Hepatic Necrosis: A Main Presentation of Systemic Lupus Erythematosus in a Previously Healthy Woman

Majid Avijgan[1], Mohsen Meidani[1], Mansour Salesi[2], Farshid Rezaei[1]

[1] MD, Department of Infectious and Tropical Diseases, Isfahan University of Medical Sciences, Isfahan, Iran.
[2] MD, Department of Rheumatology, Isfahan University of Medical Sciences, Isfahan, Iran.

Correspondence to:
Mohsen Meidani, M.D, Assistant Professor, Department of Infectious Diseases, Isfahan University of Medical Sciences,Isfahan, Iran.
Email: meidani@med.mui.ac.ir

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Case Report

ABSTRACT

Systemic lupus erythematosus (SLE) is a chronic inflammatory disease of unknown cause. In this study, we report a case of SLE that was presented with persistent vomiting and liver involvement. To our knowledge, this is the first description of a patient with hepatic necrosis as the initial presentation of SLE in a previously healthy woman without any significant past medical history. In the literature, we found few cases of SLE with liver necrosis. In addition, all the cases found had a past medical history of a missed abortion or other complications of the disease. Therefore, if a young woman presents hepatic necrosis with a background of a previously missed abortion, it is better to perform anti-nuclear antibody (ANA) and anticardiolipin antibody tests as a preventive method for early diagnosis and early treatment.

Keywords: Hepatitis, Systemic lupus erythematosus, Hepatic necrosis.

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INTRODUCTION

Lupus is an autoimmune disease characterized by acute and chronic inflammation of various tissues of the body. Any part of the gastrointestinal (GI) tract and the hepatobiliary system can be involved. Liver disease in systemic lupus erythematosus (SLE) has been reported in 8 to 23% of the patients and is usually of modest clinical relevance.[1] Subclinical liver involvement is frequent in SLE.[2] Review of the literature shows that none of the reported cases of hepatobiliary involvements secondary to lupus were as an initial presentation in the patients, i.e. the patients had suffered other complications of lupus before and had a past medical history of SLE treatment. We report a case of liver involvement due to lupus in a previously healthy woman complaining of severe persistent vomiting admitted in our hospital. It seems that it is the first report of such liver involvement as a main presentation of SLE in the literature.

CASE PRESENTATION

A 29-year-old non-pregnant female was admitted in our hospital suffering from fever, abdominal pain and vomiting. She was visited three times by her physician because of recurrent vaginitis. She reported history of menstrual irregularities and painful intermittent arthritis in her knees and wrists since three months ago. The swelling improved in a few days. Her mother and aunt had a history of abortions. In addition, eighteen days before admission, she and her husband had a history of diarrhea and fever with severe vomiting after a trip suggesting traveler's diarrhea. The problem was treated by conservative therapy. Two days later, her body temperature rose to 38 °C and she suffered vomiting and mild epigastric pain. After one week, she sought clinical attention with a complaint of severs fever, vomiting and icterus.

At this time, trifluoperazine, metronidazole and famotidine were prescribed. She was also

advised to check HBsAg but she refused. Two days later (on the third day of menstruation), with no improvements observed, she referred to another medical center. She complained of abdominal pain, severe dehydration, insomnia, loss of appetite and high grade fever. Urinary analysis showed mild pyuria (WBC count up to 5 per high power field) and a leukocytosis (WBC = 16000 /mm3; normal range = 4000-11000 /mm3). Abdominopelvic sonography revealed no abnormalities. She was injected two doses of ceftriaxone and was then discharged. Three days later, she went to another hospital again. In new laboratory tests, there were mild leukocytosis and normal hemoglobin and platelets, (WBC = 13000 /mm3, Hb = 12.3 g/dL, Plt = 175000 /mm3). Bilirubin level was in the normal range, whereas the hepatic enzymes and erythrocyte sedimentation rate were mildly elevated [SGOT (AST) = 79 IU/L (normal range: up to 40); SGPT (ALT) = 59 IU/L (normal range: up to 35); ESR = 127 mm/hr (normal rang: up to 30)]. With the suspicion of drug induced hepatitis, all previous drugs were discontinued. Three days later, she was admitted in our center with high grade fever and severe persistent vomiting. She was febrile and had dry oral mucosa and generalized abdominal tenderness, mostly on the right upper quadrant. Her pulse and respiratory rates were 120 and 42 per minute, respectively. Her oral body temperature was 39.5 °C. Her blood pressure was 120/80 mmHg. Joint examination was unrevealing. The results of laboratory tests on the 5th day after admission are presented in Table 1.

