

Clinical Significance of ^{99m}Tc -DTPA Galactosyl Human Serum Albumin Scintigram in Follow-up after Kasai Operation

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SHIMAOKA, S., OHI, R., NIO, M., IWAMI, D. and SANO, N. *Clinical Significance of ^{99m}Tc -DTPA Galactosyl Human Serum Albumin Scintigram in Follow-up after Kasai Operation.* Tohoku J. Exp. Med., 1997, **181** (1), 203-211 ——— The scintigram using ^{99m}Tc -DTPA galactosyl human serum albumin (^{99m}Tc -GSA) which binds to asialoglycoprotein receptors on hepatocytes is a good index of hepatocyte function in various liver diseases in adult patients. In 43 patients (4 months to 30 years old) who had undergone Kasai procedure, we performed 53 series of ^{99m}Tc -GSA scintigrams and checked the laboratory data of blood draw and the clinical status. The indices for blood clearance and liver accumulation were evaluated on the basis of the dynamic data after ^{99m}Tc -GSA injection. HH15 as an index of the blood clearance, and LHL15 as an index of the accumulation of the hepatocytes were calculated and the HH15/LHL15 ratio (H/L15) was examined. ^{99m}Tc -GSA scintigram correlated with liver function and clinical status. Our results revealed that 1) The deterioration of the liver functions and clinical status correlates proportionally with H/L15, 2) The results of ^{99m}Tc -GSA scintigram correlate with several liver function tests, especially direct bilirubin, albumin and choline esterase, 3) This scintigram is an useful index of clinical status and hepatic function as well as the change of the hepatic parenchymal reserve in BA patients, especially for the evaluation of liver transplantation. ——— biliary atresia; Kasai operation; asialoglycoprotein receptor; ^{99m}Tc -GSA scintigram

To know the liver functions and clinical status in following up of biliary atresia (BA) patients, we usually check the liver function tests by blood draw, abdominal ultra sonography with doppler, presence of esophageal varices for the indication of the severity of portal hypertension, weight and height for the nutritional status, episodes of ascending cholangitis and so on. It is, however, not easy to precisely predict the clinical status of biliary atresia patients. The

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scintigram using ^{99m}Tc -galactosyl human serum albumin which binds selectively to the asialoglycoprotein receptors on hepatocytes is a good index of hepatocyte function in various liver diseases regardless of cholestasis in adult patients (Sawamura et al. 1985; Torizuka et al. 1991, 1992a, b; Koizumi et al. 1992; Ohno et al. 1993). In this paper, we examined whether this scintigram reflects the clinical status and liver functions and could be practically applied to predict the clinical status in BA patients.

MATERIALS AND METHODS

From 1952 to 1995, KASAI operation was performed for 299 patients in our institute. In 43 patients (22 males and 21 females) ranging in age from 4 months to 30 years (mean age \pm S.D.; $8.17 \text{ years} \pm 8.17$), we performed 53 series of ^{99m}Tc -GSA scintigrams and checked laboratory data of blood draw, clinical status and the presence of portal hypertension. To determine the presence or absence of portal hypertension, we used the gastro-esophageal fiber scope to look for esophageal varix, and watch for the episode of continuing thrombocytopenia as well as for signs of easy bleeding from hypersplenism.

^{99m}Tc -GSA scintigram is performed by the following method. The patient is injected 3.7 megabequerel per kilogram ^{99m}Tc -GSA intravenously. The indices for blood clearance and liver accumulation are periodically evaluated on the basis of the dynamic data after ^{99m}Tc -GSA injection for 60 minutes. HH15; the ratio of the heart count of 15 minutes to that of 3 minutes after injection (H_{15}/H_3) as an index of the blood clearance, and LHL15; the ratio of the liver count to the heart and liver count at 15 minutes after injection $\{L_{15}/(H_{15} + L_{15})\}$ as an index of the accumulation of the hepatocytes, are measured and calculated. And we calculated the ratio of HH15 to LHL15 (H/L 15) to examine the correlation with laboratory data as well.

