LUPUS OR LUPOID HEPATITIS WITH MESENTERIC VASCULITIS

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SUMMARY

A 15-yr-old girl with lupus presented with hepatitis and later a mesenteric vasculitis requiring bowel resection. The gastroenterological manifestations of lupus are reviewed with particular reference to hepatic involvement.

CASE

A 15-yr-old girl of mixed race, with a Caucasian father and a mother of Spanish, Greek and Indian origin, first presented 2 weeks following a sailing holiday, with anorexia, jaundice and right upper quadrant tenderness. Investigations revealed a hepatic picture with a bilirubin of 135 µmol/l (3-22), alanine transaminase (ALT) of 2013 IU/l (7-56) and alkaline phosphatase of 213 IU/l (38-126). Viral serology, including hepatitis A, B and C, was negative. Over the following 3 months, her symptoms were confined to her joints with synovitis of the fingers and wrists. A Schirmer’s test was moist. The inflammatory markers remained elevated; Ro and Sm antibodies (by radioimmunoassay) were positive at > 800 IU, with a homogeneous staining pattern. Anti-smooth muscle antibodies were elevated at >1:40. Anti-LKM and antimitochondrial antibodies were negative. The serum IgG was 63 g/l (8-17).

The systemic features persisted, and 2 months later her ALT was elevated. She was now anaemic, with a haemoglobin of 10.3 g/dl and an albumin of 26 g/l (35-49). DNA antibodies were elevated at 640 U/ml, anticardiolipin IgG at 60 U/ml and the ENA borderline (35-49). DNA antibodies were elevated at 640 U/ml, anticardiolipin IgG at 60 U/ml and the ENA borderline to La. The complement profile was normal. Ultrasound of the abdomen showed a bulky liver and spleen. A clinical diagnosis of autoimmune chronic active hepatitis (AICAH) was made and she was commenced on corticosteroids with good effect on well-being and liver biochemistry. A liver biopsy, however, showed minor fatty change without inflammatory infiltrate, and there was preservation of the architecture.

Over the succeeding 3 months, her symptoms were confined to her joints with synovitis of the fingers and wrists. A Schirmer’s test was moist. The inflammatory markers remained elevated; Ro and Sm antibodies became positive, and the titre of anticyclic IgG increased to 200 U/ml. She was commenced on hydroxychloroquine in addition to oral steroids.

Two months later, she was admitted febrile with an acute abdomen, having passed fresh blood per rectum. At laparotomy, ischaemic ascending colon was resected with areas of infarction and ulceration. Histology revealed a vasculitis affecting the small and medium-sized vessels (Fig. 1). She was given pulsed i.v. methylprednisolone (1 g) for three consecutive days, followed by i.v. cyclophosphamide (250 mg) at weekly intervals for 3 weeks. This was followed by a further six pulses of 250 mg cyclophosphamide at three weekly intervals. The ESR and CRP fell to the normal range after the fourth pulse of cyclophosphamide. Oral prednisolone was initially 40 mg, tailed down over 3 months to a maintenance of 10 mg. She remained well at 6 month follow-up.

DISCUSSION

It is not uncommon for the gastrointestinal tract to be involved, to varying degrees, in systemic lupus erythematosus (SLE). Anorexia and weight loss may occur in >50% of patients with active disease [1]. There may be dysmotility of the oesophagus leading to symptoms of reflux; of the stomach, leading to gastric outlet obstruction; or of the small intestine, resulting in pseudo-obstruction. Peritonitis may occur as part of the serositis of lupus. It may be generalized, sometimes giving rise to ascites, or focal leading to perihepatitis or perisplenitis [2]. Mesenteric ischaemia, with or without bowel perforation, is reportedly the commonest acute abdominal complication of SLE. Acute pancreatitis is also documented [3]. Gastrointestinal vasculitis occurs in ~2% of patients with SLE and has a 50% mortality [4]. It usually presents, as in this case, with abdominal pain and diarrhoea. The role of radiology and endoscopy is not well defined [4]. Polyarteritis-like lesions on visceral arteriography have been reported, but since the vasculitis affects mainly the small vessels, rather than the medium-sized mesenteric vessels, this technique is not usually clinically useful. Treatment options include surgical intervention, which becomes essential if infarction is suspected. Corticosteroids alone are unsatisfactory, but there are anecdotal reports of good response to i.v. cyclophosphamide.

The occurrence of acute or chronic hepatitis in
patients with SLE is rare [5]. Previous studies of liver abnormalities in SLE patients have usually implicated causes other than lupus, including viral, drug or fatty infiltration. Furthermore, chronic active hepatitis, chronic persistent hepatitis, granulomatous hepatitis and primary biliary cirrhosis have occasionally been documented. There is considerable debate about the relationship between AICAH and SLE. A prospective study by Miller et al. [6] of liver involvement in 260 patients with SLE showed that, despite the multi-system characteristics of lupus, there was almost total absence of liver involvement.

