

An SLE patient with persistent elevated conjugated bilirubin as the initial symptom: a case report

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Abstract

Systemic lupus erythematosus (SLE) is an autoimmune disease that affects multiple organs. While some SLE patients may experience varying degrees of liver function abnormalities, only a small portion of these cases have clinical significance, and the majority of patients typically exhibit low levels of serum bilirubin. However, in this article, we present a case of a middle-aged female patient with SLE who exhibited persistent skin jaundice as her initial symptom, offering a fresh perspective on diagnosing and treating patients who exhibit unexplained liver dysfunction and SLE combined with liver injury.

Keywords

Systemic lupus erythematosus; Hyperbilirubinemia; Cholestasis; Lupus hepatitis

Case report

Four months ago, a 45-year-old Chinese female patient had yellow skin and sclera. The initial examination revealed elevated levels of transaminase and total bilirubin. Based on the patient's clinical manifestations and relevant diagnostic test results, the diagnosis is acute hyperbilirubinemia and liver failure. During this period, the patient experienced recurrent episodes of the disease, and the treatment was mainly focused on providing supportive care to alleviate symptoms. Two week ago, the patient visited the other hospital. The MRI of the upper abdomen revealed signs of the compensatory phase of cirrhosis and acute cholecystitis. The results of abdominal color ultrasound showed an uneven liver echo and a strong echo in the liver and gallbladder wall. Liver function test results showed: ALT 182 U/L, AST 369 U/L, TBil 250 μ mol/L, DBil 185 μ mol/L, IBil 65 μ mol/L, TBA 473.7 μ mol/L. ANA antibody panel test showed anti-nuclear antibody was positive, anti-nuclear antibody titer was positive.

The patient visited the Department of Hepatology of our hospital on October 11, 2022. The physical examination showed that the skin, mucous membrane, and sclera of the whole body were stained yellow, the capillaries on the face were dilated, and the spider nevi and liver palms appeared on the chest and neck. The patient reported a long history of alcohol consumption in the past. The equivalent alcohol intake was about 200g/time. Liver function test results showed: ALT 181.70 U/L, AST 319.30 U/L, TBil 242.41 μ mol/L, DBil 197.62 μ mol/L, IBil 44.79 μ mol/L, TBA 544.60 μ mol/L, Hypersensitivity C-reactive protein (CRP) 11.130mg/L, IL-6 8.08 pg/ml, PCT 0.25 ng/ml, Immunoglobulin IgG 24.90 g/L, complement C3 0.65 g/L, and complement C4 0.148 g/L. Urinary routine test indicated a positive result for urinary bilirubin. Five items of hepatitis B: anti-HBe>4.20PEIU/ml, anti-HBc>5.50IU/ml. ANA antibody panel test (including anti-dsDNA) showed showed positive results for anti-nuclear antibody (ANA) at a titer of 1:1000, as well as positive results for anti-double-stranded DNA (anti-dsDNA) antibodies. Additionally, anti-ribosomal P-protein antibodies were suspected to be positive. The Coombs test was positive. There was no obvious abnormality in detecting highly sensitive B DNA, blood ammonia, and autoimmune liver. Chest and abdomen CT showed suspected liver cirrhosis, the uneven density of liver parenchyma, and

