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INTERMEDIATE

CASE REPORT: CLINICAL CASE

Acute ST-Segment Elevation Myocardial Infarction as Initial Presentation of Atypical Hemolytic-Uremic Syndrome

Edward Chau, MD, MS,[a] Shiqian Li, MD,[b] Peter Z. Xu, MD,[a] Grace X. Li, MD,[c] Wesley Ghasem, MD,[a] Ilene C. Weitz, MD,[c] Brittney K. DeClerck, MD,[d] Eugene C. DePasquale, MD,[a] Bassam Yaghmour, MD[b]

ABSTRACT

A young woman presented with an acute ST-segment elevation myocardial infarction. Her clinical course was complicated by cardiogenic shock and acute renal failure. Work-up revealed thrombocytopenia and hemolytic anemia. A diagnosis of atypical hemolytic-uremic syndrome was made on the basis of clinical and pathological findings. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2021;3:561–5) © 2021 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 32-year-old woman with anxiety and obesity presented with complaints of shortness of breath, nausea, vomiting, and diarrhea for 1 day. The initial work-up revealed leukocytosis (white blood cell count, 20.62 $\times 10^3/\mu l$), elevated hemoglobin (17.6 g/dl), a normal platelet count (224 $10^3/\mu l$), and acute kidney injury (creatinine, 1.68 mg/dl). Her chest radiograph showed poor lung volumes but no opacities or pleural effusions. She was hypoxic on 4 l/min of oxygen while saturating 91%. Her troponin I level was initially 0.956 ng/ml and increased in 12 h to 36.1 ng/ml. A urine toxicology screen was negative for any substances, including cocaine and methamphetamines. The electrocardiogram revealed 2 to 3 mm of ST-segment elevation in leads II, III, aVF, and V_4 to V_6, concerning for ST-segment elevation myocardial infarction (STEMI) (**Figure 1**). She was started on heparin and taken to the catheterization laboratory, where an acute large thrombus extending the length of the proximal left anterior descending coronary artery was found (Videos 1 to 4). The rest of her coronary arteries had no angiographic evidence of coronary artery disease. Her catheterization laboratory course was complicated by an episode of ventricular tachycardia requiring amiodarone, as well as

LEARNING OBJECTIVES

- To recognize the differential diagnosis of acute STEMI in a young adult without traditional cardiac risk factors.
- To understand how aHUS is diagnosed and why early initiation of treatment can significantly improve end-organ dysfunction.
- To highlight the cardiac and other extrarenal manifestations of aHUS.

From the [a]Department of Cardiovascular Disease, University of Southern California, Los Angeles, California, USA; [b]Department of Pulmonary and Critical Care Medicine, University of Southern California, Los Angeles, California, USA; [c]Department of Hematology, University of Southern California, Los Angeles, California, USA; and the [d]Department of Dermatology, University of Southern California, Los Angeles, California, USA.

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ABBREVIATIONS AND ACRONYMS

ADAMTS13 = ADAM metallopeptidase with thrombospondin type 1 motif 13

aHUS = atypical hemolytic uremic syndrome

COVID-19 = coronavirus disease-2019

CRRT = continuous renal replacement therapy

HIT = heparin-induced thrombocytopenia

LV = left ventricular

STEMI = ST-segment elevation myocardial infarction

hypoxemia necessitating intubation. An intraoperative echocardiogram revealed an ejection fraction of 15%. A temporary transvenous pacemaker was placed for complete heart block. Left ventriculogram showed a left ventricular (LV) end-diastolic pressure of 40 mm Hg during therapy with multiple vasopressor agents; therefore, an Impella device (Abiomed, Danvers, Massachusetts) was placed for post-myocardial infarction cardiogenic shock support. After unsuccessful thrombectomy given the significant thrombus burden, the decision was made to place 1 covered stent with the goal of trapping the thrombus and preventing further embolization. The patient was eventually weaned from the vasopressor agents, and Impella support was discontinued; however, her creatinine worsened, with oliguria requiring continuous renal replacement therapy (CRRT). She tested negative for coronavirus disease-2019 (COVID-19) twice. She was noted to have worsening thrombocytopenia and several ecchymotic patches distributed over her arms and upper trunk. She was subsequently transferred to our tertiary care facility for heart transplant evaluation.

PAST MEDICAL HISTORY

Her past medical history included obesity and anxiety. She had no personal or family history of thrombosis and had never been pregnant. Home medications included desvenlafaxine and sertraline. She was not a smoker and did not use any illicit drugs.

