Role Of Liver/Kidney Microsomal Antibody Type 1 With Type 2- Autoimmune Hepatitis

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J Fac Med Baghdad
2006; Vol. 48, No.2
Received March 2005
Accepted July 2005

Summary:

Background: *anti-LKM 1 typically occurs in the absence of SMA and ANA and is the serologic marker of type 2 AIH. The 50 KD antigen of LKM-1 autoantibodies was identified as cytochrome P450 2D6(CYP 2D6). The aim of the study is to know the prevalence and clinical relevance of anti-LKM1 autoantibody in AIH*

Methods: *Anti-liver kidney microsome type 1 (LKM-1) autoantibodies were studied by indirect immuno florescence assay (IIF) and confirmed by immunoblot in the serum of 73 Iraqi patients with autoimmune hepatitis (AIH) in comparison with 20 patients control (HBV infection) and 20 healthy individuals.*

Results: *Anti-LKM1autoantibodies were present in sera of sixteen patients (22%) with AIH and never in the sera of patients or healthy controls.*

Conclusion: *it was concluded the anti-LKM 1 autoantibodies characterize patients with sever form of the autoimmune disease, poor prognosis and rapid progression to cirrhosis.*

Introduction:

Autoimmuen hepatitis is a self-perpetuating inflammation of the liver that is characterized by hypergammaglobulinemia, presence of autoantibodies in serum, and histological features of periportal hepatitis (1,2). Its diagnosis depends on the detection of non-organ specific atuoantibodies in serum such as antinuclear antibodies (ANA), smooth muscle antibodies and autoantibodies to liver/kidney microsome (LKM)(1,4). These antibodies support the diagnosis of autoimmune hepatitis, however, they are not disease specific or pathogenic (3-5).

Anti-LKM1 has been shown to be associated with a second form of ANA-negative AIH (6,8). These finding have been supported by other scientist (4,12).

Patients and Methods:

This study was conducted on 73 (53 females, 20 males) autoimmune hepatitis patients (AIH) who met the International Autoimmune Hepatitis Group (IAHG) 1999 revised criteria (9) attending the teaching hospital for gastroenterology and liver disease in a period between November 2003 and July 2004, compared with 20 patients control (HBV infection) and 20 healthy individuals (age and sex matched). All groups were subjected to immunoserological detection of anti-LKM-1 autoantibodies.

Laboratory investigation:

Anti-LKM-1 was detected using the mosaic basic profile-2: rat liver, kidney, stomach substrate and positive result was associated with positive immunoflurescence staining of the third portion of proximal renal tubules and negative staining of the distal tubules. The hepatocytes are homogeneously stained. Euroline method (as a confirmatory test) The test kit contains test strips coated with parallel lines of antigens, which have been purified by affinity chromatography.

Organ specific antibodies: antibodies to thyroid microsome and anti-thyroglobulin were detected by ELISA technique whereas anti-parietal cell antibody was detected by IIF using mouse stomach section. All these kits supplied by (Euroimmune-Germany).

Results:

Results show that the majority of patients were female (12 of 16) yielding a female to male ratio of 7.5:1 with mean age 27.2 ± 9.44. The highest frequency was between 10-29 years, which comprised 59.75% of the patients (11 of 16) figure-1

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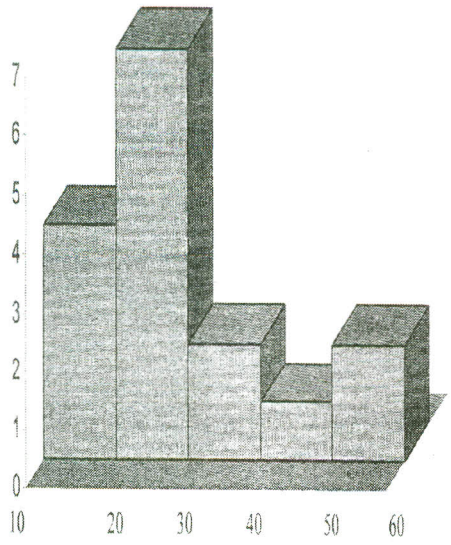

Figure (1): Bar chart showing the distribution of AIH-2 patients by age.

