CASE REPORT

Relapse of Atypical Haemolytic Uremic Syndrome After a Decade of Remission: A Case Report

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ABSTRACT

Background: Atypical hemolytic uremic syndrome (aHUS) is a rare, life-threatening form of thrombotic microangiopathy caused by dysregulation of the alternative complement pathway. Relapse following a prolonged remission is uncommon and poses diagnostic and therapeutic challenges, especially in resource-limited settings.

Case Presentation: An 18-year-old male with a past history of hemolytic uremic syndrome treated in childhood presented with decreased urine output, nausea, and fatigue for one week. He had no recent history of diarrhea or drug exposure. On examination, he was pale and normotensive without edema. Laboratory evaluation revealed hemoglobin 5.8 g/dL, platelets 1.05×10^5/µL, creatinine 6.72 mg/dL, lactate dehydrogenase 521 U/L, and reduced complement C3 (75 mg/dL). Peripheral smear showed 3–4 schistocytes per high-power field, consistent with microangiopathic hemolysis. Urinalysis revealed 3+ protein and microscopic hematuria. Ultrasound abdomen demonstrated bilateral grade II renal parenchymal changes with moderate ascites. Renal biopsy showed thrombotic microangiopathy involving glomeruli and arterioles, confirming the diagnosis of aHUS relapse. He was managed with hemodialysis, one session of plasma exchange (3 L plasma replaced with fresh frozen plasma), and high-dose corticosteroids. The patient's hematological parameters and renal function improved gradually, and he was discharged with advice for immunosuppressive therapy and follow-up for complement-targeted treatment.

Keywords: Atypical hemolytic uremic syndrome, thrombotic microangiopathy, complement dysregulation, acute kidney injury, plasma exchange, renal biopsy.

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INTRODUCTION

Atypical hemolytic uremic syndrome (aHUS) is a rare and potentially life-threatening thrombotic microangiopathy (TMA) characterized by the classical triad of microangiopathic hemolytic anemia, thrombocytopenia, and acute kidney injury (1). Unlike the typical or Shiga toxin-mediated HUS seen in children following diarrheal illness, aHUS arises from uncontrolled activation of the alternative complement pathway, leading to widespread endothelial injury and microvascular thrombosis (2). It accounts for nearly 5–10% of all HUS cases and may occur sporadically or as a result of inherited or acquired complement dysregulation involving mutations or autoantibodies directed against complement regulatory proteins such as factor H, factor I, membrane cofactor protein (MCP/CD46), and C3 (3).

The disease course is often unpredictable, with variable severity and risk of recurrence. Episodes of aHUS can be triggered by infections, pregnancy, surgery, or certain drugs. In many cases, however, no precipitating factor can be identified (2). The unregulated complement activation leads to endothelial damage, platelet activation, and thrombus formation in the renal microvasculature, resulting in ischemic injury and progressive renal dysfunction (4). Histopathological findings commonly demonstrate fibrin thrombi within glomerular capillaries and arterioles, endothelial swelling, and mesangiolysis, confirming the diagnosis of TMA (5).

The management of aHUS has evolved significantly with the advent of complement inhibitors such as eculizumab and ravulizumab, which block the cleavage of complement protein C5, thereby halting further endothelial injury (2). In regions where access to such targeted therapies is limited, plasma exchange and corticosteroid therapy remain the mainstay of acute management. Early recognition and timely intervention are crucial to prevent irreversible renal damage and improve long-term outcomes (6).

Relapse of aHUS after a prolonged remission is an uncommon but clinically significant event that may indicate persistent complement dysregulation (7). Monitoring patients with a previous episode of HUS for renal function and hematological parameters is therefore essential (8). This report describes the case of an 18-year-old male who presented with recurrent aHUS after nearly a decade of remission, emphasizing the importance of early diagnosis, renal biopsy confirmation, and prompt initiation of plasma exchange and immunosuppressive therapy in preventing disease progression and chronic renal impairment.

CASE PRESENTATION

Patient Information

An 18-year-old male presented to the nephrology department with complaints of reduced urine output, generalized weakness, and fatigue for one week. He also reported mild fever and nausea for two days prior to admission. There was no history of diarrhea, upper respiratory infection, drug use, or recent vaccination. The patient was a known case of hemolytic uremic syndrome (HUS) diagnosed in 2013, for which he had received peritoneal dialysis for nine months along with corticosteroids and mycophenolate mofetil therapy. He achieved complete recovery of renal function and remained asymptomatic until 2019, after which he was lost to medical follow-up.

Clinical Examination

On admission, the patient was conscious, oriented, and afebrile with a blood pressure of 130/80 mmHg and pulse rate of 88 beats per minute. Mild pallor was noted without icterus, cyanosis, pedal edema, or organomegaly. Cardiovascular and respiratory system examinations were unremarkable, and there were no neurological deficits.

