Case Report

Complex presentation of atypical hemolytic uremic syndrome: A case study

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ABSTRACT

This case study discusses atypical hemolytic uremic syndrome (aHUS) in a 67-year-old female who presented with hypertension and hyperlipidemia 8 days after a suspected foodborne illness. Her initial presentation included acute respiratory and renal failure in which her condition required extensive re-warming, intubation, pressor or vasopressor therapy, continuous renal replacement therapy or hemodialysis, broad-spectrum antibiotic therapy, and blood and culture workups. Kidney function also showed signs of renal failure, metabolic acidosis, thrombocytopenia, and an elevated level of lactate dehydrogenase in the laboratory results. Radiological investigations demonstrated enteritis, colitis, and an ischemic infarct without hemorrhage. Multidisciplinary consultations achieved the importance and urgency of early diagnosis and treatment of aHUS to prevent irreversible organ damage. This case highlights the role of a timely diagnosis and interprofessional patient care in the treatment of severe aHUS.

Key words: Eculizumab, multidisciplinary approach, renal failure

Atypical hemolytic uremic syndrome (aHUS) is a rare disorder with an incidence of 0.23–0.42 cases/million with potentially life-threatening complications featuring microangiopathic hemolytic anemia, thrombocytopenia, and acute kidney injury (AKI) [1]. Complement activation that causes acute endothelial inflammation is its primary cause [2]. Shiga toxin-producing *Escherichia coli* causes classic hemolytic uremic syndrome (HUS) accounting for typical clinical HUS [3], while aHUS is linked to genetic deletions or to acquired autoantibodies that control the alternative complement pathway. The clinical presentation of aHUS typically includes symptoms of AKI, thrombocytopenia, and microangiopathic hemolytic anemia, as well as, extrarenal manifestations such as neurological deficits and cardiac complications [4]. Diagnosis is challenging due to the overlap in clinical features with other thrombotic microangiopathies, such as thrombotic thrombocytopenic purpura (TTP) and disseminated intravascular coagulation. Therefore, a thorough diagnostic workup is essential to differentiate aHUS from these conditions and guide appropriate treatment strategies [5]. Early treatment with plasma exchange therapy and eculizumab is important because intervention is needed to prevent organ failure damage and improve patients' condition [6]. Because of the severity of aHUS, it is essential to employ relevant multidisciplinary clinical management including nephrologists, hematologists, and possibly infectious disease specialists [7].

Taking this case as an example, this paper seeks to explicate the difficulties in providing and accessing care for aHUS patients and the significance of a collaborative approach to care for such patients.

CASE PRESENTATION

A 67-year-old female with a history of hypertension, hyperlipidemia for 15 years, and possible polysubstance abuse presented with acute respiratory and renal failure, hypotension, and severe sepsis. She recently moved to Mexico and developed symptoms of foodborne illness, including diarrhea, nausea, vomiting, and weakness.

Upon arrival, the patient was in critical condition and needed immediate intubation and sedation. She was also started on vasopressor and vasopressin due to hypotension and shock.

Laboratory tests revealed severe renal failure with a serum creatinine level of 8.2 mg/dL and blood urea nitrogen of 63 mg/dL. Hypokalemia and hypocalcemia were noted, alongside metabolic acidosis. The patient exhibited altered mental status, possibly indicative of thrombotic microangiopathy like TTP, and had oliguric renal failure associated with rhabdomyolysis (creatine phosphokinase >7000 U/L) (Table 1). During the hospital stay, the patient was sedated and on respiratory support.

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Table 1: Renal function, metabolic, and serum electrolyte findings

Test	Normal range	Results
Glucose	70–99 mg/dL	198 mg/dL
Calcium	8.5–10.1 mg/dL	5.5 mg/dL
Phosphorus	2.5–4.9 mg/dL	3.9 mg/dL
Magnesium	1.8–2.4 mg/dL	2.3 mg/dL
Ammonia	11–32 mol/L	39 mg/dL
Lactate dehydrogenase	100–190 U/L	2167 U/L
Haptoglobin	30–200 mg/dL	106 mg/dL
CPK	26–192 U/L	>7000 U/L
Lactic acid	0.5–2.2 mmol/L	20 mmol/L
Serum creatine	0.7–1.2 mg/dL	8.2 mg/dL
BUN	5–25 mg/dL	63 mg/dL

BUN: Blood urea nitrogen, CPK: Creatine phosphokinase

Her vital signs were variable, with temperatures ranging from 96.9°F to 101.1°F, pulse from 48 to 112 bpm, respiratory rate from 17 to 30 breaths/min, and blood pressure from 80/46 mmHg to 240/107 mmHg. Her weight was recorded at 177 lb (80.4 kg).