In abdominal sonography, a little amount of free fluid was reported in the periphery of spleen, gallbladder, right side of bladder, anterior part of right kidney, and slightly in the interloop space. The thickness of the gallbladder wall was also increased. Ceftriaxone was administrated for the patient. The next morning, she was slightly better (body temperature = 37.2 °C), but in the evening, the temperature increased again (T = 39 °C).

Therefore, imipenem and vancomycin were started. In repeated sonography, similar results were reported. On day 5, Hb level dropped dramatically (Hb = 6.9 g/dL) and the results of hepatitis B surface antigen (HBS Ag), hepatitis C virus antibody (HCV Ab), hepatitis A virus antibody (HAV Ab), hepatitis E virus antibody (HEV Ab), Human immunodeficiency virus antibody (HIV Ab), cytomegalovirus antibody (CMV Ab), Epstein–Barr virus antibody (EBV Ab) and Widal tests were all negative. A mild proteinuria was also observed. Smear stool examination and echocardiography were normal, as well. Regarding the fall of Hb and appearance of petechia and purpura on her left arm, pack cell and FFP were administrated. In repeated sonography, the echo texture of the liver was slightly heterogenic and coarse. In abdominopelvic spiral CT scan, heterogeneity in the right lobe of the liver without volume expansion was detected. Right sided pleural effusion, focal hepatitis and inflammatory process were in favor of amebic abscess formation (Figure 1).

Stool examination and serology were negative for ameba. Urine and blood cultures were negative, too. Rheumatologic test results are stated in Table 1.

Considering proteinuria, malar rash and polyserositis, thrombocytopenia, positive antinuclear antibody (ANA), SLE was our first diagnosis. Due to negative test results for ameba, antibiotics were discontinued and methyl prednisolone pulse therapy was started. One day later, abdominal pain was alleviated considerably and four days afterwards platelet count rose to 59000 and body temperature was reduced steadily. New laboratory tests revealed improvement. On day 5, after corticosteroid administration, the result of thoracocentesis was exudative [LDH = 647 IU/L, PH = 7.3, amylase = 68 IU/L, glucose = 261 mg/dL, protein = 4.3 mg/dL, WBC = 200/mm3 (PMN = 80%), and RBC = 10000/mm3]. Simultaneous blood sugar and protein were 290 mg/dL and 3.4 mg/dL, respectively. Smear of effusion was negative. On day 16 of hospitalization, radiologic consult was performed. Doppler sonography of hepatic vessels demonstrated microangiopathic lesions due to SLE. On day 18, intravenous immunoglobulin (IVIG) therapy (2 gr/kg/day) was prescribed for two days. ASA 80 mg daily, heparin 5000 IU bid, prednisolone 20 mg bid were started. On day 21, liver MRI with contrast reported hemorrhagic infraction of distal vessels of the right lobe of the liver (Figure 2).

On day 25, all lab data were roughly normal and on day 27, she was discharged with a good condition while prescribed with azathioprine, metformin, prednisolone, calcium carbonate, Fero-Folic and ASA tablets. At 45th day after discharge, she was in good condition with normal lab tests.

