Complement-Mediated Atypical Hemolytic Uremic Syndrome as a Cause of Late Kidney Graft Dysfunction

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Abstract

Thrombotic microangiopathy (TMA) is a rare complication of kidney transplantation that is associated with poor patient and graft outcomes.

We present a case of a 59-year-old male patient with no other relevant medical history besides ADPKD who underwent preemptive living donor kidney transplantation from his wife in March 2020. Induction therapy was with basiliximab, tacrolimus (TAC), mycophenolate mofetil (MMF) and prednisolone (PDN). The post-transplant period was uneventful and he was discharged with base serum creatinine levels of 1.4 mg/dL, which remained stable at 1.3-1.5 mg/dL for over 3 years. His maintenance therapy consisted on TAC, MMF and PDN (with MMF being switched to Everolimus on account of CMV infection).

Three years after transplantation, the patient presented with an acute case of watery diarrhea, low-grade fever and acute kidney injury. Physical examination was unremarkable aside from dehydration. All microbiology test results were negative. At this time, hemoglobin, platelets and LDH levels were within the normal range, urine output was normal, proteinuria was not present and the urinary sediment analysis was unremarkable. The diarrhea subsided shortly after, but the patient's renal function continued to worsen despite optimized fluid therapy. A computed tomography scan of the abdomen and pelvis ruled out obstructive nephropathy and the patient was admitted for acute renal allograft dysfunction, and a renal allograft biopsy was performed that same day.

While waiting for the biopsy results and for suspected acute cellular rejection, the patient was started on methylprednisolone pulses 500 mg for 3 days, followed by PDN 40 mg/day. An initial improvement in kidney allograft function was noted. However, just 7 days after, the patient presented with worsening renal function, new-onset thrombocytopenia, hemolytic anemia with schistocytes, a negative Coombs test and allograft biopsy findings which were all consistent with TMA.

All major causes of secondary TMA were excluded, ADAMST13 activity levels were of 27% and no ADAMST13 autoantibodies were found. A heterozygous mutation in *ADAMST13* (NM_139027.8): c.3280C>T p.(Arg1094Cys) of unkown significance was found, as well as a heterozygotous deletion of *CFHR3-CFHR1* gene deletion. This last mutation is usually considered to be a benign variation, when co-inherited with another mutation, it can be considered a risk factor for TMA.

A diagnosis of atypical hemolytic uremic syndrome (aHUS) was made and the patient was started on plasmapheresis, weekly eculizumab and everolimus was replaced with mycophenolate mofetil. After the second administration of eculizumab, the patient showed continuous and sustained improvement of kidney function (SCr 1.9 mg/dL) and normalization of his hemoglobin and platelet levels. The patient was later discharged and kept on bimonthly eculizumab administrations for the first 3 months, after which eculizumab administrations were slowly spaced out until finally stopping after 12 months. At the time of writing, the patient has been off eculizumab completely for 3 months, and has displayed normal complement activity levels for the last 8 months of our eculizumab discontinuation protocol with no signs of relapse.

The purpose of this paper was to report a rare case of late-onset post-transplant acute renal allograft dysfunction, such as de novo aHUS.

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INTRODUCTION

Post-transplant thrombotic microangiopathy (PT-TMA) is a rare complication of kidney transplantation associated with poor graft and patient outcomes.[1,2] It can be classified as either recurrent TMA, if TMA was the cause of the patient's chronic kidney disease, or *de novo* TMA, if TMA only developed after the kidney transplant.[2] The incidence of PT-TMA has been reported to range from 0.8% to 14%, with kidney allograft loss rates of up to 50%.[1,3] *De novo* PT-TMA cases can be either complement-mediated or secondary to other inciting factors, whereas recurrent post-transplant TMA cases are usually complement-mediated.[3]

TMA is a highly heterogeneous condition since it does not represent a single disease entity but rather a morphologic pattern of microvascular occlusive injury that can be caused by a variety of conditions.[3] The main findings associated with PT-TMA are microangiopathic hemolytic anemia, thrombocytopenia and acute graft dysfunction.[1] The etiology of PT-TMA not only includes all known causes of native kidney TMA but also other causes unique to the transplant setting, such as calcineurin inhibitors (CNI), mammalian target of rapamycin inhibitors (mTORi), viral infections, or antibody-mediated rejection (ABMR).[1,3,4]

We describe a case of *de novo* PT-TMA as a cause of late kidney graft dysfunction in a patient with kidney failure secondary to autosomal dominant polycystic kidney disease (ADPKD).

