Case Report

Systemic Lupus Erythematosus presenting as Hemolytic Uremic Syndrome: a case report

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Abstract

Associating systemic lupus erythematosus (SLE), with an initial presentation of hemolytic uremic syndrome (HUS) is rare. We report a case of 21-year old Afghani female admitted to our hospital with an initial complaint of high grade fever and diffuse maculopapular rash and swelling of lower limbs. Diagnosis of atypical HUS was established according to the clinical triad of HUS without a veriotoxin-producing organism in her stool and the pathological finding compatible to thrombotic microangiopathy. In addition, her symptoms fulfilled the 1982 revised criteria for the classification of SLE. After pulse methylprednisolone, cyclophosphamide and plasmapheresis therapies, her laboratory findings and general condition improved. Unfortunately she was lost to follow up as she decided to return back to Afghanistan.

Introduction

Hemolytic uremic syndrome (HUS) is characterized by the triad of acute renal insufficiency, microangiopathic hemolytic anemia (MAHA) and thrombocytopenia. It is a rare cause of acute renal failure in adults. Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by production of autoantibodies and can cause alterations in components of the connective tissue of multiple organs. An association of HUS with SLE is rare.

In this report, we describe a 21-year-old female with SLE with an initial presentation of high grade fever, joint pains, photosensitivity, generalized muco-papular rash, nephrotic syndrome and non-diarrhea-associated HUS. The patient had the classic HUS triad and a compatible pathologic findings. She had no diarrhea and did not have a veriotoxin-producing organism in her stool.

Case Report

A previously healthy 21-years-old female from Afghanistan was admitted to the Aga Khan University Hospital with high grade fever, joint pains, swelling of legs and generalized maculo-papular rash for one week. In the past she had complaints of mouth ulcers and photosensitivity. There was no history of vomiting or diarrhea. She also complained of decreased urine output and coca cola-colored urine.

Figure 1. Peripheral blood smear revealed schistocytosis, fragmented RBCs and Helmet RBC.

Figure 2. Light microscopy, all glomeruli displaying diffuse proliferation. Arterioles also had fibrinoid necrosis

On examination she had diffuse maculo-papular rash. Her body temperature was 39.5°C, her blood pressure was 160/100 mmHg, she had a regular heart rate of 110 beats/min, respiratory rate was 22/min and body weight was 55 kg. The conjunctiva was pale. She had bilateral pedal edema. Systemic examination revealed bilateral pleural effusion. Anterior abdominal wall was edematous without rebound tenderness, muscle guarding or visceromegally. At admission she had oliguria (60 ml/24 hours).

Laboratory results revealed, hemoglobin 8.0 gm/dl (normal 11.1-14.5 gm/dl), MCV of 86.2 fL (normal 76-96 fL), WBC 4.5 10^9/L (normal 4.0-10 10^9/L), a platelet count of 84x10^9/L (normal 150-400x109/L),corrected reticulocyte of number fraction 0.012 (normal number fraction 0.005-0.015), serum LDH 1500 (normal 90-280 IU/L), a negative direct Coombs' test, blood urea nitrogen 48 mg/dl (normal 4-15), creatinine at 4.6 mg/dl (normal 0.6-1.3 mg/dl) and a normal coagulation profile. Urine microscopy revealed more than 20 RBC/HPF. Proteinuria was 3.5g/day. Peripheral blood smear revealed schistocytosis, fragmented RBCs, and helmet RBC (Figure 1). Her blood, urine, and stool cultures were all negative. Veriotoxin-producing organisms in the stool was negative. The initial clinical diagnosis of hemolytic uremic syndrome (HUS) was made based on the triad of hemolytic anemia, thrombocytopenia, and acute renal failure.

Figure 3. Light microscopic appearance of renal tissue showing thrombotic luminal occlusion.

Other immunology studies showed antinuclear antibodies +++ speckled, raised anti-dsDNA antibodies 32 IU (normal 0-6) and low C3 complement fraction of 0.325 GL (normal 0.738-1.80). Lupus anticoagulant and anticardiolipin antibodies IgG and IgM were negative. The diagnosis of SLE was therefore established. An ultra sound guided biopsy of the left kidney was performed. Histological examination showed that it contained 12 glomeruli. By light microscopy, all glomeruli displayed diffuse proliferation. Arterioles had fibrinoid necrosis (Figure 2)and thrombotic luminal occlusion (Figure 3). The interstitium was moderately inflamed with infiltration, including neutrophilic infiltration. Immunofluorescent microscopy showed all glomeruli stained with 3+IgG, 1+IgA, 2+IgM, 3+C3 and fibrinogen in diffuse pattern. She received methylprednisolone pulse therapy 1 g/day for 3 consecutive days. On 2nd day of pulse therapy she had an episode of brisk hemolysis and her hemoglobin dropped to 5 gm/dl and serum creatinine increased to 12 mg/dl. She subsequently received plasma pheresis therapy (total of 5 cycles) along with haemodialysis on alternate days. Oral cyclophosphamide (1.25 mg/kg of body weight) was started on day 4 along with oral steroids (1 mg/kg of body weight). Her renal func-

