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Brief report

Hepatitis in a patient with SLE: is it autoimmune hepatitis?

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Abstract

In a patient with systemic lupus erythematosus (SLE), we considered the diagnosis of autoimmune hepatitis (AIH) in view of raised serum aminotransferases, hypergammaglobulinaemia, antinuclear antibodies (titre 1:10240), seronegativity of markers for viral hepatitis and absence of recent hepatotoxic drug usage. The diagnosis of AIH was supported by using the scoring system, recently developed by the International Autoimmune Hepatitis Group and the excellent response to treatment with prednisone. Liver histology, however, showed no characteristic features of AIH. The relevance of liver histology and scoring for AIH in SLE with hepatic involvement is discussed.

Keywords: Systemic lupus erythematosus, hepatic involvement; Autoimmune hepatitis, scoring system; Liver biopsy

1. Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disorder affecting multiple organs. In SLE patients, increased serum values of liver enzymes are common [1–4]. High incidences of hepatic congestion (76%), fatty liver (73%), arteriitis (21%) and cholestasis (17%) have been reported in 53 autopsied patients with SLE, in whom drug-induced effects were not excluded [5]. Autoimmune hepatitis (AIH) has been considered to occur infrequently in SLE [5,6]. The International Autoimmune Hepatitis Group has recently presented a scoring system for the diagnosis of AIH [7]. Based on these defined diagnostic criteria, we considered the diagnosis of AIH in a patient with SLE, and discuss the relevance of the scoring system for AIH and liver histology in SLE with hepatic involvement.

2. Case report

A 20-year-old black female presented with a 3-week history of fatigue, malaise, myalgias, episodic fever and weight loss (6 kg). Three months before

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admission she started to complain of alopecia and arthralgias in both hips and knees. From a year before referral a positive Raynaud's phenomenon was noticed, and pigmented macules successively arose on the palms, soles and face. Three years before she had been adequately treated for pulmonary tuberculosis. Since then she had not taken any medication. Especially there was no history of recent hepatotoxic drug usage or parenteral exposure to blood products. There was no family history of SLE or liver disease.

On physical examination her temperature was 36.6°C increasing to 40.0°C. Pigmented macules and erythematous lesions with central atrophy and locally firmly adherent keratosis were prominent on areas of the skin exposed to cold (hands, feet and nose). Retinal vasculitis with cotton wools (cytoid bodies) were observed during fundoscopy. There was no suspicion of CMV retinitis. Further examination revealed no joint swelling, hepatomegaly or stigmata of chronic liver disease.

Laboratory data are shown in Table 1, revealing an autoimmune haemolytic anaemia, leucopenia, increased levels of liver enzymes, hypergammaglobulinaemia and hypocomplementaemia, all convalescent during treatment. Antinuclear antibodies (ANA) were prominently positive (titre = 1:10 240) with the presence of anti-Sm, anti-SS-A and anti-RNP antibodies. Anti-mitochondrial, smooth muscle, skin, granulocyte and thrombocyte antibodies were negative. Serum values of urea, creatinine, electrolytes, glucose and TSH were within normal limits. Urinalysis revealed no abnormalities. Cultures from blood and skin lesions were negative. There was no evidence of mycobacterium in sputum, gastric acid secrete or urine. Serological tests on hepatotropic viruses were negative, except for IgG and IgM anti-CMV, showing moderately elevated titres unchanged as compared with those found 6 months before. CMV IEA (= immediate early antigen) in the buffy coat and viral culture on CMV in urine were negative.

The chest X-ray showed remnants of the pulmonary tuberculosis. Ultrasound echography of the abdomen revealed no abnormalities, but histological findings in a liver biopsy specimen showed a mild hepatitis with lobular activity and degeneration of

Table 1
Laboratory data

	Before treatment	During treatment	Normal values
ESR	74	12	< 10 mm/h
Haemoglobin	6.5	7.9	7.3–9.3 mmol/l
Leucocyte count	2.3	5.9	4.0–10.0 × 10^9/l
Total bilirubin	16	8	4–14 μmol/l
Alkaline phosphatase	106	50	25–75 U/l
γ-Glutamyl transpeptidase	138	29	5–35 U/l
SGOT(= ASAT)	293	21	5–30 U/l
SGPT(= ALAT)	84	21	5–30 U/l
LDH	1 463	274	160–320 U/l
Haptoglobin	< 0.08	0.57	0.50–2.70 g/l
Dir Coombs IgG/compl.	positive		
CPK	257	34	15–110 U/l
Aldolase	5.3	2.8	1.0–3.0 U/l
Complement C3	0.37	0.79	0.80–1.60 g/l
Complement C4	< 0.08	0.08	0.15–0.40 g/l
Total complement	71	239	101–300 U/ml
IgG	24.8	19.7	8.0–18.0 g/l
IgA	4.0	3.7	0.9–4.5 g/l
IgM	1.2	1.0	0.6–2.8 g/l
Anti-cardiolipin IgG	81		0–31 U/l
Anti-cardiolipin IgM	8		0–12 U/l
ANA titre	1:10 240		
Anti-Sm/SS-A/RNP	positive		