CASE REPORT

In March 2020, a 56-year-old man with end-stage kidney disease secondary to ADPKD underwent a pre-emptive living-donor kidney transplantation, maintained on a regimen of tacrolimus, mycophenolate mofetil (MMF), and prednisolone (PDN). Although the early post-transplant course was largely uneventful, CMV viremia was detected during follow-up, at three months post-transplant, and valganciclovir was started at therapeutic dosage. This proved to be ineffective, with increasing CMV viral load being noted, and so MMF was stopped and replaced with everolimus as part of the patient's immunosuppressive regimen. This strategy resulted in an undetectable viral load and the patient's renal graft function remained stable with serum creatinine levels between 1.3 and 1.5 mg/dL for the subsequent three years.

In late September 2023, the patient presented with a 5-day history of low-grade fever and watery diarrhea. Examination revealed signs of dehydration, and laboratory tests showed acute graft dysfunction (SCr 2.91 mg/dL), slightly elevated CRP (11.74 mg/L), bland urinary sediment, and therapeutic tacrolimus (3.4 ng/mL) and everolimus (5.67 ng/mL) levels. A presumptive diagnosis of acute gastroenteritis with prerenal acute kidney injury (AKI) was made, and intravenous fluids with daily outpatient monitoring were initiated.

Three days later, the patient's symptoms had resolved; however, serum creatinine remained elevated (3.76 mg/dL). Abdominopelvic computed tomography (CT) excluded obstructive uropathy, and renal graft Doppler ultrasound showed no vascular complications. BK virus and CMV PCR were negative. Donor-specific antibody (DSAs) screening was therefore requested, the patient was admitted, and a renal graft biopsy was scheduled for the following day. Given the continued deterioration in graft function, acute rejection was suspected, and empirical treatment with intravenous methylprednisolone (MPDN) (500 mg/day for 3 days) was initiated, followed by oral prednisolone 40 mg/day.

The patient showed a steady yet small improvement during the MPDN protocol, maintaining stable levels of hemoglobin and showing moderate improvement in graft function with serum creatinine levels down from 3.76 mg/dL to 2.71 mg/dL. At the time, the screening for DSAs came back negative and the renal graft biopsy results were still pending, and so the patient was kept on IV fluids and oral PDN.

Seven days after initiation of systemic corticosteroid therapy, the patient developed worsening anemia (hemoglobin 8.4 g/dL), new-onset thrombocytopenia (67 000/µL), persistent graft dysfunction (SCr 3.13 mg/dL), and laboratory evidence of hemolysis, including markedly elevated LDH (795 U/L), indirect hyperbilirubinemia (1.31 mg/dL), undetectable haptoglobin, a negative direct Coombs test, and schistocytes on peripheral smear.

These clinical findings were consistent with PT-TMA, a diagnosis subsequently confirmed by renal allograft biopsy. Histological examination revealed normocellular glomeruli with ill-defined endoluminal fibrin thrombi and rare leukocytes, indicating mild glomerulitis. Arteriolar concentric hypertrophy and hyalinosis were prominent, resulting in near-complete luminal occlusion, while silver staining demonstrated discrete double contours along the glomerular basement membrane. Immunofluorescence studies were entirely negative, showing no deposits of immunoglobulins, complement components, or C4d. Collectively, these features indicated active TMA with underlying chronicity,[5] the absence of antibody or T cell–mediated rejection (Fig. 1).