RESULTS

Fig. 1 shows each value of HH15 as well as LHL15 for each BA patient. The closed triangle represents the patients with almost normal liver function. The open square shows the patients with severe portal hypertension i.e., the patients with esophageal varix or hypersplenism which needs some treatment. The open circle shows the patients thought to have end-stage liver dysfunction. The deterioration of the liver function correlated proportionally to HH15 and correlated inversely to LHL 15. There was no significant difference between the normal liver function and severe portal hypertension groups. Fig. 2 shows the distribution of H/L15 values for each BA patient. H/L15 correlated with HH15 and LHL15, and its correlation coefficient with HH15 was 0.968. The worse the liver function was, the higher the increase of H/L15 became. The critical point seems to be 0.8, because all patients with H/L15 over 0.8 needed or had already received liver transplantation. There was no significant difference between the normal

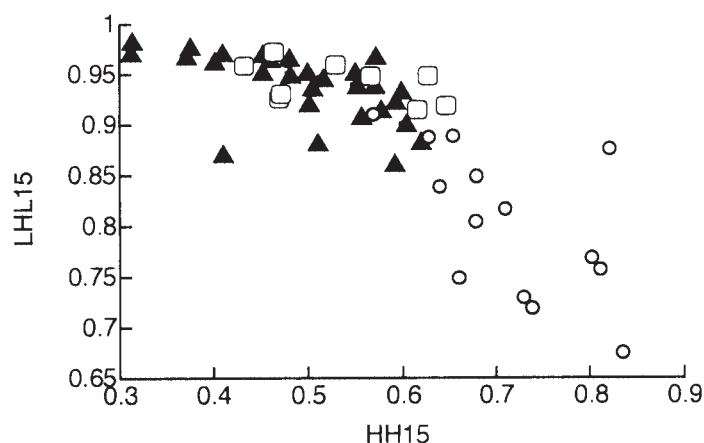


Fig. 1. The relationship between HH15 and LHL15.

▲, almost normal liver function group; □, severe portal hypertension group;
○, indication for liver transplantation.

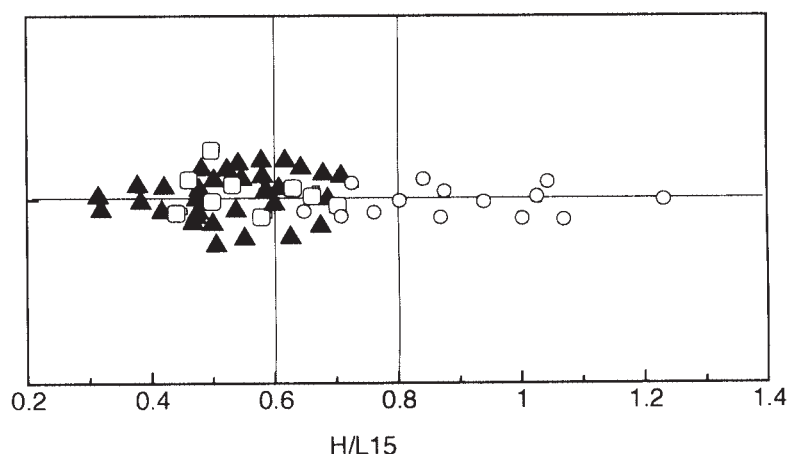


Fig. 2. Distribution of H/L15 (HH15 to LHL15 ratio).

▲, almost normal liver function group; □, severe portal hypertension group;
○, indication for liver transplantation.

liver function and severe portal hypertension groups.

We examined the relationship between H/L15 and liver function tests. Total bilirubin correlated with H/L15 as shown in Fig. 3. Direct bilirubin correlated with H/L15 (Fig. 4). Its correlation coefficient was 0.662. In all patient necessitating liver transplantation, direct bilirubin was over 2.0 mg/100 ml. There was no significant difference between the normal function and severe portal hypertension groups. Albumin also correlated with H/L15 (Fig. 5). Its correlation coefficient was -0.562 . Since the patient with severe hypoalbuminemia can get albumin supplement, this examination may not reflect precise status. Choline esterase correlated with H/L15 (Fig. 6). The correlation coefficient was -0.64 . In eleven of fourteen patients requiring liver transplantation, choline esterase was under 150 IU/ml.

In one patient ^{99m}Tc -GSA scintigram was performed twice before liver transplantation (Fig. 7). He had undergone Kasai operation on his 63rd day of life.