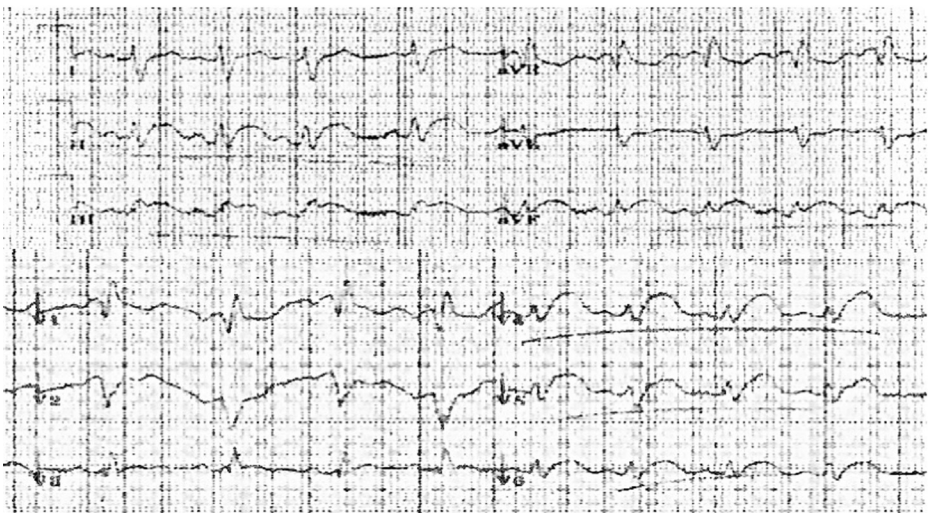
DIFFERENTIAL DIAGNOSIS

Atherosclerotic plaque rupture as a cause of acute STEMI in young adults is not common except in patients with genetically predisposed conditions such as familial hyperlipidemias or a long-standing chronic underlying inflammatory state, such as chronic human immunodeficiency virus infection with concomitant antiretroviral treatment. Non-atherosclerotic causes of STEMI include coronary vasospasm, coronary dissection or aneurysm, and coronary embolism. Considerations should include hypercoagulable states, including antiphospholipid syndrome and severe acute respiratory syndrome coronavirus 2 infection.

INVESTIGATIONS

The patient arrived afebrile with sinus tachycardia at a heart rate of 107 beats/min while being ventilated with a fraction of inspired oxygen of 60%. She was noted to be obese and sedated, and she had crackles in the lung bases with 2+ dependent edema in the arms and lower extremities. The initial complete blood count at our institution showed the following: white blood count, 21.37 $10^3/\mu l$; hemoglobin, 7.3 g/dl; and platelet count, 120 fl (Table 1). The platelets continued to downtrend to a nadir of 106 fl without

FIGURE 1 ST-Segment Elevation Myocardial Infarction Electrocardiogram



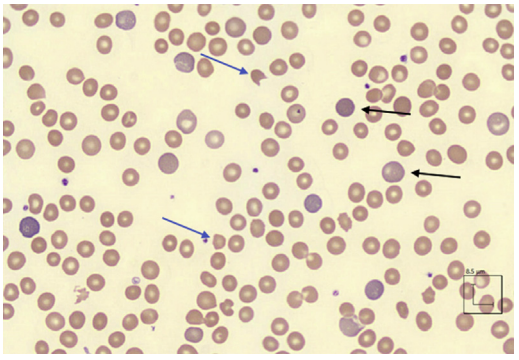
Electrocardiogram showing right bundle branch block and ST-segment elevation in leads II, III, aVF, and V_3 to V_6. The quality is poor because it is a scanned copy from an outside hospital.

TABLE 1 Pertinent Laboratory Evaluation

	Measured	Normal Values
CBC (10^3/μl), initial	21.37	4.5–11.0
Hgb (g/dl), initial	7.3	12.1–15.1 (female)
PLT (fl), initial	120,000	150,000–450,000
Total bilirubin (mg/dl)	1.2	0.1–1.2
Haptoglobin (mg/dl)	<10	41–165
Peripheral smear	Fragmented RBCs	No fragmented RBCs
CRP (mg/l)	41.0	<10
HS-CRP (mg/l)	9.0	<4.9
Ferritin (ng/ml)	221	10–120
C3 (mg/dl)	118	90–180
C4 (mg/dl)	14.4	10–40
HIT antibody screen	Positive	Negative
Serotonin release assay	Negative	Negative
Cardiolipin Ab	Negative	Negative
β_2-glycoprotein Ab	Negative	Negative
ADAMTS13 activity	Normal	Normal

Ab = antibody; ADAMTS13 = ADAM metallopeptidase with thrombospondin type 1 motif 13; HIT = heparin-induced thrombocytopenia; CBC = complete blood count; CRP = C-reactive protein; Hgb = hemoglobin; HS-CRP = high-sensitivity C-reactive protein; PLT = platelet count; RBC = red blood cell.

