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Anorexia in a Patient With Atypical Hemolytic Uremic Syndrome and Systemic Capillary Leak Syndrome: A Case Report

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Abstract

Atypical hemolytic uremic syndrome (aHUS) and systemic capillary leak syndrome (SCLS) are rare conditions with high mortality rates. Eculizumab and intravenous immune globulin (IVIG) are improving outcomes and enabling focused supportive care. We present a case of a 57-year-old male who was admitted to the hospital after a 9.07-kg weight loss over 4 weeks. He was subsequently diagnosed with aHUS, monoclonal gammopathy of undetermined significance (MGUS), and SCLS. He suffered from recurrent episodes of flash edema preceded by nausea and regurgitation that required intubation and dialysis. His condition improved after treatment with eculizumab and IVIG. The mechanism that causes anorexia in aHUS and SCLS has not previously been described. We propose that these syndromes result in delayed gastric emptying leading to anorexia, which may be a prodromal sign of an acute attack.

Keywords: Atypical hemolytic uremic syndrome; Systemic capillary leak syndrome; Monoclonal gammopathy of undetermined significance; Anorexia; Gastroparesis; Intravenous immune globulin; Eculizumab

Introduction

Atypical hemolytic uremic syndrome (aHUS) is a condition marked by the triad of hemolytic anemia, thrombocytopenia, and renal insufficiency. The disease process is linked to uncontrolled activation of the alternate complement system, leading to the formation of schistocytes and microthrombi. Studies have shown that 5-10% of patients present with life-threatening multi-organ failure from diffuse thrombotic microangiopathies [1, 2]. Etiologies include viruses, organ transplants, cancer, anti-cancer and anti-platelet medications, pregnancy, and genetic mutations. The incidence is around 1 in 500,000 people per year in the United States, making it about 10 times less common than typical HUS [3]. Adults with this syndrome typically present with a non-specific prodrome of fatigue and general distress [4]. Eculizumab was FDA approved in 2011 for treatment of aHUS, and case studies of the drug have shown reversal of thrombocytopenia and hemolysis, and a time dependent reversal of kidney dysfunction [4].

Systemic capillary leak syndrome (SCLS or Clarkson syndrome) is a rare syndrome with less than 300 cases reported since it was first described in 1960 [5, 6]. It is characterized by paroxysmal leakage of water, electrolytes, and proteins into the extravascular space, resulting in a triad of hypotension, elevated hemoglobin, and hypoalbuminemia. These patients also exhibit symptoms of fatigue, cough, abdominal pain, and nausea. Intravenous immune globulin (IVIG) is the treatment of choice and has been used prophylactically since a 2011 study on its efficacy showed an 89% drop in SCLS flares [7].

Anorexia has been described in case reports for both aHUS and SCLS. However, the mechanism resulting in anorexia has not been defined. The following case will discuss the manifestation of anorexia as a result of delayed gastric emptying in a patient diagnosed with both aHUS and SCLS.

Case Report

Our patient is a 57-year-old male with a past medical history significant for gastrointestinal candidiasis, West Nile virus, immunocompetent cytomegalovirus, viral myocarditis, bilateral carpal tunnel syndrome, and an elevated kappa-lambda IgG ratio. He initially presented to his primary care provider with a prolonged history of worsening non-specific symptoms, including fatigue, tongue swelling, bilateral pitting edema, and a body rash. His presentation was suspicious for amyloidosis, but it was ruled out after negative bone marrow, fat pad, and rectal biopsies.

Several months later, he presented with fatigue, nausea and chills, and was treated symptomatically for influenza. Over the course of the next 2 weeks, his persistent nausea resulted in a 9.07-kg weight loss. He was admitted to the hospital and within 4 h, he began having chest pain, dyspnea and a markedly elevated blood pressure. His laboratory results demonstrated acute kidney injury, anemia with numerous schistocytes, thrombocytopenia, elevated LDH, and hypoalbuminemia. His

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troponins were elevated and ECG revealed diffuse T wave inversions consistent with prior viral myocarditis. Chest X-ray showed diffuse bilateral infiltrates consistent with edema.

He received enteral nutrition upon admission, but was switched to total parenteral nutrition on the second day due to vomiting. Throughout his first week of hospitalization, he suffered from frequent episodes of flash edema, leading to intubation for 4 days and hemodialysis. Upon intubation, enteral nutrition was resumed.

