 75%, with earlier initiation shown to improve outcome [6,8,21,22]. To date, there have been no studies assessing the long-term efficacy of TPE in preventing CKD development in patients with TA-TMA. In this study we aimed to assess the incidence of CKD in patients who completed a course of TPE as per our institutional protocol to determine if TPE can prevent the renal morbidity of TA-TMA. To our knowledge this is the first study analyzing the incidence of CKD in TA-TMA pediatric patients treated with TPE.

METHODS

Data collection and analysis were performed with the approval of the Institutional Review Board of Baylor College of Medicine, Houston, Texas. The study was exempt from the requirement of obtaining informed consent because of its retrospective nature.

We reviewed records between January 2007 and June 2017 of pediatric HSCT patients diagnosed with TA-TMA who completed a course of TPE per the Texas Children's Hospital "TPE in TA-TMA" protocol. The patients were identified by review of an internal TA-TMA database maintained at our institution. These patients were diagnosed by their HSCT treating physician using our institutional TA-TMA diagnostic criteria, which include 4 major criteria and 3 additional supportive criteria that can aid in the diagnosis. The 4 major criteria are ≥2 schistocytes per high power field in the peripheral blood; lactate dehydrogenase increased above institutional baseline; doubling of baseline creatinine, proteinuria/hemoglobinuria, or hypertension; and haptoglobin < 7 mg/dL. Supportive criteria are platelets < 50×10^9/L or decreased by 50% from baseline, anemia, or plasma hemoglobin > 30 mg/dL. Patients must also have a negative direct antiglobulin test and normal ADAMTS13 (A Disintegrin And Metalloproteinase, with ThromboSpondin type 1 motif, member 13) levels.

TMA resolution was defined as platelets above 50×10^9/L without transfusion support, <2 schistocytes per high power field, and normalization of lactate dehydrogenase. CKD was defined as kidney damage for at least 3 months and stratified according to estimated GFR (eGFR) calculated by the Schwarz bedside equation: CKD 1, >90 mL/min/1.73 m^2; CKD 2, 60 to 89 mL/min/1.73 m^2; CKD 3, 30 to 59 mL/min/1.73 m^2; CKD 4, 15 to 29 mL/min/1.73 m^2; and CKD 5, <15 mL/min/1.73 m^2. "Severe CKD" was defined as CKD stage 4 or 5.

TPE procedures were performed using centrifugation with Spectra OPTIA and COBE Spectra (Teruma BCT, Lakewood, CO). Fresh frozen plasma was used for replacement fluid, and 1.2 to 1.3 plasma volume was exchanged for all TPE procedures. The total course and frequency of TPE was performed as per our institutional guidelines: 8- to 10-week course, beginning with 3 sessions per week for 3 to 4 weeks, followed by 2 sessions per week for 3 to 4 weeks, and concluding with 1 session per week for 2 to 3 weeks.

The use of other therapeutic modalities did not exclude patients from study. Beginning in 2013 the complement C5 inhibitor, eculizumab, was administered based on encouraging data demonstrating efficacy in the treatment of TA-TMA [5]. In our center eculizumab is dosed weekly by weight-based regimens (≥40 kg, 900 mg; 10-39 kg, 600 mg; 5-9 kg, 300 mg), is sequenced after TPE to prevent removal of the drug from patient plasma, and is initiated once TPE is performed no more than twice weekly (ideally once weekly). 8 independent confounding nephrotoxic variables were investigated and included the administration of nephrotoxic medications (foscarnet, vancomycin, cidofovir, amphotericin B, and calcineurin inhibitors) [23–26], the presence of BK cystitis, or a diagnosis of GVHD [17,23,27,28] in the 3 months before or during the course of TA-TMA diagnosis and a conditioning regimen consisting of total body irradiation [28,29].