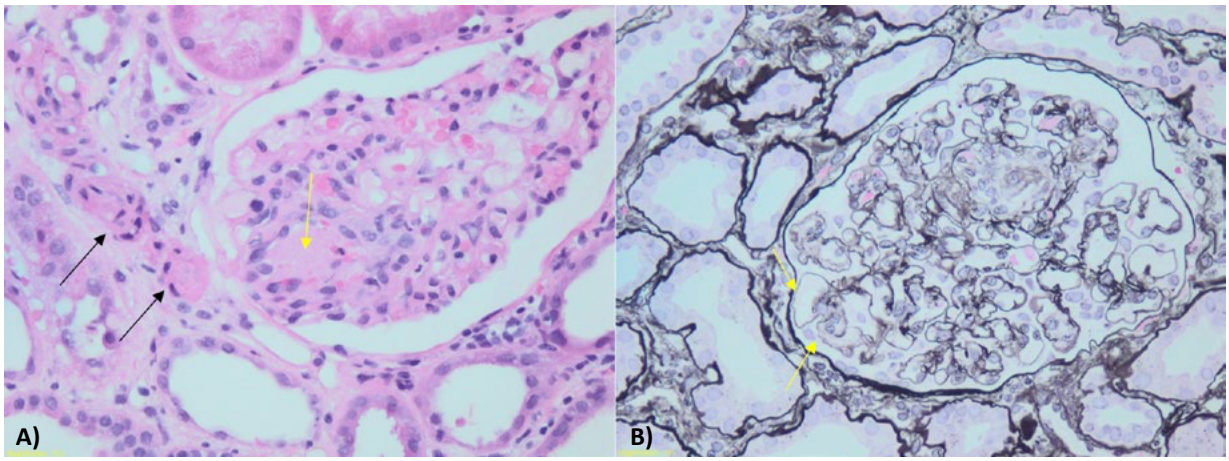

Figure 1. (A) Hematoxylin and eosin (H&E) stain shows a normocellular glomerulus, with an endoluminal fibrin thrombus (yellow arrow). Tortuous arteriole with narrowing of its lumen, concentric hypertrophy and hyalonosis of the vascular wall (black arrows) (H&E stain, under 200x magnification). (B) Silver stain shows discrete duplication of the glomerular basal membrane (yellow arrow) (Silver stain, under 200x magnification).

The patient's PLASMIC score was 4 (Supplementary Table 1), indicating a low probability of thrombotic thrombocytopenic purpura (TTP),[6] which was supported by an ADAMTS13 activity of 27%. Secondary causes of TMA, including infectious, autoimmune, and metabolic etiologies, were systematically excluded (Table 1). In the absence of alternative primary or secondary causes of TMA, a presumptive diagnosis of complement-mediated atypical hemolytic uremic syndrome (CM-aHUS) was made.

Table 1. Diagnostic workup for TMA

Test	Result
ADAMTS13 activity	27%
Viral PCR Panel (CMV, BK virus, EBV, Enterovirus, Parvovirus B19)	Negative
Blood cultures	Negative
Stool cultures	Negative
Shiga toxin-producing *E. coli* PCR	Negative
Viral Serologies (HAV, HBV, HCV, HIV, Syphilis)	Negative
Antistreptolysin O (ASO)	Negative
Autoimmunity screening	Negative
Vitamin B12	Normal (479 pg/mL)
Donor-specific antibodies (DSAs)	Negative
Complement (C3 and C4)	No consumption

Given the increased risk of PT-TMA associated with combined CNI and mTORi therapy, everolimus was replaced with MMF. The patient received appropriate immunizations and antibiotic prophylaxis while awaiting eculizumab. As per local protocol, daily plasma exchange was initiated as a bridging therapy (1.5 plasma volumes using fresh frozen plasma). The patient underwent two sessions without complications before switching to eculizumab at the 48-hour mark post-diagnosis. However, these plasma exchange sessions failed to arrest the disease progression, as evidenced by worsening anemia (hemoglobin 7.2 g/dL) and thrombocytopenia (66 000 platelets/µL), rising serum creatinine (SCr 3.4 mg/dL), and persistent hemolysis.

