

Received: 2020.05.04

Accepted: 2020.10.08

Available online: 2020.10.27

Published: 2020.12.08

Postoperative Atypical Hemolytic Uremic Syndrome in a 67-Year-Old Woman Associated with Hemolytic Anemia, Thrombocytopenia, and Acute Renal Failure

Authors' Contribution:

Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

EF 1 **Arnab Chowdhury**
E 2 **Megan P. Griffith**
E 3 **Eric Busse**
AEF 1 **Ahmed Khurshid Pasha**

1 Department of Hospital Medicine, Mayo Clinic Health System in Mankato, Mankato, MN, U.S.A.
2 Department of Pathology, Mayo Clinic Health System in Mankato, Mankato, MN, U.S.A.
3 Department of Orthopedic Surgery, Mayo Clinic Health System in Mankato, Mankato, MN, U.S.A.

Corresponding Author: Ahmed Khurshid Pasha, e-mail: Pasha.ahmed@mayo.edu
Conflict of interest: None declared

Patient: Female, 67-year-old
Final Diagnosis: Atypical hemolytic uremic syndrome
Symptoms: Anemia • renal failure • thrombocytopenia
Medication: —
Clinical Procedure: —
Specialty: Hematology • General and Internal Medicine • Pathology

Objective: Unusual clinical course

Background: Hemolytic uremic syndrome (HUS) develops from uncontrolled complement activation leading to intravascular hemolysis and thrombotic microangiopathy. Atypical HUS is diagnosed by excluding a disintegrin and metalloproteinase with thrombospondin type 1 motif, 13 deficiency, and infection-associated HUS. Patients with atypical HUS may respond to eculizumab. We present a case of a 67-year-old woman who developed atypical HUS with hemolytic anemia, renal failure, and thrombocytopenia following an elective hip arthroplasty.

Case Report: An otherwise healthy 67-year-old woman was admitted to our hospital after an elective right total hip arthroplasty. In the postoperative course, she developed vomiting and acute renal failure that was initially attributed to a prerenal cause. She continued to have worsened renal failure in spite of intravenous hydration, and she also developed mild thrombocytopenia. A peripheral blood smear was performed and showed the presence of schistocytes (red blood cell fragments) consistent with microangiopathic hemolytic anemia. In the context of anemia, thrombocytopenia, and renal failure, this finding led to a prompt and early referral to a tertiary care center and a timely diagnosis of atypical HUS. The patient underwent treatment with plasmapheresis, hemodialysis, and eculizumab.

Conclusions: This report highlights the importance of examination of the peripheral blood smear in the diagnosis of thrombotic microangiopathy. As shown in our case, the presence of schistocytes indicates the need for prompt clinical management.

MeSH Keywords: Anemia, Hemolytic • Hemolytic-Uremic Syndrome • Thrombotic Microangiopathies

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/925662>



985



—



1



6



Background

Thrombotic microangiopathy (TMA) is characterized by microvascular occlusion of capillaries and arterioles in various organs with platelet thrombi [1]. It can be broadly classified into 3 categories: thrombotic thrombocytopenic purpura, which is secondary to a disintegrin and metalloproteinase with thrombospondin type 1 motif, 13 (ADAMTS13) deficiency with variable clinical features; hemolytic uremic syndrome (HUS), which is characterized by renal failure; and other conditions associated with microangiopathic hemolytic anemia. HUS can be associated with infection due to *Escherichia coli* O157: H7 that expresses Shiga toxin, or it can be complement mediated. Atypical HUS (aHUS) is an imprecise term and broadly refers to diseases that involve TMA with some degree of renal failure in patients for whom ADAMTS13 deficiency and infection-associated HUS have been ruled out. Some of these patients have complement abnormalities as the primary underlying pathology, and a more precise term for these disorders is complement-mediated HUS. Although aHUS was initially described in children, multiple studies have shown that it can affect adults as well.

Laboratory abnormalities include hemolytic anemia, increased lactic acid dehydrogenase, low haptoglobin, schistocytes (red blood cell fragments) on peripheral smear, thrombocytopenia, and renal failure. In the differential diagnosis, one should consider systemic diseases that can be associated with aHUS, including infections, drugs, pregnancy, autoimmune disease, cancer, transplant, and metabolic abnormalities such as cobalamin deficiency-associated TMA. In many real-world hospital settings, the turnaround time for ADAMTS13 assays can be delayed. In these cases, clinical scores such as the PLASMIC score [2] can be useful to predict ADAMTS13 deficiency [3–5].

Early suspicion and timely diagnosis and treatment are of utmost importance to improve mortality and morbidity. Peripheral blood smear remains a quick, inexpensive, yet important test. We describe a case of acute renal failure and mild thrombocytopenia following an elective right total hip arthroplasty in which a diagnosis of TMA and subsequently aHUS were uncovered as a result of early peripheral blood smear.

Case Report

A 67-year-old woman was admitted to our hospital after an elective right total hip arthroplasty. She had a history of osteoporosis and previous left shoulder rotator cuff repair with an unremarkable postoperative course. She had unremarkable laboratory test results, including normal hemoglobin, platelet count, and creatinine prior to this intervention.

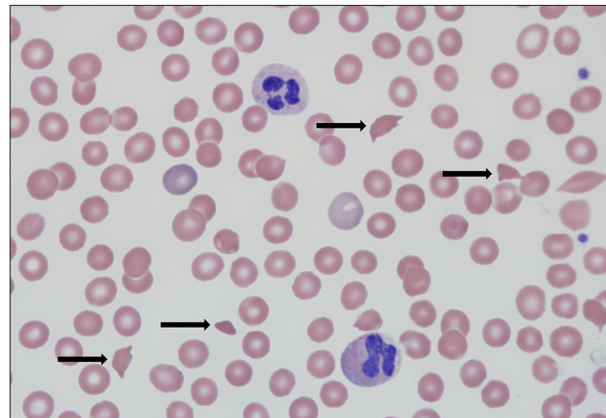


Figure 1. Peripheral smear from our patient with microangiopathic hemolytic anemia, demonstrating decreased erythrocyte numbers consistent with anemia and decreased platelets consistent with thrombocytopenia. Arrowheads highlight fragmented red blood cells (i.e., schistocytes) that have an irregular shape and lack central pallor. Wright Giemsa stain, original magnification $\times 400$.