An ADAMTS13 test for TTP was negative, leading to the diagnosis of aHUS on the second week of his hospitalization. He was started on weekly eculizumab infusions, and began consuming small amounts of food, but he continued to complain of severe epigastric discomfort with episodic regurgitation within 2 - 4 h after meals. He was also diagnosed with monoclonal gammopathy of undetermined significance (MGUS), due to elevated paraproteins. A kidney biopsy indicated that approximately 20% of his kidneys were damaged by schistocytes, so dialysis was continued.

Our patient required intubation and enteral feeding during his fifth week secondary to nightly episodes of flash edema preceded by nausea and regurgitation. After being extubated, he was able to tolerate oral intake with fewer episodes of regurgitation. Throughout his hospitalization, our patient had epigastric discomfort and postprandial regurgitation largely resistant to anti-nausea and anti-reflux medications, resulting in an additional 9-kg weight loss. Rapidly fluctuating blood pressures, nausea, coughing, and swelling of his lower extremities and face further complicated his management. These signs and symptoms, combined with MGUS, led to the diagnosis of SCLS on the sixth week of admission. He began receiving monthly IVIG infusions and had a nuclear gastric motility study performed that revealed a delayed 90-min emptying rate, with a half time of 240 min.

Treatment resulted in normalization of platelets, normalization of LDH, and a blood smear without schistocytes by week 8. Three weeks following initiation of IVIG, serum protein electrophoresis demonstrated a decreased monoclonal paraprotein and kappa-lambda ratio compared to several months prior. In the 20 weeks following the initial presentation, there has been an 11.34-kg increase in the patient's weight with improvement in appetite, but minimal return of the patient's kidney function, requiring continued dialysis.

Discussion

Anorexia has been observed in case reports of aHUS and SCLS; however, no mechanism has been described. We propose that anorexia in this patient was caused by gastroparesis. How aHUS or SCLS is linked to delayed gastric emptying remains unclear.

Inflammatory deposition of $CD4^+$ and $CD8^+$ T lymphocytes within the gastric smooth muscle layer and myenteric plexus has been implicated in delayed gastric motility [8]. aHUS may cause delayed motility through a similar mechanism. Symptoms of aHUS are due to overactivation of C5a, leading to the formation of numerous schistocytes and microthrombi. Their deposition in small gastric capillaries could potentially lead to nerve damage through ischemic mechanisms or an isolated gastric myopathy. Our patient's appetite improved after he was started on eculizumab, a monoclonal antibody that blocks the cleavage of C5 to C5a and C5b, indicating that an overactive immune response may have contributed to his anorexia.

MGUS of the IgG subtype has been found in the majority of patients with SCLS, and is believed to play a role in the pathogenesis of the disease [9, 10]. We believe a contributing factor to our patient's delayed gastric motility was bowel wall edema, secondary to hyperpermeability created by paraprotein deposition in the capillary walls. A recently proposed theory stated that large amounts of fluid leaking from the capillaries can lead to bowel wall and peritoneal edema, leading to anorexia, nausea and vomiting [11]. Significant improvement of appetite, nausea, regurgitation, and flash edema, as well as a decrease in the paraprotein levels was noticed in our patient with monthly infusions of IVIG.

This patient's episodes of flash edema and aHUS findings were preceded by nausea and regurgitation, from 24 h to several weeks in duration. Therefore, we suggest that anorexia may be a prodromal sign indicating an acute attack. As both aHUS and SCLS are diseases prone to lethal episodes of relapse, this may give providers enough time for lifesaving interventions in patients diagnosed with either of these conditions.

aHUS and SCLS are rare systemic diseases capable of disrupting gastric motility, a previously undescribed phenomenon. Anorexia caused by delayed gastric emptying may be overshadowed by more imminently life-threatening complications. Treatment with eculizumab and IVIG has led to improved outcomes in patients with aHUS and SCLS, and continued improvement in these patient populations will enable more focused supportive care. We recommend that patients with aHUS or SCLS presenting with decreased appetite have a nuclear gastric motility study and receive motility stimulating agents as needed to improve nutrition and decrease recovery times, and be educated on the importance of contacting their providers if they have sudden onset nausea and vomiting.

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Conflicts of Interest

The authors declare that they have no competing financial interests.

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