Statistical Methods

Descriptive statistics were used to summarize the data. Normality assumptions were checked. A log transformation was applied to achieve normal distribution of data if appropriate. Comparisons were made between groups using the Wilcoxon rank-sum test or *t*-test for continuous variables. Overall survival was calculated from the time of TA-TMA diagnosis to death from any cause; observations were censored at the date of last follow-up. Cumulative incidence was estimated for severe CKD after TA-TMA with death as a competing risk. A $P < .05$ was considered statistically significant.

RESULTS

Patient Characteristics

Patient characteristics are provided in Table 1. 15 patients completed TPE per our institutional protocol for treatment of TA-TMA in the 10-year time frame, 11 male and 4 female patients. The median age at TA-TMA diagnosis was 8 years (range, 10 months to 18 years). All 15 HSCTs were allogeneic: 9 (60%) matched unrelated donor, 2 (13%) matched related donor, 2 (13%) haploidentical, 1 (7%) mismatched related donor, and 1 (7%) cord blood transplant. 12 patients (80%) received HSCT secondary to malignant disease, whereas 3 patients (20%) received HSCT for nonmalignant disease. Most patients received total body irradiation–based conditioning regimens (12, 80%). 12 patients (80%) received calcineurin inhibitors as immune suppression post-transplant. In 8 of these patients the calcineurin inhibitors were discontinued before the diagnosis of TA-TMA as part of the routine post-transplant care; in the other 4 patients these drugs were stopped upon making the diagnosis of TA-TMA. 6 patients (40%) had a concurrent diagnosis of acute GVHD, and in all cases the GVHD was well controlled and mild (skin, grades I to II). Median baseline (pre-HSCT) creatinine levels and eGFR in all patients were 0.4 mg/dL (range, 0.2 to 0.6) and 144 mL/min/1.73 m^2 (range, 107 to 220), respectively.

Patient Presentation and Treatment Characteristics

Patient presentation and treatment characteristics are described in Table 2. 12 patients met all 4 major criteria for TA-TMA diagnosis, and 3 patients met 3 of 4 major criteria and 2 of 3 minor criteria to make the diagnosis. The median lactate dehydrogenase level at TPE initiation was 1684 U/L (range, 594 to 3280). Creatinine and eGFR levels at TPE initiation were 0.9 mg/dL (range, 0.44 to 2.6) and 67 mL/min/1.73 m^2 (range, 21 to 137), respectively. The median hemoglobin level and platelet count at TPE initiation were 8.1 g/dL (range, 6.3 to 9.2) and 49×10^9/L (range, 7 to 117), respectively.

In all 15 patients internal jugular vein pheresis catheters were placed 24 to 72 hours before the initiation of TPE. TPE was initiated at a median of 5 days after the TA-TMA diagnosis

Table 1
Patient Characteristics and Demographics (N = 15)

Characteristic	Value
Median age at TA-TMA diagnosis (range)	8 (10 months to 18 years)
Sex	
Male	11 (73)
Female	4 (27)
Race/ethnicity	
White/Hispanic	11 (73)
White/non-Hispanic	4 (27)
HSCT type	
MUD	9 (60)
MRD	2 (13)
Haploidentical	2 (13)
MMRD	1(7)
Cord blood	1 (7)
Underlying diagnosis	
Malignant	12 (80)
Nonmalignant	3 (20)
TBI conditioning	12 (80)
Calcineurin inhibitor	12 (80)
GVHD	6 (40)
Median pre-HSCT creatinine, mg/dL (range)	0.4 (0.2-0.6)
Median pre-HSCT eGFR, mL/min/1.73 m^2 (range)	144 (107-220)

Values are n (%) unless otherwise defined. MUD indicates matched unrelated donor; MRD, matched related donor; MMRD, mismatched related donor; TBI, total body irradiation.