Table 2. Evolution of laboratory parameters during hospitalization.

Parameter	Day 0	Day 3 (MPDN start)	Day 7	Day 10	Day 12 (Eculizumab start)	Day 21 (Discharge)
Hemoglobin (g/dL)	11.2	9.2	9.0	8.4	7.2	9.4
Platelets (/µL)	165 000	221 000	153 000	67 000	66 000	120 000
Creatinine (mg/dL)	2.91	3.76	2.71	3.13	3.4	1.95
LDH (U/L)	362	426	571	795	731	252
Bilirubin (mg/dL)	0.5	0.6	0.8	1.81	1.7	0.55
Haptoglobin (mg/dL)	-	-	-	Undetectable	Undetectable	103
Urinalysis	-	Trace hematuria/ +++ proteinuria	+++ proteinuria	+++ proteinuria	-	No active sediment
Blood smear	-	Negative for schistocytes	Negative for schistocytes	5.7% schistocytes	7.2% schistocytes	Negative for schistocytes
Direct Coombs Test	-	-	-	Negative	Negative	-

Following initiation of eculizumab (900 mg every week for 4 weeks), the patient rapidly demonstrated improvement in kidney graft function, with normalization of hemolysis parameters and peripheral blood smear findings. Nine days later, the patient was discharged with improving hemoglobin (9.4 g/dL), platelet count (120 000/µL), and serum creatinine (1.95 mg/dL). The patient's analytical evolution throughout his hospital stay is detailed in Table 2.

Complement factor H autoantibody testing came back negative and the complement genetic test panel revealed two relevant mutations:

- A heterozygous missense mutation in *ADAMTS13 (NM_139027.8): c.3280C>T p.(Arg1094Cys)* which is described as a variant of uncertain significance[7];
- A heterozygous deletion encompassing the entire *CFHR1* and *CFHR3* genes, usually described as a benign variant, a polymorphism present in many of European descent,[8] despite it being associated with CM-aHUS in a few case reports.[9,10]

In this case, none of these complement gene variants were known to be pathogenic. Given the absence of pathogenic complement variants, the late onset of *de novo* PT-TMA, and the successful resolution of modifiable triggers, we elected to gradually taper eculizumab. Therefore, after 3 months of biweekly eculizumab (1200 mg every 2 weeks) therapy, we started spacing out eculizumab administrations one week at a time every 3 months (i.e. 1200 mg every 3 weeks by months 4-6; every 4 weeks by months 7-9; every 6 weeks through months 10-12), eventually stopping it after twelve months. Close monitoring of kidney graft function and hemolysis parameters was maintained on a monthly basis throughout this phase.

Table 3. Evolution of laboratory parameters throughout eculizumab tapering and discontinuation.

Parameter	Discharge (Month 0)	4 Months (eculizumab every 4 weeks)	8 Months (eculizumab every 6 weeks)	12 Months (eculizumab discontinuation)	20 Months
Hemoglobin (g/dL)	9.4	12.9	14.1	15.3	14.7
Platelets (/µL)	120 000	187 000	218 000	172 000	163 000
Serum creatinine (mg/dL)	1.95	1.64	1.58	1.51	1.53
LDH (U/L)	252	438	274	227	256
Total bilirubin (mg/dL)	0.55	0.50	0.96	0.45	0.51
Haptoglobin (mg/dL)	103	153	128	134	141
Urine P/C ratio (g/g)	-	0.082	0.070	0.106	0.078
CH50 (%)	6.4	4.0	69	59	61
AH50 (%)	5.6	3.0	85	71	75

Complement activity was suppressed (CH50 4%; AH50 3%) up until eculizumab started being administered every 4 weeks, at which time both alternative and common complement pathways showed no sign of inhibition (CH50 69%; AH50 85%). Yet, the patient did not experience recurrence of TMA, showing continuous signs of improving graft function (Table 3). His last Eculizumab administration was in November 2024, with the subsequent blood work showing

normal hemoglobin levels (15.3 g/dL) and platelet count (172 000 platelets/µL), as well as kidney graft function returning to baseline levels with serum creatinine levels of 1.51 mg/dL, even though complement activity was not suppressed (CH50 59%; AH50 71%). To date, the patient remains clinically stable with no signs of TMA recurrence, sustaining the recovered allograft function even in the absence of complete complement blockade (Table 3).