Investigations

Initial laboratory evaluation revealed severe anemia with a hemoglobin level of 5.8 g/dL and thrombocytopenia with platelets at $1.05 \times 10^5/\mu L$. Peripheral smear demonstrated schistocytes (3–4 per high-power field), suggestive of microangiopathic hemolytic anemia. Lactate dehydrogenase was elevated to 521 U/L, indicating ongoing hemolysis. Serum creatinine was markedly elevated at 6.72 mg/dL, and blood urea was 112 mg/dL, consistent with acute kidney injury. Complement C3 level was reduced (75 mg/dL), while C4 remained normal. Coagulation profile, including PT/INR and APTT, was within normal limits, excluding disseminated intravascular coagulation. Serological tests for HIV, hepatitis B, and hepatitis C were negative. Urinalysis revealed 3+ proteinuria, microscopic hematuria, and granular casts. Ultrasound abdomen demonstrated bilateral Grade II renal parenchymal changes with moderate ascites and no hydronephrosis.

Renal biopsy showed characteristic findings of thrombotic microangiopathy in both glomeruli and arterioles, with fibrin thrombi, mesangiolysis, and double-contoured basement membranes. There was moderate tubular atrophy and interstitial fibrosis involving less than 50% of the cortex, confirming the diagnosis of atypical hemolytic uremic syndrome (aHUS) relapse.

Management and Clinical Course

The patient was initiated on hemodialysis via a right internal jugular venous catheter. One session of plasma exchange was performed with a total replacement volume of three liters, using two units of fresh frozen plasma and two units of packed red blood cells. Intravenous methylprednisolone 500 mg daily was administered for two days, followed by oral prednisolone 60 mg per day. Supportive management included proton pump inhibitors, calcium and vitamin D supplementation, antiemetics, and fluid restriction of

750 mL per day.

Over the next few days, the patient's clinical status improved with stabilization of renal function and hematological parameters. His hemoglobin increased to 8.3 g/dL, platelet count improved to $1.06 \times 10^5/\mu L$, and creatinine levels plateaued following dialysis. He was discharged in stable condition with instructions for strict fluid and salt restriction, continuation of immunosuppressive therapy, and close nephrology follow-up for consideration of complement inhibition therapy with eculizumab.

Follow-Up and Outcome

At discharge, the patient was clinically stable with improved urine output and no further hemolytic episodes. He was advised regular follow-up to monitor renal function and hematological parameters. Genetic testing for complement pathway abnormalities and evaluation for long-term eculizumab therapy were recommended to prevent further relapses and preserve renal function.

DISCUSSION

Atypical hemolytic uremic syndrome (aHUS) represents a complement-mediated thrombotic microangiopathy characterized by microangiopathic hemolytic anemia, thrombocytopenia, and renal impairment (9). It differs from the typical, infection-associated form of HUS, which is secondary to Shiga toxin-producing Escherichia coli (8). In aHUS, the pathogenesis involves uncontrolled activation of the alternative complement pathway, leading to endothelial damage, platelet aggregation, and thrombus formation within the renal microvasculature (2). Mutations in genes encoding complement regulatory proteins such as factor H, factor I, MCP (CD46), C3, and factor B have been implicated in approximately 50–60% of cases, while in others, autoantibodies against factor H are responsible (10).

This case is noteworthy because it describes a relapse of aHUS after a decade of remission, an uncommon but recognized phenomenon. The patient had previously recovered completely after peritoneal dialysis and immunosuppressive therapy but later presented with acute kidney injury, anemia, and thrombocytopenia, suggesting reactivation of complement dysregulation (11). Low complement C3 levels, normal coagulation profile, and the absence of infection or toxin exposure reinforced the diagnosis of a complement-mediated process (12). The renal biopsy findings of thrombotic microangiopathy involving both glomeruli and arterioles, with fibrin thrombi and double-contoured basement membranes, provided histological confirmation (13).

In the acute setting, plasma exchange remains the initial therapeutic intervention, particularly in resource-limited environments where complement inhibitors such as eculizumab or ravulizumab are unavailable (14). Plasma exchange removes circulating autoantibodies and supplies functional complement regulatory proteins, thereby temporarily controlling disease activity. High-dose corticosteroids are often administered adjunctively to modulate immune-mediated endothelial injury (15). Despite the absence of targeted complement blockade in this case, the patient demonstrated clinical improvement and stabilization of renal function following plasma exchange and steroid therapy (6).

Eculizumab, a humanized monoclonal antibody against complement component C5, is currently the treatment of choice for aHUS, as it prevents terminal complement activation and subsequent endothelial damage. Early initiation has been shown to improve renal recovery and reduce recurrence risk (16). Genetic and serologic evaluation for complement abnormalities is essential for prognostication and long-term management. This case underscores the need for heightened clinical suspicion, timely renal biopsy, and early institution of therapy to prevent irreversible renal failure and optimize patient outcomes, especially in recurrent or complement-mediated cases of aHUS (17).

CONCLUSION

This case highlights the recurrence of atypical hemolytic uremic syndrome after a prolonged remission, emphasizing the importance of early recognition and timely intervention. Prompt diagnosis, supportive management, and plasma exchange stabilized renal function. Regular follow-up and consideration of complement inhibitor therapy are crucial for preventing future relapses and preserving kidney function.

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