Table 2
Patient Presentation and Treatment Characteristics

Characteristic	Value
LDH at TPE initiation, U/L	1684 (594-3280)
Creatinine at TPE initiation, mg/dL	0.9 (0.44-2.6)
eGFR at TPE initiation, mL/min/1.73 m^2	67 (21-137)
Hemoglobin at TPE initiation, g/dL	8.1 (6.3-9.2)
Platelet count at TPE initiation, 10^9/L	49 (7-117)
TPE initiation after TA-TMA diagnosis, days	5 (1-175)
Length of TPE course, days	80 (48-174)
TPE + eculizumab, n (%)	5 (33)
Eculizumab initiation after TA-TMA diagnosis, days	42 (6-123)

Values are median (range) unless otherwise defined. LDH indicates lactate dehydrogenase.

but ranged from 1 to 175 days after diagnosis because some providers chose to trial other therapies before TPE initiation. When further stratifying into "early" and "late" TPE initiation, 12 patients (80%) underwent TPE initiation early, at a median of 4 days after TA-TMA diagnosis (range, 1 to 13), whereas the remaining 3 patients underwent TPE initiation late, at 59, 78, and 175 days after TA-TMA diagnosis, respectively.

Patients were treated with a median TPE course of 80 days (range, 48 to 174), equivalent to 11.5 weeks (range, 7 to 25). 1 patient received 7 total weeks of TPE (1 less than our institutional protocol recommends) secondary to thrombosis of his central line 7 weeks into his TPE course. Because he demonstrated hematologic resolution of TA-TMA at that time, the decision was made to remove the line and forego additional TPE sessions. One patient was treated with high-dose intravenous immune globulin, prednisone, and rituximab in addition to TPE. Five patients (33%) received eculizumab at a median of 42 days (range, 6 to 123) after TA-TMA diagnosis as an additional therapy to TPE. In 4 of these patients eculizumab was initiated after TPE was weaned to less frequent dosing. In the 5th patient eculizumab was used initially as sole therapy for TA-TMA; however, TPE was eventually added secondary to lack of improvement with eculizumab alone. Eculizumab was dosed at weekly intervals in all 5 patients. One patient only received 4 doses, 2 patients received 9 total doses, 1 patient received 13 doses, and 1 patient received 28 doses. CH50 levels were followed in 3 of 5 patients, but changes to the eculizumab dose or frequency were not made based on the levels.

Overall Survival

Figure 1 presents the overall survival of patients who completed a course of TPE per our institution's protocol. 2 patients

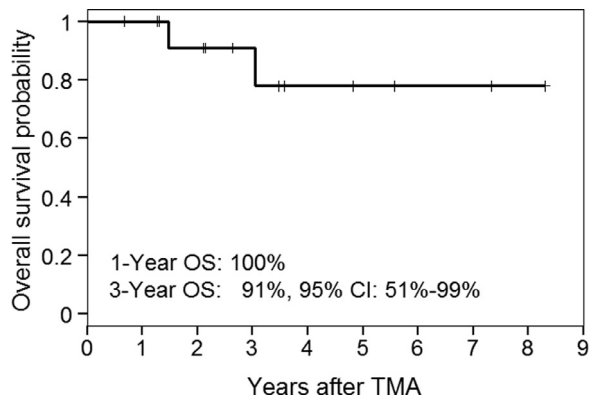

Figure 1. Overall survival of patients who completed a course of TPE per the Texas Children's Hospital "TPE in TA-TMA" protocol.

(13%) died of complications related to HSCT (bronchiolitis obliterans and cytomegalovirus pneumonitis) but unrelated to their diagnosis of TA-TMA or CKD or due to complications from TPE. The 1- and 3-year overall survival rates were 100% and 91% (95% confidence interval, 51% to 99%), respectively.

Outcomes

Patients were followed for a median of 963 days (range, 243 to 3032). All patients demonstrated a hematologic response with TPE treatment at a median of 82 days (range, 46 to 372). 10 patients (66.7%) suffered from complications, which included both catheter-related and TPE-related complications (Table 3). Some of these patients suffered from more than 1 complication during the TPE course. Catheter-related issues included bleeding from the line site (26.7%), resuturing of the line (26.7%), complete dislodging of the line (6.7%), and thrombosis (6.7%), whereas TPE-related issues included hypocalcemia (26.7%) and allergy/transfusion reaction to fresh frozen plasma (46.7%). All 4 cases of hypocalcemia resolved by increasing the calcium chloride infusion rate during the procedure, and all 7 transfusion reactions resolved with antihistamine and/or steroid administration. There were no infections associated with the pheresis catheter in any patient, and there were no cases of anaphylaxis reported. As mentioned above, the patient with catheter-related thrombosis required removal of the line and discontinuation of TPE 1 week premature of completing an 8-week course per protocol.