DISCUSSION

PT-TMA is a rare but severe complication of kidney transplantation, characterized by endothelial injury and microvascular thrombosis leading to unexplained allograft dysfunction.[2] It may occur as recurrent disease or, more commonly, as *de novo* PT-TMA without prior manifestations.[3] *De novo* PT-TMA is typically multifactorial, with major risk factors including CNI and mTORi, ABMR, and viral infections (e.g., CMV, BKV, parvovirus B19).[11] Although most cases occur within the first 3–6 months post-transplant, late-onset presentations up to 6 years after transplantation have been reported.[11]

The patient initially presented with acute graft dysfunction attributed to dehydration in the setting of a gastrointestinal infection. Progressive graft dysfunction and new-onset anemia—initially attributed to hemodilution—raised concerns for acute rejection, prompting a renal graft biopsy and empirical systemic corticosteroids. However, there was minimal response to therapy. Seven days later, the diagnosis of systemic PT-TMA was established following the onset of microangiopathic hemolytic anemia and thrombocytopenia, accompanied by TMA findings in the biopsy. Given the absence of prior personal or familial TMA and end-stage kidney disease due to ADPKD, *de novo* PT-TMA was considered the most likely diagnosis.

The etiology of PT-TMA is often multifactorial, resulting from the interaction of multiple acquired risk factors; therefore, identifying predisposing causes is essential for appropriate management and prevention of recurrence.[3] In this case, negative stool cultures and STEC testing, along with ADAMTS13 activity >10%, excluded typical HUS and TTP. Secondary etiologies of TMA, including viral or bacterial infections, autoimmune disorders, metabolic causes, and malignant hypertension, were considered unlikely given the negative infectious and serological workup (Table 1) and the patient's consistently controlled blood pressure. The renal graft biopsy revealed features of acute-on-chronic TMA. Acute injury was evidenced by fibrin thrombi, while chronicity was indicated by discrete double contours and severe arteriolar hyalinosis (Fig. 1). Concurrently, the absence of tubulitis or significant interstitial inflammation ruled out T-cell-mediated rejection. Furthermore, the lack of DSAs, C4d deposits, or significant microvascular inflammation argued against ABMR, pointing instead toward other drivers of PT-TMA, such as medication toxicity or genetic susceptibility.

CM-aHUS is caused by the dysregulation of the alternative pathway of the complement system, resulting in permanent activation of the common terminal pathway. Complement overactivation leads to systemic endothelial injury and microvascular thrombosis, which, in turn, perpetuates the activation of the complement cascade.[12] Approximately 50%-60% cases of CM-aHUS are caused by genetic variants of complement genes,[12,13] however, about 50-80% of patients' family members who present the same variations are healthy individuals without any history of TMA.[14] As such, current evidence suggests that the presence of additional triggers like infections, drugs, surgery or pregnancy, are needed to clinically manifest an episode of CM-aHUS.

Immunosuppressive drugs like CNIs and mTORi are well-established risk factors for *de novo* PT-TMA.[3] CNIs promote endothelial injury through arteriolar vasoconstriction and platelet activation, while mTORi exert prothrombotic and antiangiogenic effects that impair endothelial repair.[2] Their combined use therefore markedly increases TMA risk.[2,3]

When immunosuppression is thought to be implicated in *de novo* PT-TMA, the most commonly used strategies are suspending CNIs temporarily, or switching them for another drug within the same class or even for an mTORi[11,15]; however, these approaches are controversial, as mTORi are also strongly associated with PT-TMA, with some evidence suggesting a higher risk than CNIs. Accordingly, we discontinued everolimus and switched to MMF, while maintaining tacrolimus and PDN.