DISCUSSION

GI manifestations of SLE are protean. Any part of the GI tract and the hepatobiliary system can be involved. Up to two-third of SLE patients develop GI symptoms at some stage of their illness. The association between enhanced thrombosis and the lupus anticoagulant is discussed, and previously reported thrombotic

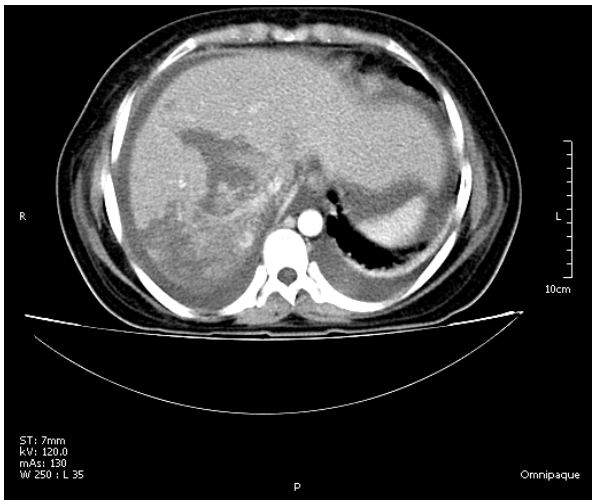

Figure 1. CT scan of liver with branching hypodense lesions due to hepatic necrosis.

Table 1. Rheumatologic and routine laboratory tests on the 5th day after admission

Laboratory tests		Rheumatologic Tests
WBC = 29400 /mm3	Bilirubin total = 2.4 mg/dL	ANA = 1/140 titer
Hb = 6.9 g/dL	Bilirubin direct = 0.9 mg/dL	Anti LKM = 1 U/ml (Normal ≤ 15)
Plt = 20000 /mm3	ALT = 755 IU/L	ANCA = Negative
Fibrinogen = 459 mg/dL	AST = 451 IU/L	Anti-ds-DNA = 129 (Normal ≤ 20)
Amylase = 103 IU/L	ALkp = 660 IU/L	C_3 = 65 mg/dL (Normal 55-170)
D-dimer = 3600 ng/mL	Albumin = 2.3 g/dL	C_4 = 12 mg/dL (Normal 10-55)
LDH = 4090 IU/L	PT = 20 second	CH_{50} = 60 units (Normal 60-220)
INR = 2.9	PTT = 65 second	Retic count = 0.8 %
		Coombs Direct = Negative
		Coombs Indirect = Negative

WBC: White Blood Cell; Hb: Hemoglobin; LDH: Lactate Dehydronase; ACT: Alanine AST: Aspartate Aminotransferase
ALKP: Alkalane Phosphatase; Anti LKM: Anti Liver-Kidney Microsomes; PT: Prothrombin Time PTT: Partial T
ANA: Antinuclear Antibody; ANCA: Antinuclear Cytoplasmic Antibody; INR: International Normalized Ratio

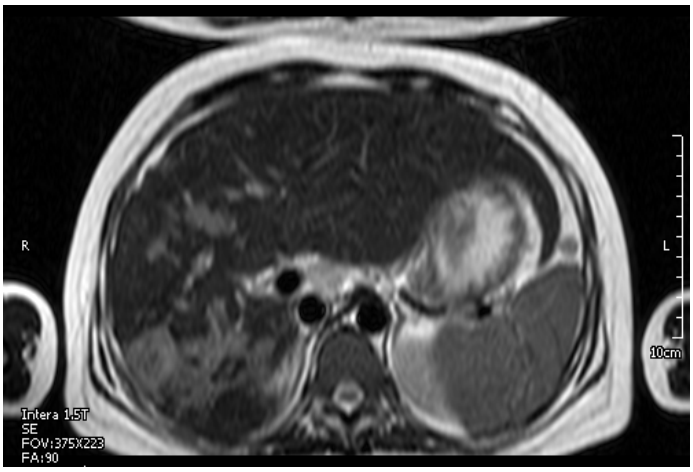

Figure 2. Liver MRI with hemorrhagic infraction of distal vessels of right lobe of the liver.

