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An Atypical Cause Of Atypical Hemolytic Uremic Syndrome

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An atypical cause of atypical hemolytic uremic syndrome

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Abstract

Atypical hemolytic syndrome is an extremely rare, life threatening, progressive disease. Approximately one to two cases per million are seen annually in the US.[3,4] It is known to be associated with variety of conditions including infections, drugs, autoimmune conditions, vaccination, malignancy, organ transplantation, pregnancy, and metabolic conditions.[11,13] We hereby describe a case of atypical hemolytic uremic syndrome associated with CABG surgery. A 58 year old female presented to the emergency department (ED) with three days of worsening shortness of breath and cold like symptoms including nausea, vomiting and rhinorrhea. Twenty six days prior to presentation she had undergone Coronary Artery Bypass Graft (CABG) for three vessel disease. The physical examination was unremarkable. Labs showed anemia, acute renal injury and thrombocytopenia. A peripheral smear demonstrated over 10 per high-power field of schistocytes. She was presumptively diagnosed with Thrombotic Thrombocytopenic Purpura (TTP) and started on plasmapheresis. ADAMSTS-13 was normal and autoimmune workup was negative. After an extensive workup she was diagnosed with Atypical Hemolytic Uremic Syndrome (aHUS). To our knowledge this is the first case of aHUS associated with CABG. In fact, there has been only one other case of aHUS related to cardiac surgery which was found in a child who underwent Tetralogy of Fallot repair.[1]

Key Words

Atypical hemolytic uremic syndrome, CABG, TTP, Acute renal failure, Thrombocytopenia

Introduction

Atypical Hemolytic Uremic Syndrome is associated with a mortality of 25% in the acute phase and a morbidity of 50%.[2] The patient is often assumed to have TTP and is treated with immediate plasmapheresis. Eventually once the ADAMSTS-13 results return at normal values, TTP is ruled out and if results for Shiga toxin- producing bacteria or streptococci are also negative, the diagnosis of aHUS is made.[3] Both TTP and HUS usually have similar presentation as they both depict thrombotic microangiopathy with a known triad of thrombocytopenia, microangiopathic hemolytic anemia and end organ involvement (kidney, GI and neurological).TTP is associated with low ADAMSTS-13 levels and aHUS is associated with non-Shiga toxin etiologies. There has been only one other cardiac surgery reported to have led to atypical hemolytic uremic syndrome, which was a pediatric cardiac surgery to repair tetralogy of fallot.[1]

Case presentation

This is a 58-year-old female who is status post CABG less than one month prior to presentation. She presented to the ED complaining of shortness of breath that worsened over 2-3 days. She denied lower extremity edema, fever, chills or night sweats. She reported cold like symptoms of rhinorrhea associated with nausea and decreased appetite. Patient suffered an ST elevation myocardial infarction (STEMI) one month prior to this, was found to have multi-vessel CAD that required CABG for definitive revascularization. Patient denied new medications as she had been on Aspirin and Plavix for several years prior to her MI and CABG.

On Examination: Vitals- Temp-97.9, Pulse-80, RR-18, BP-179/96, Oxygen saturation-96% on room air. She was in minimal respiratory distress, had dry oral mucosa and no signs of fluid

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overload or edema. Laboratory studies showed her hemoglobin was down from 9.5g/dl to 7.7g/dl and platelets went down from 177,000μL to 83,000μL since her discharge. She was hyperkalemic with an elevated creatinine of 3.4mg/dl (up from 1.1mg/dl). Peripheral smear showed schistocytes over 10 /hpf.

A presumptive diagnosis of TTP was made and ADAMSTS-13 level was immediately drawn, and plasmapheresis urgently initiated. She failed to clinically improve with plasmapheresis. Once ADAMSTS-13 came back normal, an extensive investigation for Hemolytic Uremic Syndrome(HUS) was commenced and eventually ECOLI, Shigella, Streptococcus, Influenza and RSV infections were all ruled out. Total complement (CH50), C3 and C4 levels came back to be normal. Anti-Glomerular BM Ab, anti-CCP IgG, anti-cardiolipn IgG/IgM, anti-neutrophil cytoplasmic Ab, anti-nuclear Ab, IFA, anti-dsDNA Ab, anti-scleroderma70(scl-70) Ab, anti-centromere Ab were tested as a part of diagnostic workup for autoimmune conditions and were all negative. Genetic testing was not addressed, however this patient lacked key diagnostic clues to familial aHUS being infection or pregnancy.[14] Atypical Hemolytic Uremic Syndrome was diagnosed. She was then started on Eculizumab, and found to respond well to therapy.[8,10] Eventually renal biopsy revealed occlusive lesions of arterioles and small arteries with tissue micro infarcts suggestive of HUS in the given clinical setting.

The patient showed significant improvement in her symptoms. Finally she was discharged on Eculizumab after a hospital stay of thirty-four days. Her labs at discharge showed platelet count of 256,000, BUN- 52, Cr-4.8, peripheral smear showed no signs of hemolysis. She has been dialysis dependent since then and has been following up as an outpatient. On her last outpatient visit on September 14, 2016, twenty months since her discharge, she was still in remission and still taking Eculizumab, with her labs as follows: platelets 331,000, BUN-47, Cr- 5.3 with no signs of hemolysis on peripheral smear. The patient continues to need dialysis.

Discussion

Atypical Hemolytic Uremic syndrome is a rare entity that is known to have sudden onset. It is often defined as a triad of hemolytic anemia, thrombocytopenia and renal failure.[4] It predominantly affects renal arterioles and interlobar arteries by causing swelling and retraction of endothelial cells which leads to exposure of the basement membrane. This predisposes vessels to becoming occluded by red blood cells and platelet fibrin thrombi.[5,6] Often times TTP and aHUS can be treated the same way, plasmapheresis. When aHUS is resistant to plasmapheresis there is one other non-invasive option, which does not exist for TTP patients. In these cases Eculizumab, a humanized monoclonal antibody to C5, is a life altering tool.[7,8]

Although Plavix is known to cause TTP/HUS independent of ADAMSTS-13 levels, most cases occur within two weeks of initiation of the drug. Our patient had been on Plavix for years making Plavix induced TTP/HUS unlikely in this case.[9]

aHUS has been strongly associated with transplant surgeries and infections but never with Coronary Artery Bypass Grafting. TTP, on the other hand, has had a strong correlation with this procedure.[10,11] Our patient had extensive workup that ruled out infections, autoimmune states, and revealed no new medications; this, however, was less than one month post CABG. To our knowledge this is the first case of atypical hemolytic uremic syndrome associated with CABG surgery.

Conclusion

This case report suggests CABG may be associated with atypical hemolytic syndrome. Although this is the first reported case of aHUS associated with CABG surgery, awareness of the possible problem may result in increased reporting.

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