Antibody to Ribosome in Liver Diseases

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INTRODUCTION

The presence of antibodies reacting with constituents of various human and other mammalian organs has been demonstrated in sera from patients with liver diseases[1-5], but further studies into the nature of antigenic material in the extract of the organ are necessary.

We detected an antibody to constituents of ribosomes in sera from patients with liver diseases by the bentonite ribosomes flocculation test. The incidence of ribosome antibodies in patients with liver disease, its diagnostic significance and the nature of antigen and antibodies will be described in the present study.

MATERIALS AND METHODS

Sera of 132 patients with various liver diseases and 20 normal individuals were examined. The diagnoses were mainly made on the basis of liver biopsies. The histological criteria used were essentially those described by Ichida et al.[6] for chronic hepatitis.

Preparation of ribosomes : Differential centrifugation of 0.25 M sucrose extracts of rabbit liver was performed by a modification of the method of Littlefield et al.[7] as shown in Table 1. Spectrophotometric analysis of the suspension solution of the ribosomes showed a single absorption peak at 260 and a 260/280 ratio of 1.5.

Detection of antiribosome antibody : Bentonite ribosomes flocculation test described by Sturgill et al.[8] was used (Table 2).

Miscellaneous procedures : The complement fixation test was performed by the method as previously described[9]. Human liver homogenates were used as antigens for the detection of complement fixing antibodies.

The Hyland "RA-test" for rheumatoid factor and the Hyland "TA-test" for antibody to thyroglobulin were employed. Anti-nuclear factor was detected by the indirect immunofluorescence technique described by Weir et al.[1].

Table 1.

Preparation of Ribosomes

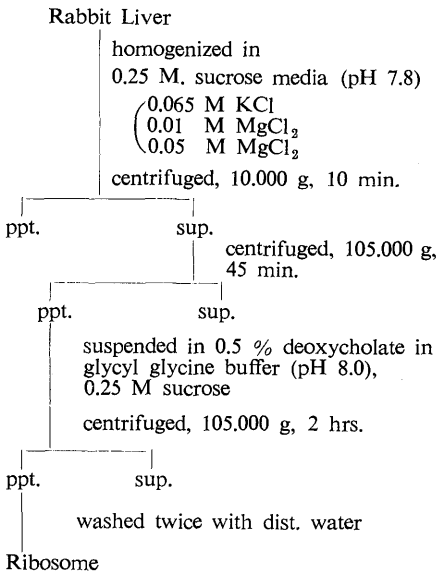
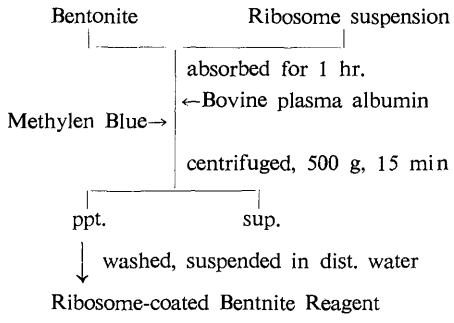
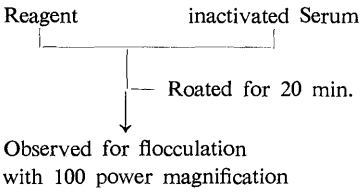


Table 2.

1) Coating Bentonite with Ribosome



2) Bentnite Ribosome Flocculation test



The serum immunoglobulin levels were measured by radical immunodiffusion method modified by Fahey et al.[10].

RESULTS

The result of the bentonite ribosomes flocculation tests in liver diseases is shown in Table 3. One of 38 patients with acute hepatitis had a positive bentonite test. Retrospectively the patient was considered to have chronic active hepatitis rather than acute hepatitis, for a liver biopsy revealed distortion of the lobular pattern by fibrosis and the heavy infiltration of lymphocytes. Seven of 41 patients with chronic hepatitis were found to have a positive bentonite test. Histological findings revealed chronic active hepatitis in 6 of these 7 patients. Three of them had long-standing jaundice and persistently high values of transaminase activity and high levels of gammaglobulin in sera for more than one year. The ribosome antibody was also detected in 3 of 39 patients with liver cirrhosis. Two of them had chronic active hepatitis which persisted for more than 2 years. One of the patients (F.M.) had a titer of 1,024 for rheumatoid factor, while the other patient (N.T.) had a marked reactivity in the complement fixation test. Sera from 24 patients with hepatoma, cholestasis or primary biliary cirrhosis and from 20 healthy

Table 3. Incidence of Antibody to Ribosomes in Liver Diseases

Clinical Diagnosis	No. of Cases	No. of Positive
Acute Hepatitis	35	1 (3 %)
Subacute Hepatitis	2	1 (50 %)
Chronic Hepatitis	41	7 (17 %)
Active	19	6 (32 %)
Inactive	22	1 (5 %)
Liver Cirrhosis	39	3 (8 %)
P B C	1	0
Liver Carcinoma	8	0
Obstructive Jaundice	7	0
Toxic Hepatitis	2	0
Normal	20	0

Table 4. Correlation between Antibody to Ribosomes and other Circulating Antibodies