The blood glucose levels were 198 mg/dL, and lactic acid was 20 mmol/L (Table 1). Hematological findings included white blood cell 8200/µL, Hgb 10.1 g/dL, and platelets 53,000/µL. Prothrombin time/international normalized ratio and activated partial thromboplastin time were also elevated. Liver enzymes were elevated and there were also findings of low calcium and albumin levels (Table 2). Lactate dehydrogenase (LDH) was markedly elevated at 2167 U/L and haptoglobin was within the normal range at 106 mg/dL (Table 1).

A computed tomography (CT) scan of the abdomen revealed enteritis and colitis (Fig. 1), while a CT of the head showed a non-hemorrhagic ischemic infarct in the left parietal lobe (Fig. 2). A chest X-ray indicated mild bilateral retrocardiac atelectasis (Fig. 3).

The patient was promptly started on broad-spectrum antibiotics, including doxycycline, piperacillin/tazobactam, and vancomycin. IV fluids were initiated, and dopamine, norepinephrine, and vasopressin were added due to ongoing hemodynamic instability. She was also treated with potassium chloride, magnesium sulfate, famotidine, and human insulin lispro every 6 h according to a sliding scale. Despite these measures, her urine output remained minimal, necessitating the initiation of continuous renal replacement therapy (CRRT). She was closely monitored for complications related to AKI, electrolyte imbalances, and rhabdomyolysis. Consultations with multiple specialties were initiated, including nephrology, infectious disease, and hematology/oncology.

The patient's condition remained critical, necessitating close monitoring and ongoing interventions. The assessment included continued supportive care with CRRT, vasopressor support, and antibiotic therapy. The plan involved monitoring for complications, including renal function, anemia, and neurologic sequelae. Further evaluation for complement-mediated causes was also considered. Possible diagnoses being considered include HUS due to enteropathogenic *E. coli* infection, based on the clinical presentation and laboratory findings.

Table 2: Laboratory investigations showing hematological, liver function tests, and coagulation profile

Test	Normal range	Results
Hemoglobin	12–16 g/dL	10.1 g/dL
White blood cells	4500–11,000/µL	8200/µL
Platelets	1.5–4 lakh/µL	53,000/µL
Alanine transaminase	30–65 U/L	1848 U/L
Aspartate aminotransferase	15–40 U/L	989 U/L
Total bilirubin	0.0–1.0 mg/dL	1.2 mg/dL
Albumin	3.4–5.0 g/dL	1.5 mg/dL
Fibrinogen	166–580 mg/dL	468 mg/dL
Prothrombin time	11.6–14.9 s	16.8 s
Activated partial thromboplastin time	22.0–37.0	41.2 s
International normalized ratio	0.8–1.20	1.38

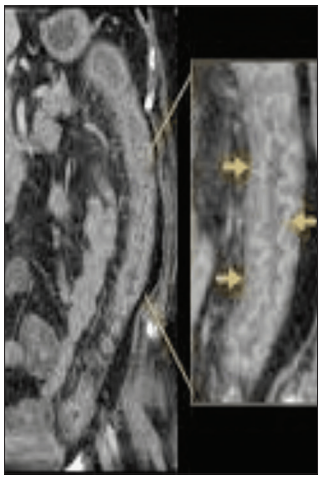

Figure 1: Computed tomography abdomen which shows bilaminar mural enhancement with asymmetrical mucosal hyperenhancement

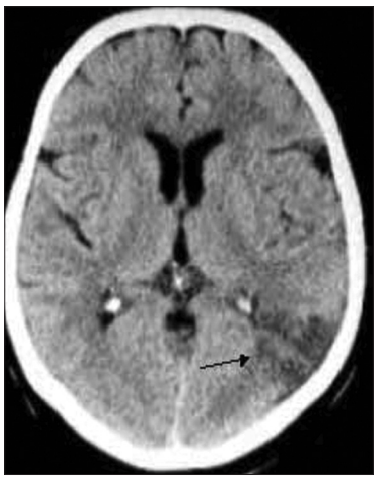

Figure 2: Wedge-shaped hypodensity with loss of gray white matter differentiation and adjacent sulcal effacement, likely watershed infarct