14 patients (93%) developed CKD, with 5 (36%) developing severe CKD by a median of 92 days (range, 63 to 159) after TA-TMA diagnosis (Table 4). The CKD stages in the 3 patients who underwent late TPE initiation at 59, 78, and 175 days were 2, 4, and 2, respectively. One patient who died was CKD

Table 3
TPE Complications

Complication	No. of Cases (%)
Catheter-related	
Bleeding	4 (26.7)
Resuturing	4 (26.7)
Dislodged	1 (6.7)
Thrombosis	1 (6.7)
TPE-related	
Hypocalcemia	4 (26.7)
Allergy/transfusion reaction	7 (46.7)

Table 4
TA-TMA Outcomes

Outcome	Value
Length of follow-up, days	963 (243-3032)
TA-TMA resolution, days	82 (46-372)
CKD, n (%)	14 (93)
Severe (stage 4 or 5), n (%)	5 (36)
Severe CKD after TA-TMA diagnosis, days	92 (63-159)
Cumulative incidence of severe CKD in all patients, % (95% CI)	33 (11-57)
Dialysis, n (%)	6* (40)
Renal transplant, n (%)	2† (13)
Creatinine at last follow up,‡ mg/dL	1.2 (0.6-6.4)
eGFR at last follow up,‡ mL/min/1.73 m^2	38 (11-98)

Values are median (range) unless otherwise defined.

* One patient with CMV pneumonitis required dialysis after multiorgan failure unrelated to TA-TMA.

† Two additional patients were listed for renal transplant at the time of last review.

‡ For patients on dialysis, "last follow-up" was considered the day dialysis was initiated.

stage 2, and the other patient who died did not have CKD at the time of death. The cumulative incidence of severe CKD was 33% (95% confidence interval, 11% to 57%) (Figure 2). There were no significant differences in either creatinine or eGFR between mild/moderate CKD patients (stages 1 to 3) and severe CKD patients (stage 4 or 5) before HSCT or at TPE initiation (Table 5).

4 of 5 patients with severe CKD required dialysis; the 5th patient was being considered for renal replacement therapy at the time of last review. 2 of 5 patients with severe CKD survived renal transplant and did not have recurrence of TA-TMA in their transplanted kidneys, and at the time of last review 2 other patients were listed for renal transplant (Table 4). 2 patients without severe CKD underwent dialysis. The first patient required dialysis around TA-TMA diagnosis for acute kidney injury but demonstrated improved renal function and at the time of last review was CKD stage 2 off of dialysis. The second patient required dialysis for acute kidney injury at end of life for multiorgan failure in the setting of cytomegalovirus infection not related to TA-TMA (Table 4). No other patients required dialysis for acute kidney injury. 4 of 5 patients who received eculizumab in addition to TPE developed severe CKD. Median creatinine levels and eGFR at last follow-up were 1.2 (range, 0.6 to 6.4) and 38 (range, 11 to 98), respectively; "last follow-up" was defined as the study end date in non–dialysis-dependent patients or the date of initiation of chronic dialysis in dialysis-dependent patients (Table 4).

Additional Nephrotoxic Variables

All 15 patients had at least 2 nephrotoxic insults before or during the course of TA-TMA diagnosis, and the median number per patient was 4. The number of nephrotoxic variables per patient was not different between the mild/moderate and severe CKD groups. The patient with the most nephrotoxic insults (7/8 investigated variables) had CKD stage 2 at last study follow-up, and the 1 patient who did not develop CKD experienced 3 nephrotoxic variables.