Diagnosis	Name	Age	Sex	AR-T*	RF-T**	AICF	TA	ANF
Acute Hepatitis	Y. K.	39	♂	1 : 1	1 : 80	1 : 16	−	−
Subacute Hepatitis	I. K.	42	♂	1 : 6	1 : 160	N.D.	−	−
Chronic Hepatitis								
Active	H. K.	33	♂	1 : 6	1 : 160	−	+	−
	K. K.	23	♀	1 : 6	1 : 640	−	−	+
	H. T.	52	♂	1 : 6	1 : 40	−	−	−
	A. M.	40	♂	1 : 2	1 : 160	1 : 16	−	−
	K. K.	34	♂	1 : 1	1 : 320	1 : 256	−	+
	S. N.	23	♂	1 : 1	1 : 160	1 : 64	+	−
Inactive	T. S.	42	♀	1 : 1	1 : 20	−	−	−
Liver Cirrhosis	N. T.	56	♂	1 : 1	1 : 160	1 : 512	−	−
	M. T.	58	♂	1 : 1	1 : 80	−	−	−
	F. M.	48	♂	1 : 1	1 : 1024	−	+	−

* Anti-Ribosome titer ** Rheumatoid factor titer

individuals showed no reactivity with ribosomes coated bentonite.

As shown in Table 4, 11 patients who had a positive bentonite test had a higher incidence of serological abnormalities. All of the 11 patients had a rheumatoid factor, and 5 of these patients reacted to a crude saline extract of human liver homogenates. Sera from 2 patients contained an antibody to thyroglobulin, while sera from 2 other patients had an antinuclear factor. The highest antiribosome titer was observed in a patient (K.H.) in whom chronic hepatitis progressed to postnecrotic cirrhosis. The titer was at a 1 : 6 serum dilution.

In order to detect immunoglobulin which is particularly effective in the bentonite ribosomes flocculation test, serum immunoglobulin levels in liver diseases with the ribosome antibody were measured as shown in Fig. 1. No correlation was found between the levels of the 3 classes of immunoglobulin G, M and A and the antiribosomes titer.

The antigenecity of ribosome suspension solution was digested by either trypsin or ribonuclease. The effects of trypsin and RNase suggest that antigenic determinants are related to both protein and RNA.

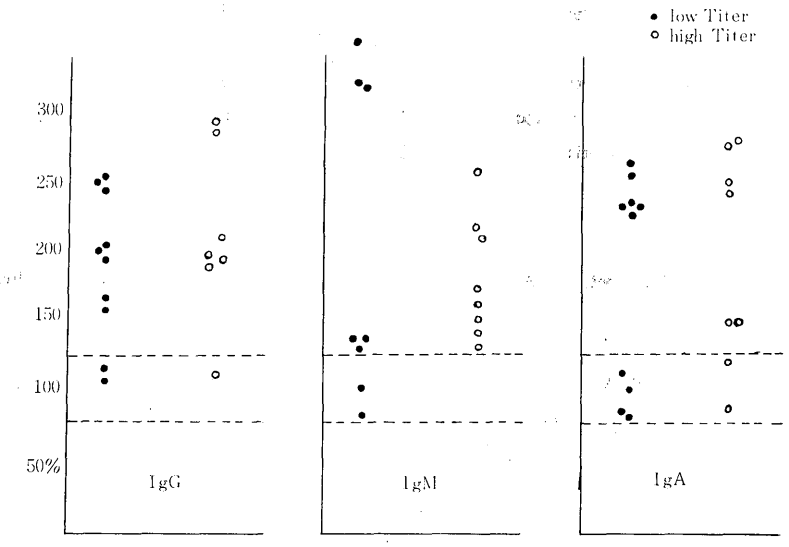


Fig. 1. Serum Immunoglobulin Levels in Liver Diseases with Anti-Ribosome Antibody.

DISCUSSION

It is well known that complement fixing antibodies against microsomal fractions are detected in sera from patients with liver diseases[11)12)]. Since the microsomal fractions contain ribosomes, there is a posibility of the presence of an antibody to ribosome in liver diseases. Sturgill et al.[8)] reported that ribosome antibody was present in serum from one patient with primary biliary cirrhosis but only in low titer. In the present study, ribosome antibodies are detected in 11 of 132 patients with various liver diseases. The highest rate of incidence was found to be 32% in patients with active chronic hepatitis. Dodd et al.[13)] have reported the incidence of antibody to ribosomes by injecting rabbit liver ribosomes into rabbits. Histological examination of these animals showed marked loss of cytoplasm in liver cells and focal collections of plasma cells in the connective tissue septa of the liver. All these findings suggest that ribosome antibodies are present in the sera of patients with chronic active hepatitis.

It was unclear which immunoglobulin is particularly effective in the bentonite ribosomes flocculation test. Further observations are need for understanding of relationship between the immunoglobulin and the ribosome antibodies.

The effects of trypsin and RNase on ribosomes suggest that antigenic determinants are related to both protein and RNA. Anti-DNA antibodies and an antinuclear factor are frequently found in sera from patients with chronic liver diseases. These antibodies are also detected in sera of patients with systemic lupus erythematosis together with antibodies to cytoplasmic antigen. Although there is no evidence that organ specific antigen and antibodies are present in sera from patients with liver diseases, the serological abnormality seems to have some role in the progress of chronic liver diseases.

SUMMARY

The sera of 132 patients with liver diseases were examined for antibody to constituents of ribosomes by the bentonite ribosomes flocculation test. The ribosome antibody was detected in 11 of 35 cases (3 %) of acute hepatitis, in 7 of 41 cases (17 %) of chronic hepatitis, in 3 of 39 cases (8%) of liver cirrhosis. The ribosome antibody was absent detected in the 36 patients with primary biliary cirrhosis, liver carcinoma, obstructive jaundice and toxic hepatitis or in the 20 normal donors. The ribosome antibody seemed to be present only in sera of patients with chronic active hepatitis.

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