Her renal function and hematological parameters improved gradually as she became hemodialysis free and her hemoglobin remained stable. She was discharged 1 month later with a hemoglobin level of 12 gm/dl, a platelet count of 230 10^9/L, and serum creatinine at 3.2 mg/dl. She was readmitted after one week with cellulitis of right leg and was discharged after treatment with antibiotics. Unfortunately she was lost to follow-up as she decided to return to Afghanistan.

Discussion

HUS is characterized by the triad of acute renal insufficiency, MAHA and thrombocytopenia. In HUS, lesions are confined mainly to the kidney and thus renal failure is the dominant feature. In addition the makeup of the clot is of a mixed thrombus, which occludes arterioles and capillaries in microcirculation. HUS and thrombotic thrombocytopenic purpura (TTP) are mainly distinguished from each other by the location of the lesion and the defect of von Willebrand factor, or a deficiency of the von Willebrand factor-cleaving protease.[1] Unlike TTP patients with HUS show normal von Willebrand factors and cleaving protease activity. Clinically, ours was a case of HUS with prominent renal involvement but without any neurological symptoms, though the von Willebrand factor and cleaving protease were not checked.

Kwaan introduced the term thrombotic microangiopathic hemolytic anemia (TMHA) to comprise classic TTP and HUS, as well as their association with pregnancy, neoplasm, certain drugs, and connective tissue disorders such as systemic lupus erythematosus. Others have used TTP/HUS to describe the combined condition.[2]

In SLE, microangiopathic anemia, usually associated with diffuse vasculitis or malignant hypertension, may rarely be detected. According to Nesher et al. and other reports, the estimated incidence of thrombotic microangiopathy complicating SLE occurs in at least 2% to 3% of patients, presenting this manifestation during the course of SLE.[3]

Nesher et al. described the association of TTP/HUS with SLE, however, their cases lacked patients with definite HUS and SLE, as reviewed by Ogawa et al.[2-4] Ogawa et al. described a girl with SLE who also presented symptoms of HUS. The additional diagnosis of HUS was established by a peripheral blood smear finding and not by pathological findings.[4] Our patient presented with the diagnostic triad of acute renal insufficiency, MAHA (Coombs'-negative reaction) with fragmented erythrocytes, and thrombocytopenia. Her renal biopsy revealed the characteristic pathologic lesions of thrombotic angiopathy in HUS, in addition to the finding of lupus nephritis of diffuse proliferative glomerulonephritis. There were never any neurological symptoms. Though she did not have tests for von Willebrand factor or the von Willebrand factor-cleaving protease evaluation, HUS was diagnosed by both clinical and pathological means. She also met the 1982 revised criteria for the classification of SLE.[5] She presented with symptoms of HUS simultaneously with SLE and was thus diagnosed as having both.

Though SLE is a sporadic, noninfectious cause of HUS, it is not known whether a pathogenic relationship exists between these two diseases. Several hypotheses have been proposed to explain the mechanism of the association between TTP/HUS and SLE, including the presence of circulation antiplatelet antibodies, antiendothelial antibodies, or immune complexes.[6,7] The role of antiphospholipid antibodies is also speculative.[8] Anticardiolipin antibodies was negative in our patient. However, the precise mechanisms for these correlations are still to be defined.

It may be difficult to differentiate clinically between antiphospholipid syndrome and TMHA. Careful laboratory testing should greatly help in the differentiation. To diagnose HUS, a peripheral blood smear should reveal the presence of schistocytes (fragmented erythrocytes). In addition, Coombs' test results are usually negative.[3]

Prognosis of HUS in adults is poor. Tonshoff et al. demonstrated that 33% of HUS patients developed CRF/ESRD, or they died.[9] Fitzpatrick et al. suggested that plasmaphresis might improve the poor prognosis of atypical HUS in adults.[9] From reviews of the published cases of TTP/HUS in SLE by Nesher et al, plasmapheresis and/or plasma infusion appear to be beneficial adjuncts to therapy with steroids.[3]

Our patient's condition also improved after we initiated plasmapheresis treatment. We believe that the clinical improvement of our case with plasmapheresis appears to support the opinion of Fitzpatrick et al.[9]

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