Her procedure was performed under regional anesthesia with negligible blood loss, and she was subsequently started on aspirin twice daily for venous thromboembolism prophylaxis. She had normal vitals in the postoperative period, and she had follow-up complete blood counts on postoperative days 1 and 2. On day 1, results showed mild anemia with hemoglobin of 10.8 g/dL but were otherwise unremarkable. The platelet count was noted to be $271 \times 10^9/L$. On postoperative day 2, hemoglobin was 10.6 g/L and platelets were $184 \times 10^9/L$. The patient was asymptomatic, and no other investigations were pursued. Renal function was not assessed on postoperative days 1 and 2 because there were no clinical indications. On postoperative day 3, the patient started having episodes of nonbloody, bilious emesis. Laboratory tests were conducted and were significant for increased creatinine of 5.57 mg/dL. Further, the tests showed blood urea nitrogen 48 mg/dL, hemoglobin 10.0 g/L, and platelets $111 \times 10^9/L$. Fluid resuscitation was started, but the patient continued to have increased creatinine and decreased platelet count. A peripheral smear was obtained, which showed fragmented red blood cells, moderate thrombocytopenia, and unremarkable white cells (Figure 1). These observations were consistent with microangiopathic hemolytic anemia. The patient's lactate dehydrogenase level was elevated and her haptoglobin level was reduced. The patient was subsequently transferred to a tertiary care center where she underwent plasmapheresis and temporary hemodialysis. ADAMTS13 activity was noted to be normal. A fecal polymerase chain reaction test for Shiga toxin was negative. A diagnosis of aHUS was made, and the patient was started on eculizumab, with an excellent response. After a protracted stay, the patient's laboratory tests (creatinine and platelets) returned

to baseline and she was discharged. Further genetic workup was obtained and revealed an MCP/CD46 heterozygous mutation, which placed her at a higher risk for developing aHUS.

Discussion

The patient in this report received a diagnosis of aHUS, for which there is no specific laboratory test. Exclusion of thrombotic thrombocytopenic purpura and Shiga toxin *E. coli* HUS in the proper clinical context marks the diagnosis of aHUS. The results of specific tests needed for this exclusion can take time. Given a high index of suspicion, early involvement of a hematology team and prompt initiation of plasmapheresis along with hemodialysis, if indicated, are lifesaving. Furthermore, eculizumab approval from the Food and Drug Administration for treatment of aHUS has revolutionized its management [6].

Anemia, thrombocytopenia, and renal dysfunction should alert physicians to the possibility of TMA. A simple peripheral smear is a quick and rather inexpensive test that can detect schistocytes and confirm microangiopathic hemolytic anemia. In our case, rapidly worsening anemia, thrombocytopenia, and acute kidney injury in an otherwise healthy patient prompted obtaining a peripheral smear, which pointed toward TMA and led to the patient's transfer to a tertiary care facility. A

diagnosis of aHUS was eventually made at that facility, and with timely treatment, the patient recovered without complications. aHUS is a type of TMA and should be considered after ruling out ADAMTS13 deficiency, Shiga-toxin-mediated HUS, and other systemic conditions causing TMA. Eculizumab has revolutionized the treatment of aHUS.

Conclusions

Given the potential mortality and morbidity associated with TMA syndromes, physicians should always consider TMA as a differential for anemia, thrombocytopenia, and renal failure. Furthermore, physicians should have a low threshold of suspicion to perform a peripheral blood smear, which is a quick, inexpensive, yet important tool in the detection of microangiopathic hemolytic anemia. This report of a case of postoperative aHUS associated with hemolytic anemia and thrombocytopenia with acute renal failure highlights the importance of examination of the peripheral blood smear. As shown in our case, the presence of schistocytes indicates the need for prompt clinical management to prevent mortality and morbidity.

Conflict of interest

None

References:

1. Manrique-Caballero CL, Peerapornratana S, Formeck C et al: Typical and atypical hemolytic uremic syndrome in the critically ill. *Crit Care Clin*, 2020; 36(2): 333–56
2. Bendapudi PK, Hurwitz S, Fry A et al: Derivation and external validation of the PLASMIC score for rapid assessment of adults with thrombotic microangiopathies: A cohort study. *Lancet Haematol*, 2017; 4(4): e157–64
3. Nester CM, Barbour T, de Cordoba SR et al: Atypical aHUS: state of the art. *Mol Immunol*, 2015; 67(1): 31–42
4. Go RS, Winters JL, Leung N et al: Thrombotic microangiopathy care pathway: A consensus statement for the Mayo Clinic Complement Alternative Pathway-Thrombotic Microangiopathy (CAP-TMA) Disease-Oriented Group. *Mayo Clinic Proc*, 2016; 91(9): 1189–211
5. Scully M, Cataland S, Coppo P et al., International Working Group for Thrombotic Thrombocytopenic Purpura: Consensus on the standardization of terminology in thrombotic thrombocytopenic purpura and related thrombotic microangiopathies. *J Thromb Haemost*, 2017; 15(2): 312–22
6. Berger BE: Atypical hemolytic uremic syndrome: A syndrome in need of clarity. *Clin Kidney J*, 2019; 12(3): 338–47