Most mutations associated with CM-aHUS are not directly causative but instead increase disease susceptibility. Many complement gene variants identified in CM-aHUS are missense mutations of uncertain significance that also occur in healthy individuals. Nevertheless, such variants may increase the risk of TMA when combined with other complement gene mutations.[16]

Genetic testing revealed a heterozygous missense *ADAMTS13* mutation and a heterozygous CFHR3–CFHR1 deletion. While severe ADAMTS13 deficiency is associated with TTP, partial ADAMTS13 deficiency, as in our patient (27% activity), has been linked to other TMA phenotypes, including CM-aHUS, in the presence of additional triggers.[7] The heterozygous CFHR3–CFHR1 deletion is a common, typically benign polymorphism (>18% prevalence in British and Italian populations [8]), although it has been rarely associated with CM-aHUS in case reports.[9,10]

These genetic variants, although not known to be pathogenic, may collectively increase the risk of PT-TMA when combined with triggering events.[1] In this patient, a gastrointestinal infection, CNI/mTORi combination therapy, and underlying genetic susceptibility likely acted together to precipitate post-transplant CM-aHUS.

Given the multifactorial pathogenesis of PT-TMA, treatment should be individualized according to the most likely

etiology.[2] In CM-aHUS, early initiation of eculizumab, a monoclonal antibody targeting complement C5, can halt complement activation, prevent further organ damage, and promote rapid recovery of hematologic parameters and graft function.[1] The optimal duration of eculizumab therapy for PT-TMA remains uncertain and is influenced by underlying complement genetic variants. In patients without confirmed pathogenic variants, treatment duration should be individualized, with most authors suggesting that eculizumab can be safely discontinued after 6–12 months.[1,12,17]

In our case, no pathogenic complement variants were identified, and PT-TMA developed *de novo* more than three years post-transplant and in the presence of modifiable triggers. Eculizumab was therefore gradually tapered after three months and discontinued at twelve months, with close monitoring for relapse (Table 3). The patient has remained off eculizumab for twelve months, with normal complement activity and no evidence of TMA recurrence.

CONCLUSION

Our case report highlights the intricacies of diagnosing PT-TMA and its multifactorial nature, showcasing the importance of identifying as many possible predisposing factors, in order to optimally treat the condition and prevent further recurrences. Immunosuppression protocols play a causative role in PT-TMA and should be carefully planned. Combining CNIs and mTORi in the same immunosuppressive regimen increases the risk of PT-TMA, even if the patient has no personal or familial history of TMA. As for the case of CM-aHUS patients who do not possess known pathogenic complement variants, the decision to stop eculizumab therapy should be individualized, and more studies are required as to the best way to proceed in doing so.

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HR: Drafting of the article, data acquisition and analysis.
MG: Patient follow-up, contributed to the diagnosis, critical reviewing of the article.
LR and GGS: Contributed to the diagnosis, critical reviewing of the article.
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REFERENCES