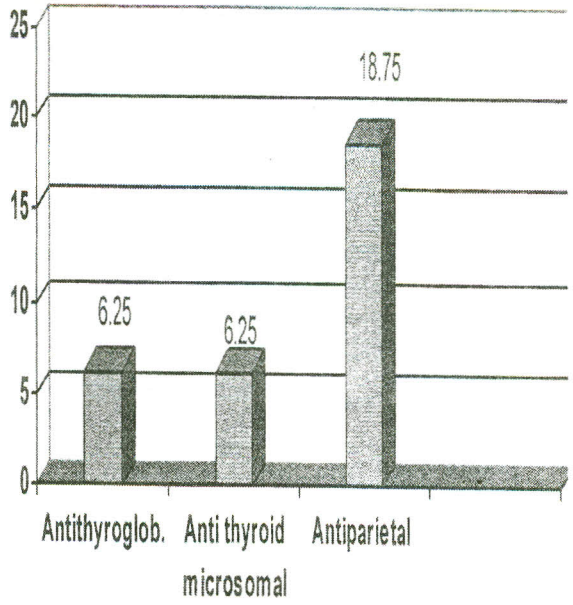

Figure 2: The distribution of organ specific autoantibodies (%) in AIH-2.

Immunologically sixteen patients (22%) out of seventy-three patients were positive for anti-LKM1 Abs and negative for other immunoserological marker of autoimmune hepatitis (ANA, SMA, AMA and SLA/LP Abs). The concomitant positivity of LKM-1 was observed only in AIH patient's sera, and never in the sera of patients or healthy control groups.

It was shown that in 7 patients (43.7%) a second or third disease was present. Totaling 9 associated diseases (Table 1). The majority of these diseases had an autoimmune etiology. The distribution of patients by organ specific autoantibodies is given in figure 2.

Table (1): The distribution of concurrent immune diseases in patients with anti-LKM1.

Disease	No	%
Vitiligo	2	12.5%
Insulin dependent diabetes (IDDM)	2	12.5%
Thyroid disorders	2	12.5%
Alopecia	1	6.25%
Nail dystrophy	1	6.25%
Celiac disease	1	6.25%
SLE	1	6.25%

Interestingly, the present work showed that one or several autoimmune diseases were found in first-degree relatives from 8 families, one or two members presented with an autoimmune disease: insulin-dependent diabetes (4 cases); autoimmune thyroid disease (2 cases); vitiligo (2 cases), psoriasis (1 case), and alopecia (1 case).

In ten patients (62.5%), the onset of the disease was insidious, the diagnosis was made at the stage of chronic hepatitis in 2 patients and the remaining 8 patients had cirrhosis at the time of initial presentation .At present all surviving patients had cirrhosis.

Discussion:

The observation in this study that the mean age of the disease was 27.2 ± 9.44, these finding was almost comparable to other abroad studies who observed that the mean age was 25 years (7, 10).

Regarding the sex differences, the present work showed the F: M ratio was 7.5:1 which is nearly comparable to that of abroad study (7) who reported 8:1.

It is generally accepted that, in patients with autoimmune hepatitis (AIH) the immunological markers, including anti-LKM1, are usually mutually exclusive (6,7,11).

Interestingly, our study revealed that anti-LKM1 Abs was not detected in patients control as well as healthy control, but was found in patients with AIH. These findings proved that anti-LKM1 characterize a further subgroup of AIH.The specificity of this Abs for the diagnosis of AIH makes them important for diagnostic purposes.

Obviously, the result in this work was in agreement with the previous studies (13,14), in which organ specific antibodies in patients with

anti-LKM1 exhibit 31.25% which include anti-thyroglobulinb Abs, anti thyroid microsomal Abs (6.25%) for each, and anti-partial cell Abs (18.75%).

One clue in diagnosing autoimmune diseases (AIH) may be the coexistence of other disease with immune or autoimmune feature, this fact was very clear in this study since, 62.5% of our patients had concurrent immunological disease most commonly IDDM, autoimmune thyroid disease and vitiligo. On the other hand, a probably genetic background suggested by autoimmune disorders found in first-degree relatives.

Our results were in agreement with many investigators (15,16) who collectively cited that, in hepatitis associated with anti-LKM1, the period of chronic hepatitis before onset of cirrhosis was short. This fact was true since 66.6% of patients with acute onset developed cirrhosis within 3 years.

The fore mentioned findings reinforce the belief that AIH-2 was a special entity of disease characterized by: female predominance, no history of contact with hepatitis patients and no blood transfusion, presence of anti-LKM1 autoantibodies and absence of ANA,SMA and SLA/LP Abs, frequent association with autoimmune disorders, a poor prognosis with an ultimate progression to cirrhosis and probably genetic background suggested autoimmune disorders found in first-degree relatives.

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