FIGURE 2 Peripheral Blood Smear



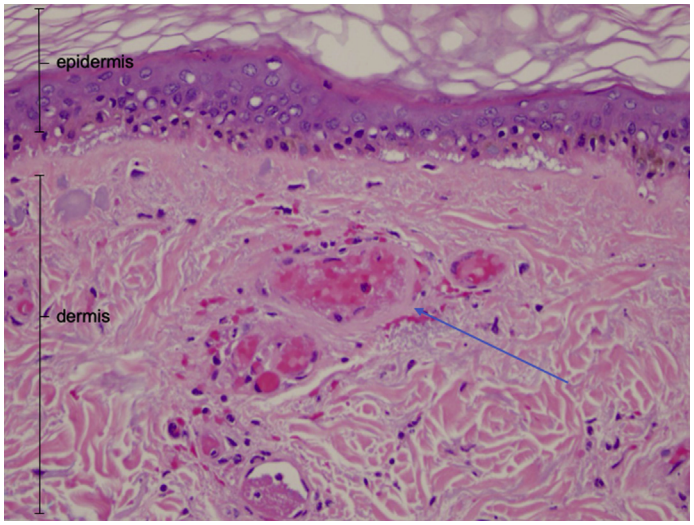
Peripheral blood smear demonstrating schistocytes **(blue arrows)** and reticulocytosis **(black arrows, larger round blue cells).**

concurrent Impella use. Given concern for heparin-induced thrombocytopenia (HIT) with a 4T score of 6 (64% probability), she was switched from heparin to argatroban. Results of an HIT antibody screen were positive but, results of a serotonin releasing assay confirmatory testing were negative. Other relevant laboratory findings include the following (Table 1): D-dimer, 5,205 ng/ml (normal high,<249 ng/ml); C-reactive protein, 41.0 mg/l (normal high, <4.9 mg/l); high-sensitivity C-reactive protein, 9.0 mg/l (normal high, <4.9 mg/l); ferritin, 221 ng/ml (normal high,<204 ng/ml); haptoglobin, <10 mg/dl; and total bilirubin, 1.2 mg/dl. There was still concern for COVID-19, but the result of the third test, performed using mini-bronchoalveolar lavage, was negative. A peripheral blood smear showed significantly increased fragmented red blood cells and reticulocytosis (Figure 2). Thrombotic microangiopathy, such as thrombotic thrombocytopenic purpura and atypical hemolytic-uremic syndrome (aHUS), was suspected because of the hemolytic anemia, thrombocytopenia, and end-organ dysfunction. Further work-up showed a normal C3 (118 mg/dl; normal, 90 to 180 mg/dl) and normal C4 (14.4 mg/dl; normal, 10 to 40 mg/dl). Test results for cardiolipin and β_2-glycoprotein antibodies were negative. ADAM metallopeptidase with thrombospondin type 1 motif 13 (ADAMTS13) activity was 110 (normal). An atypical targetoid, mottled-appearing 2 × 2 cm patch was noticed on her left forearm. A skin biopsy was performed and showed microthrombi within the small vessels in the papillary dermis (Figure 3). There was associated reactive inflammation but no evidence of vasculitis. Results of special stains for microorganisms (periodic acid-Schiff diastase stain, Grocott methenamine silver stain, and Gram stain) were negative.

MANAGEMENT

Review of the outside hospital angiogram did not reveal any intrinsic or structural coronary abnormality. A repeat echocardiogram obtained while the patient was intubated showed grossly normal biventricular systolic function. The patient was continued on CRRT because of anuria; however, her dialysis catheter and CRRT machine clotted 3 times, suggesting ongoing coagulopathy. The microangiopathic hemolytic anemia, thrombocytopenia, and acute renal damage were consistent with a diagnosis of aHUS in a patient without a history suggestive of an infectious or other thrombotic microangiopathic cause. Eculizumab, a recombinant humanized monoclonal antibody against the complement protein C5, was initiated. A few days later, her platelets normalized, and there were no further clotting issues with dialysis. She was eventually extubated and found to be neurologically intact except for persistent right upper extremity weakness. Magnetic resonance imaging of the brain demonstrated multifocal punctate acute to early subacute infarcts involving the periventricular and subcortical white matter consistent with a possible embolic event but not likely contributing to the upper extremity weakness. Magnetic resonance imaging of the right

FIGURE 3 Dermatopathologic Hematoxylin and Eosin Stain of Left Arm Skin Biopsy



A microthrombotic vasculopathic process with associated inflammation. The epidermis is unremarkable. Within the dermis, there is evidence of edema with occlusion of the superficial and mid-dermal vessels by proteinaceous debris, erythrocytes, and some neutrophils **(blue arrow).** The dermis also shows a variable, mostly perivascular lymphohistiocytic infiltrate with some neutrophils and extravasated erythrocytes.

brachial plexus revealed mild brachial plexitis, and the patient was started on a course of steroids.