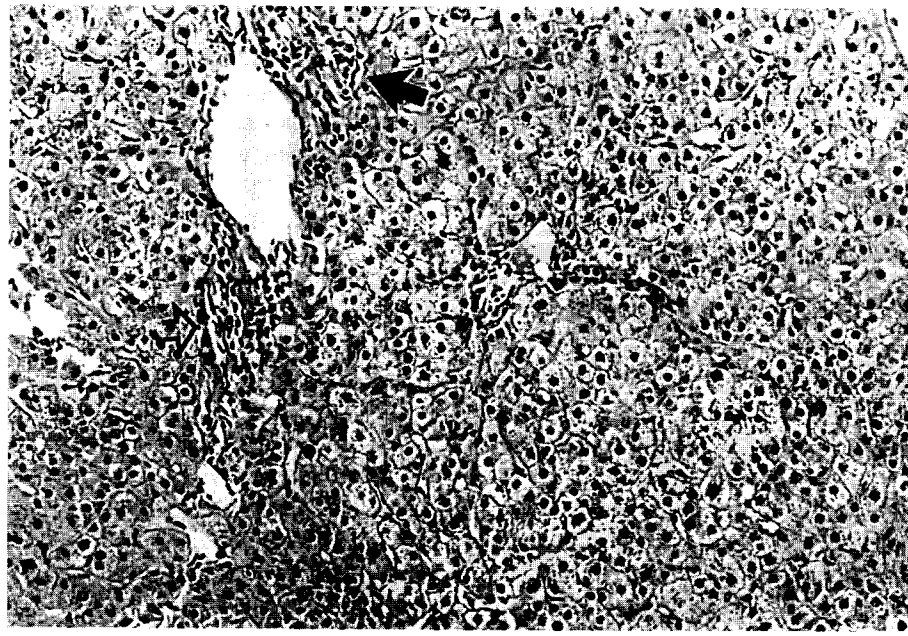

Fig. 1. Liver biopsy specimen shows only a limited portal infiltrate (open arrow) and isolated degeneration of hepatocytes (solid arrow) in a patient with SLE.

hepatocytes, without piecemeal necrosis or evident rosetting of liver cells (Fig. 1). Copper stains were negative. Frozen sections of a biopsy specimen from macroscopically normal skin showed depositions of IgG and complement along the basal membrane of the epidermis and that of skin appendages. ANA

Table 2
Diagnosis of autoimmune hepatitis in our patient according to scoring system [a]

Required parameters	
Female	+2
Ratio of serum alkaline phosphatase to aminotransferase activities (in IU/l) < 3.0	+2
Total serum globulin or gammaglobulin or IgG: times upper limit = 1.0–1.5	+1
Autoantibodies (titres ANA/SMA/LKM-1); adults > 1:80; children > 1:20	+3
Seronegative for markers hepatitis A, B and C	+3
No history of recent hepatotoxic drug usage or parenteral exposure to blood products	+1
Alcohol average consumption < 25 g/day	+2
Other autoimmune disease in patient	+1
Additional parameters	
Complete response to therapy	+2
Total aggregate score [b]	
Before treatment	15
After treatment	17

[a] Scoring system for autoimmune hepatitis recently defined by the International Autoimmune Hepatitis Group (7).
[b] Interpretation of scores before and after treatment:

Before	*After*	*Diagnosis*
> 15	> 17	definite autoimmune hepatitis
10–15	12–17	probable autoimmune hepatitis

were also present. The clinical picture combined with the haematological and immunological findings are consistent with a diagnosis of SLE according to the revised ACR criteria [8]. In SLE, raised serum aminotransferases (especially SGOT) may also fit in with the diagnosis of (dermato)myositis [9]. Indeed, in this patient a mild myositis was present, but the concurrent increase of SGPT, τ-glutamyl transpeptidase and alkaline phosphatase is clearly indicative for hepatitis.

According to the scoring system defined by the International Autoimmune Hepatitis Group [7] the diagnosis of AIH was probable in our patient (Table 2). She was treated with prednisone 30 mg and hydroxychloroquine 200 mg, both once daily. The clinical picture improved excellently, and the ESR, leucocyte counts, serum levels of liver enzymes, haptoglobin and complement normalized completely within 4 weeks. Review of the liver biopsy by an independent hepatologist and pathologist cast doubt on the diagnosis of AIH in view of the absence of characteristic abnormalities such as piecemeal necrosis and rosetting of liver cells.

3. Discussion

Hepatic involvement in SLE is common. Varying incidences of hepatic congestion, fatty liver, arteriitis and cholestasis are reported, but the relation to hepatotoxic drug usage and the presence of viral hepatitis is unknown [3–7]. From a prospective study it becomes clear that in about one third of patients with SLE and raised serum transaminases, usually mild (often lobular, as in this patient) hepatitis is not associated with drugs or alcohol as a cause, but reflects disease activity of SLE [10]. AIH and SLE-associated hepatitis have been defined as two different entities [6], although both have features of an autoimmune disorder, such as polyarthralgia, hypergammaglobulinaemia and presence of ANA, anti-Sm, anti-RNP and anti-cardiolipin antibodies [6,10,11]. This may lead to diagnostic confusion. Several histological and clinical features discriminate AIH from SLE [6,10,11]. Periportal piecemeal necrosis variably associated with lobular activity, rosetting of liver cells and dense lymphoid infiltrates are prominent in AIH, while in SLE the inflammation is usually lobular and occasionally (peri)portal with a paucity of lymphoid infiltrates [6,10,11]. Leucopenia, hemolytic anaemia and malar rash are clearly in favour of SLE [6]. Coexistence of SLE with primary biliary cirrhosis has been described [12]. Histological findings and the absence of antimitochondrial antibodies did not support this diagnosis in our patient.

We report a probable AIH according to the scoring system for this diagnosis (7) in a 20-year-old woman with active SLE [8]. The absence of piecemeal necrosis and rosetting of liver cells in the present case, however, points to SLE-associated hepatitis rather than to AIH. This case emphasizes that increased serum levels of liver enzymes in active SLE ask for liver histology to differentiate between SLE-associated hepatitis and AIH. Further refinement of the scoring system for AIH appears desirable. We think that the actual scoring system for AIH should be used with caution if histopathological findings are not available in patients with liver enzyme abnormalities in the context of SLE and other autoimmune diseases; the minimal histological requirements for the diagnosis of AIH should be present.

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