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CASE REPORT

Autoimmune Hemolytic Anemia following Septic Shock with Escherichia Coli; a Case Report

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Abstract: Sepsis is a severe, life-threatening illness caused when the immune system responds inappropriately to infections, causing organ deterioration and negatively affecting the systems inside the body, one of which is the coagulation system. Most hematologic changes in red blood cells (RBCs) are non-antibody-mediated hemolytic anemia (NAHA). Autoimmune hemolytic anemia (AIHA) is a rare condition, challenging in diagnosis, requiring prompt recognition and management. Warm hemolytic anemia has recently been reported in patients with septic shock. This report presents a sepsis-induced autoimmune hemolytic anemia case. A 44-year-old Vietnamese female with no chronic disease came to the emergency department because of sudden periumbilical colicky pain after consuming a fresh garden salad. The abdominal pain appeared nine hours after the meal, following vomiting. Twelve hours later, she developed diarrhea, subsequently a fever, and chills. She was admitted to the emergency department in the fifteenth hour of the first symptom. Septic shock, multiple organ failure, and warm autoimmune hemolysis were all present in the patient. Hemolytic anemia and multiorgan failure made the situation worse, leading to death. Autoimmunity hemolytic anemia in sepsis or septic shock is rare, but treating both emergency hemolytic anemia and potential infectious etiology is crucial in acute situations.

Keywords: Anemia, hemolytic, autoimmune; Coombs test; Blood coagulation; Hemolysis

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1. Introduction

Autoimmunity hemolytic anemia (AIHA) involves hemolysis, affecting red blood cells (RBCs), involving autoantibodies, complement, macrophages, T-lymphocytes, and cytokines. A positive direct antiglobulin test (DAT) indicates the presence of immunoglobulins (most commonly IgG, but also IgM, IgA, and/or complement - consistently C3d) on erythrocytes. AIHA, classified into warm (WAIHA) or cold autoimmune hemolytic anemia, has primary or secondary etiologies depending on the underlying condition. In approximately 50% of circumstances, the primary form of AIHA is identified, while secondary etiologies are associated with autoimmune diseases, lymphoproliferative diseases, infections, solid tumors, or solid organ transplantation (1, 2). The incidence of AIHA is currently estimated to be approximately 1.77 cases per 100,000 people per year, with WAIHA accounting for almost two-thirds of cases. Sepsis is a severe, life-threatening illness caused when the immune system responds inappropriately to infections, causing organ deterioration. The coagulation system, among other systems, is negatively impacted by sepsis. Coagulopathy in sepsis may take the form of sepsis-induced coagulopathy (SIC) (early stage) or sepsis-associated disseminated intravascular coagulation (DIC) (late stage). Sepsis can cause both quantitative and qualitative changes in RBCs (3). Alterations in RBCs include volume, morphology, deformability, metabolism, antioxidant status, and hemolysis. Intravascular hemolysis is common in sepsis and septic shock cases, with recent reports of sepsis-induced autoimmune hemolytic anemia (4). Although the precise mechanism and causal relationship between AIHA and sepsis is unknown, it is conceivable that hemolysis is also an indicator of sepsis and contributes to the poor prognosis of septic patients. For proper initial management in a critical illness scenario, it is essential to recognize the emergency hematological disease. This report presents

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a case of sepsis-induced autoimmune hemolytic anemia in a 44-year-old Vietnamese female following sudden periumbilical colicky pain after consuming a fresh garden salad.