The commonest abnormality of liver biochemistry in SLE is an elevated serum bilirubin, usually due to Combs’ positive haemolysis. Patients with antiphospholipid antibodies may develop a Budd-Chiari syndrome due to hepatic vein thrombosis. Drug therapy, especially aspirin, but also azathioprine and other immunosuppressants, may be the cause of abnormal liver biochemistry in these patients.

An elevation in the serum transaminases is found in 20-30% of patients with SLE at some time during their disease. It is usually mild and transient, and related to disease activity, probably reflecting subclinical liver disease. Rothfield [7] noted that 30% of 365 lupus patients had abnormal liver function tests at the time of diagnosis, which resolved in the majority with corticosteroid therapy. Gibson and Myers [8] found that 19 (23%) of 81 patients with SLE had abnormal liver function tests for which no cause was apparent other than the lupus itself. Of seven patients who underwent liver biopsy, an inflammatory infiltrate of the portal areas was seen in five, fatty liver in one and chronic active hepatitis in one.

HEPATOLOGIST’S VIEW (MFM)

In discussing this case, a rheumatologist and a hepatologist may well arrive at the same point, but from different directions, partly for historical reasons. Most of the classical descriptions of autoimmune hepatitis are reports from the 1950s and 1960s, and such reports are weakened by the lack of knowledge of the viral causes of chronic hepatitis. The first reports were of young women with chronic liver disease associated with jaundice, acne, amenorrhoea, hepatosplenomegaly and hyperglobulinaemia [9]. Because these patients had positive LE cells, the term lupoid hepatitis arose [10]. In the 1960s and 1970s [11], autoimmune chronic active hepatitis was reported to be associated with multi-system autoimmune disease, such as Sjögren’s syndrome, renal tubular acidosis, pulmonary diffusion defects, haemolytic anaemia, arthropathy, peripheral neuropathy and ulcerative colitis. In the 1990s, the diagnosis of AICAH is still based on clinical, biochemical, immunological and histological findings, and the exclusion of identifiable
causes, such as hepatitis B, C and drugs. However, even within the sphere of hepatology, overlap between AICAH and primary biliary cirrhosis, and AICAH and primary sclerosing cholangitis, may occur.

Runyon et al. [12], in a retrospective study of 238 patients with SLE, found severe clinical liver disease occurring in many patients and that 4/33 patients with SLE had features of AICAH on liver biopsy. Other groups have applied the ARA criteria for lupus to patients with AICAH and found patients with features sufficient for a diagnosis of SLE [12].

The case described in this report seems to demonstrate an overlap syndrome in evolution. In the initial presentation, there was a hepaticitis illness and a subsequent autoimmune profile in keeping with AICAH. Five months after the onset of the illness, the patient became progressively unwell with vasculitis, although now the transaminases were improved. This is not usually the case where the liver is the main target of the autoimmune process. This is further supported by the relative normality of the liver biopsy.

Gough et al. [13] describe 34 cases of a minocycline-induced SLE and AICAH-like syndromes. A single known cause is seen here to initiate both processes in different patients, with some overlap. It is likely that we may be looking at a spectrum of disease.

RHEUMATOLOGIST'S VIEW (AB)

This case illustrates the unsatisfactory nature of the diagnosis SLE; this disease state is defined by clinical and pathological criteria, many of which can be present in primary Sjögren's syndrome, AICAH and systemic vasculitides. The Sm antibody is reputedly highly specific for SLE (if relatively insensitive, occurring in <30% of cases of the condition) [14]. Currently, a pragmatic approach (treat what needs to be treated), based around cyclophosphamide, is used in the management of systemic vasculitis, whatever the exact diagnostic label [15], and this case illustrates the efficacy of this approach. This patient, whose parentage includes Indian and Italian antecedents, had particularly aggressive vasculitis. Patients of Indian origin with SLE have, anecdotally, more severe disease. This case also illustrates the difficulties in drawing conclusions about the nature of dynamic liver disease from a single liver biopsy.

Klippel [16], in his study of 131 patients with SLE, found six patients with liver involvement. These six patients have anti-ribosomal P autoantibody. These may prove to be useful in detecting lupus hepatitis.

In conclusion, it is difficult to categorize patients with hepatitis who have clinical criteria for SLE. They may be labelled as 'lupoid' hepatitis. This could, however, lead to under-representation of the prevalence of significant liver disease in SLE and possibly inadequate treatment. It is proposed that AICAH and SLE be clinically regarded as part of a continuum. Genetic and HLA studies may be helpful in defining differences in aetiopathogenesis.

Our patient was unusual in presenting with hepatitis and later mesenteric vasculitis with bowel infarction. She had the serological markers of SLE/Sjögren's syndrome, and responded to immunosuppression with corticosteroid and pulsed i.v. cyclophosphamide.

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REFERENCES