1. Godara A, Migliozzi DR, Pilichowska M, Goyal N, Varga C, Gordon CE. Use of eculizumab in transplant-associated thrombotic microangiopathy in a patient with polycystic kidney disease immediately post–kidney transplant: a case report. Kidney Med. 2020;2:652-6. doi:10.1016/j.xkme.2020.06.007
2. Abbas F, Kossi M El, Kim JJ, Sharma A, Halawa A. Thrombotic microangiopathy after renal transplantation: Current insights in de novo and recurrent disease. World J Transplant. 2018;8:122-41. doi:10.5500/wjt.v8.i5.122
3. Mubarak M, Raza A, Rashid R, Sapna F, Shakeel S. Thrombotic microangiopathy after kidney transplantation: Expanding etiologic and pathogenetic spectra. World J Transplant. 2024;14 :90277. doi:10.5500/wjt.v14.i1.90277
4. Rolla D, Fontana I, Ravetti JL, Marsano L, Bellino D, Panaro L, et al. De novo post-transplant thrombotic microangiopathy localized only to the graft in autosomal dominant polycystic kidney disease with thrombophilia. J Renal Inj Prev. 2015;4:135-8. doi:10.12861/jrip.2015.28
5. Schwimmer J, Nadasdy TA, Spitalnik PF, Kaplan KL, Zand MS. De novo thrombotic microangiopathy in renal transplant recipients: A comparison of hemolytic uremic syndrome with localized renal thrombotic microangiopathy. Am J Kidney Dis. 2003;41:471-9. doi:10.1053/ajkd.2003.50058
6. Paydary K, Banwell E, Tong J, Chen Y, Cuker A. Diagnostic accuracy of the PLASMIC score in patients with suspected thrombotic thrombocytopenic purpura: A systematic review and meta-analysis. Transfusion. 2020;60:2047-57. doi:10.1111/trf.15954
7. Feng S, Eyler SJ, Zhang Y, Maga T, Nester CM, Kroll MH, et al. Partial ADAMTS13 deficiency in atypical hemolytic uremic syndrome. Blood. 2013;122:1487-93. doi:10.1182/blood-2013-03-492421
8. Holmes LV, Strain L, Staniforth SJ, Moore I, Marchbank K, Kavanagh D, et al. Determining the Population Frequency of the CFHR3/CFHR1 Deletion at 1q32. PLoS One. 2013;8 :e60352. doi:10.1371/journal.pone.0060352
9. Park J, Yhim HY, Kang KP, Bae TW, Cho YG. Copy number variation analysis using next-generation sequencing identifies the CFHR3/CFHR1 deletion in atypical hemolytic uremic syndrome: a case report. Hematology. 2022;27:603-8. doi:10.1080/16078454.2022.2075121
10. Diep J, Potter D, Mai J, Hsu D. Atypical haemolytic uremic syndrome with refractory multiorgan involvement and heterozygous CFHR1/CFHR3 gene deletion. BMC Nephrol. 2023;24. doi:10.1186/s12882-023-03153-x
11. Leong ZCW, Kong JHL, Khor SY, Liew YF. Everolimus-associated thrombotic microangiopathy following renal transplant: a case report. Cureus. 2024;16:e71535. doi:10.7759/cureus.71535
12. Genest DS, Patriquin CJ, Licht C, John R, Reich HN. Renal thrombotic microangiopathy: a review. Am J Kidney Dis. 2023;81:591-605. doi:10.1053/j.ajkd.2022.10.014

13. Zipfel PF, Wiech T, Stea ED, Skerka C. CFHR gene variations provide insights in the pathogenesis of the kidney diseases atypical hemolytic uremic syndrome and C3 glomerulopathy. J Am Soc Nephrol. 2020;31:241-56. doi:10.1681/ASN.2019050515
14. Leon J, LeStang MB, Sberro-Soussan R, Servais A, Anglicheau D, Frémeaux-Bacchi V, et al. Complement-driven hemolytic uremic syndrome. Am J Hematol. 2023;98:S44-S56. doi:10.1002/ajh.26854
15. Cho W, Jo SK, Jung CW, Kim MG. Characteristics and management of thrombotic microangiopathy in kidney transplantation. Korean J Transplant. 2023;37:11-8. doi:10.4285/kjt.23.0011
16. Thompson GL, Kavanagh D. Diagnosis and treatment of thrombotic microangiopathy. Int J Lab Hematol. 2022;44:101-13. doi:10.1111/ijlh.13954
17. Fakhouri F, Schwotzer N, Frémeaux-Bacchi V. How I diagnose and treat atypical hemolytic uremic syndrome. Blood. 2023;141:984-95. doi: 10.1182/blood.2022017860.

Supplementary Table 1. PLASMIC score at the moment of TMA diagnosis.

Parameters	Patient Results	Score
Platelets < 30,000/µL	67 000	0
Hemolysis	Yes	1
Active Neoplasm (Cancer)	No	1
Hx of Organ Transplant	Yes	0
MCV <90 µm³ (fL)	84	1
INR < 1.5	1.1	1
Creatinine < 2.0 mg/dL	3.1	0
Total		4