2. Case presentation

A 44-year-old Vietnamese female with no chronic disease came to the emergency department because of sudden periumbilical colicky pain after consuming a fresh garden salad. The abdominal pain appeared nine hours after the meal, following vomiting. Twelve hours later, she developed diarrhea, subsequently a fever, and chills. She was admitted to the emergency department in the fifteenth hour of the first symptom. She denied any chest pain, difficulty breathing, headache, urinary urgency or dysuria, vaginal bleeding, melena, hematochezia, any new medications, traveling, trauma, or any recent illnesses. Her vital signs demonstrated a heart rate of 120 beats per minute, a blood pressure of 90/60 mmHg, and a temperature of 101.2 degrees Fahrenheit (F). The patient's physical examination showed light jaundice, mottle and dry skin, generalized fatigue, a distended abdomen with moderate ascites, periumbilical tenderness, dark urine, and no neurologic deficits. Table 1 and figure 1 display laboratory findings and imaging results. The patient's mental status rapidly deteriorated. Therefore, she was intubated, given a resuscitated infusion with normal saline at 30 milliliters per kilogram within one hour, and initiated with noradrenaline at 0.05 micrograms per kilogram per minute to maintain the mean blood pressure above 65 mmHg. Simultaneously, one gram of Meropenem was infused intravenously into the patient. After three hours of being admitted to the emergency department, the patient was transferred to the intensive care unit (ICU) under vasopressors. In the ICU, the dramatically dropped hemoglobin and the elevated indirect bilirubin and lactate dehydrogenase levels pointed toward the new onset of hemolytic anemia. Her condition required a transfusion, but the blood bank could not identify compatible units. At this time, after the acute hemolytic anemia workup shown in Table 1, disseminated intravascular coagulation (DIC) and WAHA were confirmed. Ultimately, we decided to inject 40 milligrams of dexamethasone and transfuse two units of packed red blood cells at the twentieth hour from the onset of her first symptom. However, the anemia worsened because of the synergistic effect of DIC and warm autoimmunity hemolysis. Unfortunately, her condition began declining as a result of multiple organ failures, particularly the hematologic problem. The patient was declared dead after two days of hospitalization. The final diagnosis was septic shock resulting in multi-organ failure, DIC, and WAIHA.

3. Discussion

Thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS), DIC, and hemolytic anemia are the top acute hemolysis conditions in hematologic emergencies, categorized into non-antibody-mediated hemolysis (NAHA) and AIHA. These medical conditions might be misdiagnosed and necessitate greater attention to get appropriate management (5-7). Except for WAIHA, which has distinct clinical manifestations and laboratory results when compared to non-antibody-mediated hemolysis, the majority of the disorders listed above are intravascular hemolytic anemias. In addition to the dysregulated red blood cells that cause intravascular hemolysis in sepsis, antibody-mediated hemolysis, particularly WAIHA, has recently been identified.

AIHA involves the antibody-mediated destruction of red blood cells. AIHAs are classified as cold AIHA (CAIHA) and WAIHA (1), based on antibody interaction with human red blood cells. Cold antibodies respond best between 0-4 degrees Celsius, while warm antibodies respond best at 37 degrees Celsius. CAIHA and WAIHA share common features, including severe anemia symptoms and hemolysis evidence. WAIHA evaluations reveal hemolysis biochemical results such as decreased haptoglobin, increased LDH concentration, positive hemoglobinuria, urobilinogen in urine, and difficulties finding crossmatch-compatible blood for transfusion. Critically ill WAIHA patients should receive corticosteroids as first-line therapy to slow hemolysis. Prednisone or methylprednisolone can be used as an alternative. Splenectomy may be considered a third-line therapy option. Rituximab combined with corticosteroids is more effective than corticosteroids alone. Intravenous immune globulin can be beneficial as an adjuvant to other therapies.

In this specific case report, the patient typically presented with signs and symptoms of multiorgan failure, and septic shock resulting from gastroenteritis. From the beginning, the symptoms included pallor, jaundice, and dark urine after acute illness onset, and laboratory results both confirmed hemolysis. Up until the patient's condition deteriorated and a pRBC transfusion was necessary, it was empirically assumed that the dropped hemoglobin and dysregulation of the coagulation panel in the septic shock were caused by the DIC. Disseminated intravascular coagulation is common in hematologic complications from sepsis or septic shock. Laboratory results are compatible with septic-induced DIC. On the other hand, the difficulty finding crossmatch-compatible blood for transfusion in the hemolysis scenario raised suspicion about other hematologic disorders in combination with the DIC. In this case, the positive DAT in conjunction with spherocytes determined the WAIHA diagnosis. In this scenario, infection, particularly septic shock, might have served as the underlying cause. In the event rituximab is not avail-