complications are described.[3] Clinical presentations of GI lupus are non-specific and can be difficult to differentiate from infective, thrombotic, therapy-related and non-SLE etiologies.[3] Appropriate endoscopic, biopsy and imaging procedures are essential for establishing the correct diagnosis. Acute abdominal pain in SLE patients can herald an intra-abdominal catastrophe and should be evaluated promptly. Surgical intervention should be instituted without delay if conservative management fails or when there is clinical or radiological suspicion of visceral perforation or intra-abdominal collections.[3] Hepatic infarction can be recognized preoperatively only with a high index of suspicion. Young reported a case of a thirty-one year-old postpartum patient, with SLE and antibodies to cardiolipin causing hepatic infarction due to hepatic vascular thrombosis. No previous record is found in the literature.[4] Hepatic infarction remains a rare and dramatic presentation of an acute abdomen in patients with SLE. Imaging studies such as abdominal CT scan may aid in making the diagnosis. Although it is not yet proved that lupus anticoagulant and anticardiolipin antibodies cause thromboses, investigating these antibodies can identify the patients more prone to thrombotic episodes. Occurrence of vascular thrombosis is said to be less likely in hemodialysis patients, but Kaplan reported a case of histologically documented hepatic infarction secondary to thrombosis in an end-stage renal disease patient on hemodialysis with SLE and a circulating lupus anticoagulant.[5] Mor reported the first description of liver infarction associated with the lupus anticoagulant in a 31-year-old patient with missed abortion, thrombocytopenia, and clinical, laboratory, and radiologic evidence of hepatic infarction. On evaluation, she was found to have the lupus anticoagulant.[6] Nakamura reported the first case of a patient with SLE who developed an occlusion of small hepatic veins attributable to the lupus anticoagulant and anticardiolipin antibody. Occlusion of the small hepatic veins was confirmed by hepatic venography, but the lumen of the large hepatic veins showed a smooth appearance. Since a high incidence of thromboembolic diseases in patients with the lupus anticoagulant or anticardiolipin antibody has been reported, the presence of this type of anticoagulant may provide an explanation for hypercoagulability and subsequent development of hepatic vein thrombosis in this patient. Nakamura proposes that a systematic search for hepatic vein occlusion should be made in patients with systemic lupus erythematosus who have developed inexplicable hepatomegaly, especially in those with positive tests for the lupus anticoagulant and/or anticardiolipin antibody.[7] In Caramaschi et al. study, evidence of liver disease was found in 23.2% of patients; in six cases liver abnormalities were not directly caused by SLE: in three subjects the abnormalities found were induced by drugs, in two patients by infection and in the last one by fatty liver. In the remaining 14 cases (16.2%), whose hepatic involvement was really due to SLE, a higher frequency of positivity for anti-ds-DNA antibodies than in the other patients was observed (92.8% and 51.3%, respectively in the two groups; $p < 0.05$).[1] In the literature, the cases are dominantly female. Similar to previous studies, in our case study anti-ds-DNA was high and anticardiolipin antibody was positive. Our case was not pregnant and had no history of previous abortion, unlike most of the past reports, but she had a positive history of recurrent abortion in her family.

We offer considering hepatic involvement due to SLE in approach to young female patients who are admitted with a complaint of severe persistent vomiting and family history of recurrent abortion or past medical history of abortion or other symptoms related to lupus. Antiphospholipid antibody may be responsible for recurrent abortion in young women, and SLE is the most connective tissue disease that has a relationship with this phenomenon. Therefore, it is better to perform ANA and anticardiolipin antibody tests as a preventive method for early diagnosis and early treatment in young women presenting hepatic necrosis with a background of previous missed abortion. We know that early diagnosis and early treatment can be life saving in SLE.

Conflict of interest statement: All authors declare that they have no conflict of interest.

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