DISCUSSION

The efficacy of TPE in the treatment of TA-TMA has been evaluated by other studies, but our report is the first to evaluate long-term development of CKD in TPE-treated TA-TMA. CKD is a well-described complication of TA-TMA [6,16]. In one retrospective review Glezerman et al. [17] analyzed the incidence of CKD in 100 adult patients in the 2 years after HSCT.

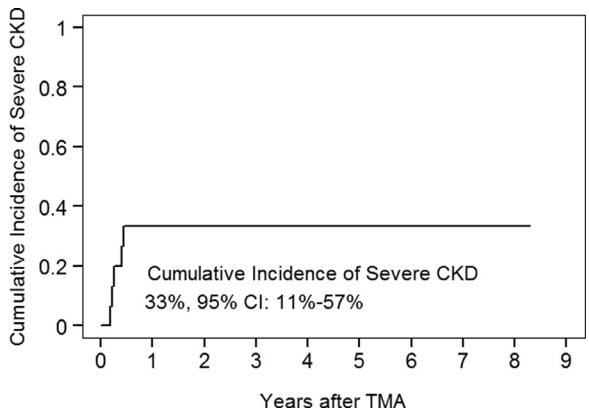

Figure 2. Cumulative incidence of severe CKD in patients who completed a course of TPE per the Texas Children's Hospital "TPE in TA-TMA" protocol.

Table 5
Comparison of Creatinine and eGFR between Mild/Moderate CKD and Severe CKD

	Mild/Moderate CKD (1-3) Median (range)	Severe CKD (4 and 5) Median (range)	*P**
Creatinine			
Pre-HSCT, mg/dL	0.4 (0.2-0.6)	0.6 (0.3-0.6)	0.186
TPE Initiation, mg/dL	0.9 (0.4-2.6)	1.0 (.7-1.1)	0.674
eGFR			
Pre-HSCT, mL/min/m^2	132 (107-196)	165 (110-214)	0.606
TPE Initiation, mL/min/m^2	58 (21-91)	67 (45-137)	0.519

* Wilcoxon rank-sum test

11 patients developed TA-TMA. The authors found that the risk of developing CKD was 4.3 times higher for patients with versus without TA-TMA, and TA-TMA was the only risk factor identified in a univariable analysis to be associated with development of severe CKD. Treatment modalities for TA-TMA were not discussed. In a recent review by Postalcioglu et al. [30], the authors evaluated the impact of TA-TMA on renal outcomes and found that TA-TMA was significantly associated with worse kidney dysfunction–free survival. Specifically, the cumulative incidence of renal replacement therapy at 2 years post-HSCT was 17% for patients with a diagnosis of definite TA-TMA and 3% for patients with a diagnosis of probable TA-TMA, compared with 0.4% in patients without TA-TMA. Additionally, the cumulative incidence of kidney dysfunction (defined as doubling of serum creatinine relative to the baseline value or the need for renal replacement therapy) at 2 years was 31% in patients with definite TA-TMA, 16% in patients with probable TA-TMA, and 7.4% in patients without TA-TMA. Finally, among the patients diagnosed with TA-TMA, 3 patients (1.2%) with definite disease and 2 patients (0.4%) with probable disease underwent kidney transplantation after developing TA-TMA. Finally, 9 of 45 patients with a clinical diagnosis of TA-TMA (20%) were treated with TPE, but renal outcomes were not correlated with this treatment modality.

Most of the literature reporting on the efficacy of TPE in the treatment of TA-TMA has focused on the resolution of the hematologic parameters of the disease, with little evidence assessing efficacy of TPE in preventing CKD. A 2013 study by Jodele et al. [22] assessed outcomes, including renal function, in 10 consecutive pediatric TA-TMA patients treated with TPE, with the hypothesis that initiation of TPE earlier after TA-TMA diagnosis would result in improved outcomes. Patients in this study were followed over 997 days (range, 689 to 1249). 5 of 10 patients survived TA-TMA. TPE was initiated earlier after TMA diagnosis in the survivor group compared with the nonsurvivor group, at medians of 17 days versus 35 days, respectively. 7 patients required renal replacement therapy—3 in the survivor group and 4 in the nonsurvivor group—but no patients underwent renal transplantation. 9 of 10 patients demonstrated laboratory resolution of TA-TMA; however, only 5 patients recovered renal function (defined by recovery of nuclear GFR) and survived. Although this study did not specifically stratify CKD development in the surviving patients, it does suggest that TPE does not effectively prevent renal dysfunction in TA-TMA. Additionally, because all 5 patients who did not recover renal function were in the nonsurvivor group, the study indicates that failure to resolve renal dysfunction in TA-TMA can lead to significantly worse outcomes. Although length of follow up in our study was similar to that in the Jodele et al. study [22], ours is different in that we specifically evaluated development of CKD in TA-TMA patients treated with TPE.