Table 1: Laboratory data of the patient upon diagnosis

Parameter	Normal range	Result	Parameter	Normal range	Result
WBC (G/L)	4-10	19.63	Urea (mmol/L)	3.3-8.3	14.8
Neutrophil (%)	40 – 60	82	Creatinine (mol/L)	44-80	183
Lymphocyte (%)	20 - 40	12	AST (U/L)	<40	82
RBC (T/L)	3.8 - 5.0	2.06	ALT (U/L)	<40	67
Hb (g/L)	120 - 150	62	Bil. T (µmol/L)	<21	64.8
Hct (%)	33.5 - 45	49	Bil. D (µmol/L)	<3.4	2.0
MCV (fl)	80-100	89	PCT (ng/mL)	0-0.05	14.4
RDW (fl)	40.0 - 55.0	69	Fibrinogen (mg/dL)	200 -400	135
PLT (G/L)	140-350	114	D – Dimer (ng/mL)	< 250	2890
PT (seconds)	10-15	212	LDH (units/L)	140 - 280	421
APTT (seconds)	25-35	102.7	Haptoglobin (g/L)	0.5-2.2	3.6
Reticulocyte (%)	0.5-1.5	2.3	DAT	Negative	Positive
RPI	1	2.68	PBS	Reticulocytes, spherocytes, schistocytes	
Urinalysis - Dipstick			**Microbiological studies**		
RBC	Negative	Positive	Blood cultures	Negative	Escherichia coli (ETEC)
Leukocyte esterase	Negative	Negative			
Ketone	Negative	Negative			
Nitrite	Negative	Negative	Stool bacterial PCR panel	Negative	Escherichia coli (ETEC)
Bilirubin	Negative	Positive			
Urobilirubin	Negative	Positive			

WBC: White blood cells; RBC: Red blood cells; PLT: Platelet count; Hb: Hemoglobin; Hct: hematocrit; MCV: Mean corpuscular volume; RDW: Red cell distribution width; LDH: Lactate dehydrogenase; RPI: Reticulocyte production index; PBS: Peripheral blood smear; DAT: Direct Coombs test; AST: Aspartate aminotransferase; ALT: Alanine transaminase; Bil.T: Total bilirubin; Bil.D: Direct bilirubin; PCT: Procalcitonin; APTT: Activated partial thromboplastin time; PT: Prothrombin time; PCR: Polymerase Chain Reaction; ETEC: Enterotoxigenic Escherichia coli; fl: Femtoliter; G/L: Giga/Liter.