DISCUSSION

The case presented in this study presents the clinical situation of a 67-year-old female, with complex clinical presentation and laboratory findings. It leads to a diagnosis of aHUS because of

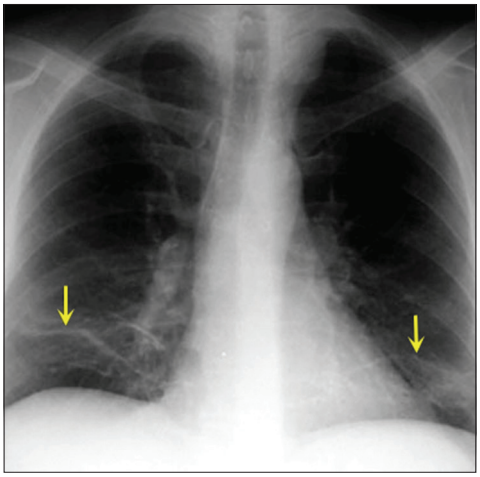

Figure 3: Bilateral lower lobe atelectatic bands

an infection due to an enteropathogenic E. The main findings include severely compromised renal function, thrombocytopenia, and microangiopathic hemolytic anemia; all these are classic signs of aHUS [8]. These findings correlate with the current knowledge that aHUS is frequently related to complement system dysfunction that causes endothelial cell injury and manifests as thrombotic microangiopathy [9]. Other studies have shown that aHUS may arise from diverse causes of infection, for instance, enteropathogenic *E. coli*, as well as, from exposure to medication or variations in genetic code [10]. One of the important aspects in this case is the tremendously high LDH, which is a clear indicator of cellular damage and hemolysis [11].

The multi-organ dysfunction syndrome (MODS) and non-hemorrhagic ischemic infarct in the left parietal lobe can also highlight the need for considering the serious and potentially complex nature of aHUS. This case best fits complement dysregulation as it shows the impact of this condition on different organ systems not only on the kidneys [12].

Eculizumab is a powerful terminal complement inhibitor that has proven effective in mending the outcomes of aHUS patients by stopping more injury to the endothelium and reducing the chances of requiring further dialysis for life [13]. Because of such findings, it has been shown that earlier initiation of eculizumab in aHUS has a better renal outcome and decreased mortality when compared with supportive care only [14]. This shows that early stages and intervention in aHUS cases would have a big impact on the patients in terms of improving their survival rate and avoiding kidney transplants in the future.

Data from previous research have indicated that mutations in complement regulatory proteins, particularly C3, are risk factors for negative renal outcomes and increased incidence of end-stage renal disease [15]. These patients need continued follow-up to track post-operative BP and renal function as well as to improve their management experience in case of relapse.

Numerous studies indicated that if eculizumab is initiated early, then the outcomes are favorable but the patients who have some genetic mutation in C3 have severe consequences of the disease. This re-emphasizes the role of genetic testing in aHUS and long-term assessment of the patient [16].

The clinical presentation of this case highlights the importance of early detection and diagnosis of aHUS in patients who have thrombotic microangiopathy and MODS but do not show evidence of typical infection-related hemolytic-uremic syndrome. Complement-inhibitory therapy, most importantly with eculizumab, should be promptly administered to avoid progression to irreversible renal injury and to maximize the likelihood of recovery [17]. This case also provides evidence on how appropriate patient management of aHUS requires a multidisciplinary team including nephrologists, hematologists, and infectious disease specialists. Further research needs to be performed to examine specific genetic markers and complement regulatory protein mutations that confer an increased risk of developing aHUS as well as to develop better test protocols to improve early diagnosis. Further studies are also required to determine the long-term effects on these individuals and to optimize treatment with the use of new agents for C3 complement inhibition. More studies in aHUS will clarify the molecular mechanisms involving the dysregulation of complement patterns to enhance the development of new therapeutic targets and management approaches that can improve the morbidity and mortality outcomes of the disease.

CONCLUSION

This study describes the presentation of a 67-year-old female with dysregulated activated complement, associated with an infection with enteropathogenic E. coli and a complex and rare variant of aHUS. The patient showed kidney failure and MODS together with a thrombotic microangiopathy caused by thrombocytopenia combined with microangiopathic hemolytic anemia. The initial introduction of therapies directed against dysregulation of the complement system, like eculizumab, was fundamental to the management of this disease and the betterment of various outcomes. It shows that early diagnosis and treatment combined with coordinated comprehensive management and monitoring is crucial for reducing the occurrence of renal injury and other serious consequences in aHUS.

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