cholecystitis sign. Upper abdominal MRI showed abnormal signal in liver parenchyma and cholecystitis. MR enhancement scan of upper abdomen showed large abnormal enhancement focus in the liver, hepatic sinus obstruction syndrome? Signs of cholecystitis. DWI of upper abdomen: slightly high signal in the liver. MR cholangiography (MRCP) showed gallbladder effusion and cholecystitis are considered. Color Doppler ultrasound of liver and portal vein system showed intrahepatic echo changes and intrahepatic patch echo areas; there were many strong echo spots in the liver, and the portal vein blood flow was smooth. After admission, the patient was treated with symptomatic support such as liver protection, anti-jaundice, enzyme lowering, and intestinal microflora regulation. The patient's jaundice did not show significant improvement during hospitalization. The relevant immunologic tests were completed, and the results showed abnormalities. Considering the possibility of SLE, lupus liver, and biliary system impairment, the patient was transferred to our department for a liver function test, which revealed ALT 194.70U/L, AST 487.40U/L, TBIl 228.20 μ mol/L, DBil 159.90 μ mol/L, IBil 68.30 μ mol/L, and TBA 372.77 μ mol/L. The patient's immunity was inhibited by methylprednisolone sodium succinate (40mg/Qd) and mycophenolate mofetil (0.75g/d); Polyolefinylcholine (20ml/d) and glutathione (0.6 g/Qd) improve liver function and promote bile excretion; The patients were also treated with nutritional support. Following the aforementioned treatment for two weeks, a significant reduction in the patient's yellow skin and sclera was observed. The patient underwent a liver function test, which showed ALT 141.50U/L, AST 72.00U/L, TBIl 87.50 μ mol/L, DBil 58.60 μ mol/L, IBil 28.90 μ mol/L, TBA 86.43 μ mol/L. The patient presented with an acute onset of the disease and significant liver function impairment, along with a significant elevation in TBA levels. The presence of positive anti-dsDNA and anti-nuclear antibodies was observed, but the absence of AMA and other AIH-related indicators led to the exclusion of AIH. The patient's Coombs test was positive. According to the patient's medical history, clinical manifestations, and relevant examinations, it was determined that the primary cause of the persistent unconjugated bilirubin elevation was lupus hepatitis.

Discussion

SLE is a heterogeneous disease characterized by chronic autoimmune dysfunction of both the innate and adaptive immune systems^[16]. However, the commonly used classification criteria for SLE diseases do not include liver function impairment and biliary tract involvement. According to the epidemiological survey^[6], up to 60% of SLE patients may have abnormal liver function but often have no apparent clinical significance. Multiple studies have demonstrated a significant decrease in serum bilirubin levels among SLE/LN patients, which is closely related to disease activity^[26]. Atsushi Takahashi^[20] et al. investigated SLE patients with liver function impairment and concluded that drugs, SLE, and fatty liver are the primary causes of liver function impairment in SLE patients. Currently, most clinicians overlook abnormal liver function as the primary manifestation of SLE, resulting in many patients not receiving timely treatment. According to previous reports^[3], more than half of the 15 patients with abnormal liver function as their initial symptom were diagnosed several weeks or even years after treatment. They were more likely to be misdiagnosed as hepatitis or delayed SLE. Liver function impairment is often characterized by abnormal levels of liver enzymes and the changes in bilirubin and albumin levels. Jaundice is a recognizable "distress signal" that is visible to the naked eye, making it one of the common reasons that most patients seek medical attention.

For patients presenting with liver function impairment, it is important to consider liver diseases and hemolytic conditions, as well as autoimmune diseases. Ellen C Ebert et al. The ANA antibody panel test of this female patient also showed that anti-rRNP was suspiciously positive. As early as 1993, there were literature reports that^[10, 11], SLE patients complicated with chronic active hepatitis were also anti-rRNP positive. Therefore, the positive result of anti-rRNP antibody may indicate an association with SLE-related hepatitis and autoimmune hepatitis (AIH), in addition to its potential predictive value for neuropsychiatric symptoms in SLE patients. The presence of the anti-rRNP antibody suggests a possible association with hepatitis activity in immune-related diseases. In SLE patients who test positive for this antibody, it is important to consider whether the antibody is continuously expressed in the body and monitor changes in liver function levels.