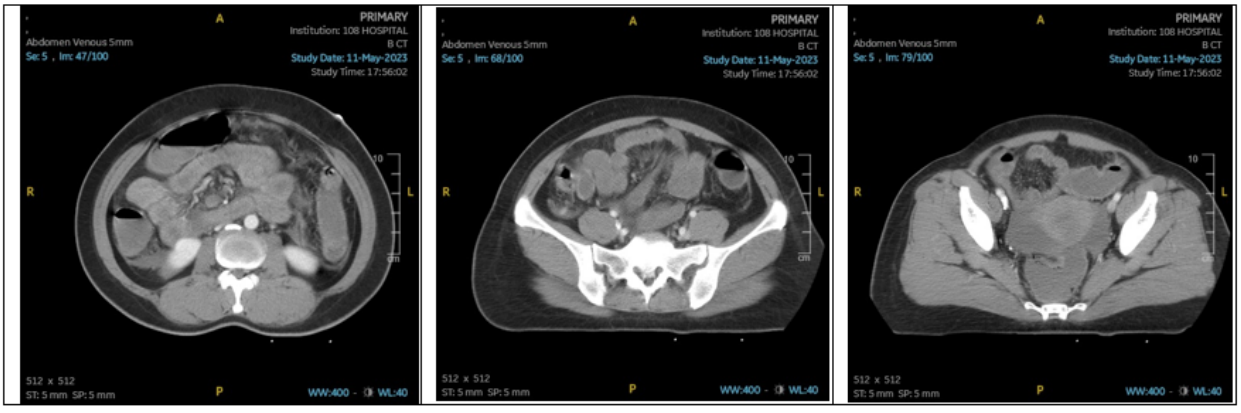

Figure 1: Abdominal computed tomography scan with contrast of patient shows moderate abdominal ascites, thickening of the bowel wall, and fluid-filled bowel loops in the small intestine with no pathological findings in the stomach, appendix, or colon, and no hepatosplenomegaly.

able, hemolysis must be halted as soon as possible using an intravenous high-dose corticosteroid to prevent further deterioration. We were unable to detect any improvement in hemolysis despite using 40 mg of dexamethasone, which was approximately three times higher than the dose that was advised for the 60-kg patient (0.8 to 1.6 mg/kg per day of methylprednisolone). This could be explained by a delayed or underdiagnosis, and in this case, the coexistence of WAIHA and DIC had a synergistic negative impact on the patient's prognosis.

4. Conclusion

Approach to the hemolysis as an emergency perspective, especially in a severe scenario, needs to be appropriated with the optimal algorithm from the beginning to avoid diagnostic bias. AIHA is a rare hemolysis disorder in sepsis and the exact relationship between these conditions is not known. This

case highlights the autoimmune hemolytic anemia in septic shock from the clinical manifestation to the laboratory evaluation. Emergency physicians should be aware of the symptoms and risk factors of warm autoimmune hemolytic anemia to enhance patient outcomes and ensure appropriate treatment and pathophysiology.

5. Declarations

5.1. Acknowledgments

None.

5.2. Ethics approval

The study was approved by 108 Military Center Hospital ethics committee in biomedical research.

5.3. Informed consent

Written informed consent was obtained for publication of this case report.

5.4. Author contribution statement

All authors listed have significantly contributed to the investigation, development, and writing of this article.
• Data curation: Nhi Vo Thuy Tran, Giang Le Duc.
• Formal analysis: Nhi Vo Thuy Tran, Giang Le Duc.
• Supervision: Duong Le Xuan.
• Writing – original draft: Nhi Vo Thuy Tran.
• Writing – review & editing: Duong Le Xuan, Hoa Do Thanh.
• All authors read and approved the final version.

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5.6. Data availability statement

Data will be made available on request.

5.7. Declaration of competing interest

The authors declare no conflict of interest.

5.8. Using artificial intelligence chatbots

None.

References

1. Barcellini W, Fattizzo B. How I treat warm autoimmune hemolytic anemia. Blood. 2021;137(10):1283-94.
2. Hill A, Hill QA. Autoimmune hemolytic anemia. Hematology Am Soc Hematol Educ Program. 2018;2018(1):382-9.
3. Effenberger-Neidnicht K, Hartmann M. Mechanisms of Hemolysis During Sepsis. Inflammation. 2018;41(5):1569-81.
4. Edwards Z, DeMeo S. Sepsis-induced Autoimmune Hemolytic Anemia: A Case Report. Clin Pract Cases Emerg Med. 2020;4(4):668-70.
5. Robertson JJ, Brem E, Koyfman A. The Acute Hemolytic Anemias: The Importance of Emergency Diagnosis and Management. J Emerg Med. 2017;53(2):202-11.
6. Wada H, Matsumoto T, Suzuki K, Imai H, Katayama N, Iba T, et al. Differences and similarities between disseminated intravascular coagulation and thrombotic microangiopathy. Thromb J. 2018;16:14.
7. Spring J, Munshi L. Hematology Emergencies in Critically Ill Adults: Benign Hematology. Chest. 2022;161(5):1285-96.