In our study we found that a course of 7 or more weeks of TPE was not effective in the prevention of CKD: Nearly all patients developed CKD, and about one-third progressed to severe CKD. Because there were only 2 deaths in our study (both unrelated to TPE) and because the complications of TPE were mild except for 1 pheresis catheter–related thrombosis, it is unlikely that TPE worsened outcomes but rather was unsuccessful in preventing CKD development. The number of catheter-related and TPE-related complications in our study was similar to that observed in other reports, although the severity of the complications in our study was less [31–33]. The lack of line-associated infections may be attributable to the internal jugular vein location of these lines in all patients. 3 patients in our study initiated TPE late in their TA-TMA course; however, the other 12 patients were initiated within 2 weeks of TA-TMA diagnosis. The timing of TPE initiation in this study did not have significant impact on the incidence or severity of CKD because 4 of 5 patients (80%) with severe CKD were in the group of patients who initiated TPE early in their TA-TMA course. CKD severity was not associated with creatinine levels or eGFR obtained before HSCT or at TPE initiation (Table 4).

All 15 patients in our study experienced at least 2 additional nephrotoxic insults around the time of TA-TMA diagnosis, including foscarnet, vancomycin, cidofovir, amphotericin B, calcineurin inhibitors, BK cystitis, GVHD, or total body irradiation. The number of confounding variables present was not correlative with CKD stage, and therefore the differences between incidences of mild/moderate and severe CKD cannot be explained by presence of these variables. However, because all patients did experience at least 2 nephrotoxic insults in addition to TA-TMA, it is likely that renal disease observed in our patients is multifactorial. The reasons for the more severe renal disease in one-third of the studied patients are unclear, and additional studies are necessary to assess risk factors leading to severe CKD in such a large proportion of TA-TMA patients. Even though 40% of our patients had a concurrent diagnosis of acute GVHD, in all cases the GVHD was mild at grades I to II. Therefore, it is unlikely that in our study the endothelial damage from acute GVHD worsened TA-TMA or prolonged recovery. Interestingly, although our follow-up was long, patients developed severe CKD relatively soon after diagnosis (92 days), suggesting that severe CKD development does not occur remotely after TA-TMA diagnosis or cessation of TPE therapy. Finally, it does not seem that severity of CKD had significant impact on survival because the 5 patients with severe CKD were still living at last review, whereas the 2 patients who died had either mild CKD or no CKD at the time of death.

The literature reports that TA-TMA patients have variable eculizumab clearance and require a dosing regimen based on pharmacokinetics to achieve effective complement blockade [5,19,34]. In 2014 Jodele et al. [5] found that all children with TA-TMA treated with eculizumab in their study required higher dosing and/or more frequent administrations to reach adequate eculizumab trough levels. The authors reported that CH50 levels < 4 CAE units strongly correlated with a therapeutic eculizumab level, indicating successful complement blockade and drug dosing. Because eculizumab dosing in our patients was not optimized based on CH50 levels, because eculizumab was initiated fairly late after TA-TMA diagnosis, and because our numbers were small, it is likely that the rate of CKD in our study was not affected by the addition of eculizumab. Finally, although our study demonstrated that renal outcomes in TA-TMA patients are poor, it is important to note that severe CKD could still be rescued by a renal transplant, leading to long-term survival and decreased morbidity.

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