Monocytes and macrophages destroy aging red blood cells in the circulation through hemolytic destruction

by heme oxygenase (HO) and cathepsin [8,9]. Later, uridine diphosphate glucuronic acid transferase 1A1 (UGT1A1) in the liver, combines free bilirubin with glucuronic acid to form binding bilirubin[7]. Various metabolic substances in the human body are in a dynamic state of balance. The stable levels of various metabolic substances in the human body are maintained through a dynamic balance between their production and the consumption of excess metabolites [1]. In this case, we reported a middle-aged female patient with a significant elevation of combined bilirubin. After further investigations, all abnormal indicators were found to be related to non-specific digestive system symptoms. Recently, N Ferdous[27] et al. also reported a patient with severe lupus hepatitis. Unlike the patient in Ferdous’s report, our patient only presented with apparent jaundice. Through physical examination, we observed typical signs of cirrhosis, such as spider nevus and liver palm, but did not detect any symptoms of discomfort such as ascites. Biochemical indicators improve liver function impairment, but it is not accumulated kidney. Before the first visit, the patient did not take any medications, and the disease has a relatively short duration, mainly characterized by elevated levels of conjugated bilirubin; there are specific variations in the disease background and laboratory findings for this patient compared to others.

As we reported, for the female patient with lupus hepatitis, the liver impairment was mainly attributed to SLE. Bile is produced by hepatocytes and is closely linked to the liver cell metastasis function[13]. However, when hepatocyte impairment occurs, it can cause bile production dysfunction. Bile cannot be transferred in time, leading to cholestasis, which increases the local oxidative stress of the liver and increases the level of heme oxygenase and bilirubin; when the function and expression of intrahepatic transport proteins are disturbed, toxic bile acids will accumulate in the cells, thus aggravating the impairment of hepatocytes and creating a vicious cycle [12]. Prolonged cholestasis can cause enlargement of the intrahepatic and extrahepatic bile ducts.

For SLE-related liver diseases, Gonz á lez Regueiro JA[21] and others have emphasized the importance of firstly determining whether the liver injury is associated with SLE. First, SLE-related lupus hepatitis should be considered. Second, other autoimmune diseases , such as AIH, PBC, PSC, AIH-PBC/PBS(table 1), and alternative liver diseases (mainly including SLE combined with non-immune diseases, such as viral hepatitis, non-alcoholic hepatitis, drug-induced hepatitis, liver injury, biliary injury, vascular injury, and hemolysis-related disorders) should also be considered.

Liver disease	Characteristics of clinical manifestations and biochemical indicators
AIH PBC[23] PBS Overlap syndrome (AIH-PBC/PBS)	Various clinical manifestations Characterized by hypergammaglobulinemia

Table. 1 Characteristic of non-SLE-related autoimmune liver diseases

PBC: Primary biliary cholangitis; PSC: Primary sclerosing cholangitis; AIH-PBC: Autoimmune hepatitis/primary biliary cirrhosis overlap syndrome; ANA: anti-nuclear antibody; anti-SMA: smooth muscle actin; anti-LKM-1: anti-liver kidney type 1; anti-LC-1: anti-liver cytosol type 1.

Conclusion

In summary, we report a case of SLE with lupus hepatitis and secondary biliary tract involvement. During the diagnosis and treatment of SLE, particularly in regions with a high prevalence of hepatitis B cirrhosis like China, it is important to exclude hepatitis B or alcohol-related liver injuries and also consider differential diagnosis from other autoimmune liver diseases. Liver biopsy and liver fibrosis examination are also necessary, especially for identifying unknown causes of liver dysfunction and cirrhosis. Cholestasis provides a more comprehensive diagnosis. Hormone therapy combined with immunosuppressive therapy is recommended for these patients. In this case, the combined treatment of methylprednisolone and mycophenolate has been implemented and has demonstrated favorable results.

Authorship List

Jun Liu: conceptualization.

Ying Huang: methodology.

Tingting Shen: validation.

Xingyi Li: Formal analysis, writing-original draft.

Fang Zhao: review and editing.

Xiaoxia Liu: formal analysis.

Shan Zhang: : investigation.

Pengjia Wu: data curation.

Na Li: visualization.

Long Li: project administration.

Jiashun Zeng: supervision .

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