DISCUSSION

We report a case of a young woman who presented with STEMI caused by thrombotic microangiopathy that was complicated by cardiogenic shock. Her initial condition was severe enough to warrant transfer to a tertiary care center for advanced heart failure therapies, including consideration of heart transplant evaluation, and to help elucidate the origin of her STEMI. She later received a diagnosis of aHUS.

Given the acuity of her respiratory symptoms and development of thrombosis, there was high clinical suspicion for COVID-19. However, test results were negative on 3 separate occasions, including once from specimen obtained via mini-bronchoalveolar lavage. Further laboratory investigation revealed hemolytic anemia, thrombocytopenia, and renal failure. The differential diagnosis was initially focused on the Impella device as the cause of hemolysis and thrombocytopenia, with cardiogenic shock contributing to renal failure. HIT was also considered early on. But after switching the patient to argatroban from heparin and removing the Impella device, thrombocytopenia persisted. A peripheral blood smear revealed schistocytes, suggesting a microangiopathic process. Thrombotic thrombocytopenia purpura was ruled out with a normal ADAMTS13 activity level. Antiphospholipid syndrome was also considered because the entity can present with stroke and myocardial infarction in young women, but it was also ruled out with normal C3 and C4 levels and negative cardiolipin and β2-glycoprotein antibodies. A skin biopsy demonstrated a microthrombotic process. She received a diagnosis of aHUS and started clinically recovering after initiation of empirical therapy with eculizumab, thus further supporting the diagnosis.

The origin of the massive thrombus in the left anterior descending coronary artery is likely secondary to microcirculation thrombosis and not LV thromboembolism. In the presence of LV thrombus, Impella implantation is not recommended, and the operators did not identify any thrombus before implantation of the device. To help further elucidate the cause of coronary thrombus in future cases, operators can use intracoronary optical coherence tomography imaging to assess the morphological features of the lesion and the architecture of the native vessel (1). Although LV thromboembolism can cause strokes, the patient had only a mild peripheral neurological deficit. Moreover, aHUS thrombotic microangiopathy commonly manifests as punctate ischemic lesions in the brain (2).

Hemolytic uremic syndrome (HUS) is a rare disease process characterized by hemolytic anemia, thrombocytopenia, and renal failure (3). Most cases are associated with Shiga toxin-producing *Escherichia coli* infection, but approximately 10% are classified as atypical because they are not caused by Shiga toxin-producing bacteria (3,4). Most aHUS cases are the result of alternative complement pathway dysregulation secondary to genetic or sporadically acquired abnormalities, such as the development of autoantibodies. Levels of complement can be normal when measured in aHUS, however. Other cases occur idiopathically. As a result of endothelial damage and complement activation, fibrin or platelet thrombi form, which cause vascular occlusion and induce tissue ischemia (4).

The glomerular arterioles of the kidneys are often affected, progressing to end-stage renal disease in nearly one-half of the patients affected with aHUS (3). Extrarenal involvement, including the brain, heart, lungs, gastrointestinal tract, and pancreas, can occur as well (3). Myocardial infarction, cardiomyopathy, and heart failure have been reported in 3% to 10% of patients with adult or pediatric complement-related aHUS (5,6).

Treatment of aHUS is with eculizumab, a monoclonal antibody against C5. Earlier intervention with

the drug was associated with greater improvements in estimated glomerular filtration rate, clinical outcomes, and health-related quality of life (7).

FOLLOW-UP

The patient continues to make a meaningful recovery. She is taking aspirin and ticagrelor for her stent. Another echocardiogram showed a recovered ejection fraction of 50% to 55%. With continued eculizumab treatments, her hemoglobin is improving, platelets have normalized, and lactate dehydrogenase is decreasing. After 2 weeks of being dialysis dependent, she is now making a significant amount of urine with medical management.

CONCLUSIONS

In a young adult, aHUS may manifest as a non-atherosclerotic cause of STEMI.

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ADDRESS FOR CORRESPONDENCE: Dr. Edward Chau, University of Southern California, Cardiovascular Medicine, 2020 Zonal Avenue, IRD 620, Los Angeles, California 90033, USA. E-mail: edchau89@gmail.com. Twitter: @drEdChau.

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KEY WORDS acute heart failure, autoimmune, cardiovascular disease, myocardial infarction

APPENDIX For supplemental videos, please see the online version of this article.