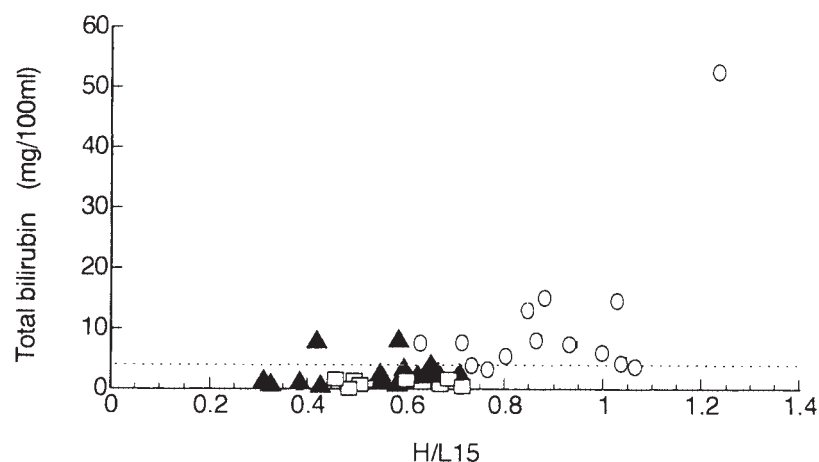


Fig. 3. The relationship between H/L15 and total bilirubin.

$$y = -12.093 + 25.44x \quad \text{CC}; 0.654$$

▲, almost normal liver function group; □, severe portal hypertension group;
○, indication for liver transplantation.

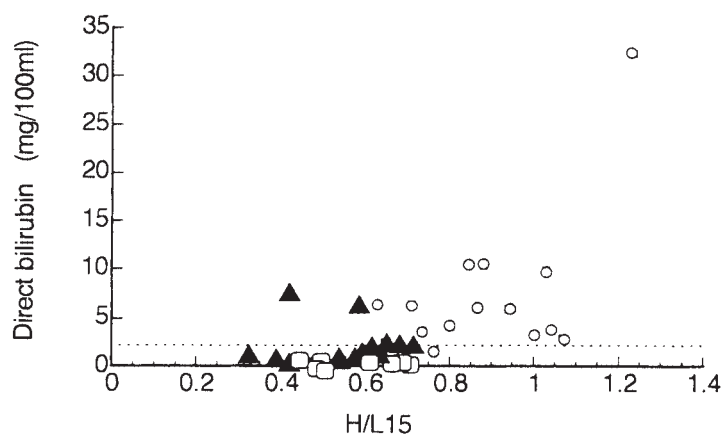


Fig. 4. The relationship between H/L15 and direct bilirubin.

$$y = -7.878 + 16.625x \quad \text{CC}; 0.662$$

▲, almost normal liver function group; □, severe portal hypertension group;
○, indication for liver transplantation.

His total bilirubin decreased once to 1.9 mg/100 ml on the 56th post-operative day. He suffered ascending cholangitis 3 times (on 87th, 103th and 143th POD), and he needed an operation to resolve the lysis of adhesion and to reconstruct intussuscepted valve at the Roux-en-Y limb on the 155th day after the first Kasai operation. But his liver function deteriorated, and he finally needed liver transplantation. In this case we performed ^{99m}Tc -GSA scintigram on 108th and 206th POD (Fig. 8). H/L15 on 108th POD was 0.6451, that is, both the accumulation of the liver and the reduction of activity from blood pool were good. On the other hand, H/L15 on the 206th POD increased to 1.0277. The accumulation of the liver was worse than that on the 108th POD and the remaining activity of the heart as the blood clearance was high. The results of H/L15 of this case are shown in Fig. 9. H/L15 increased from 0.6451 to 1.0277 crossing the critical 0.8

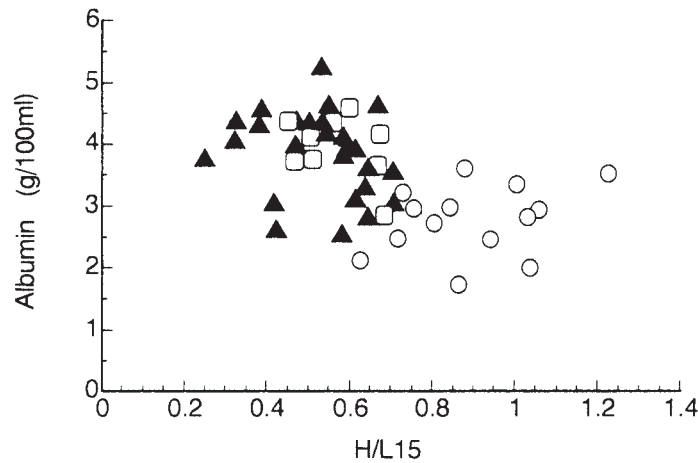


Fig. 5. The relationship between H/L15 and albumin.

$$y = 5.489 - 3.187x \quad CC; 0.605$$

▲, almost normal liver function group; □, severe portal hypertension group;
○, indication for liver transplantation.

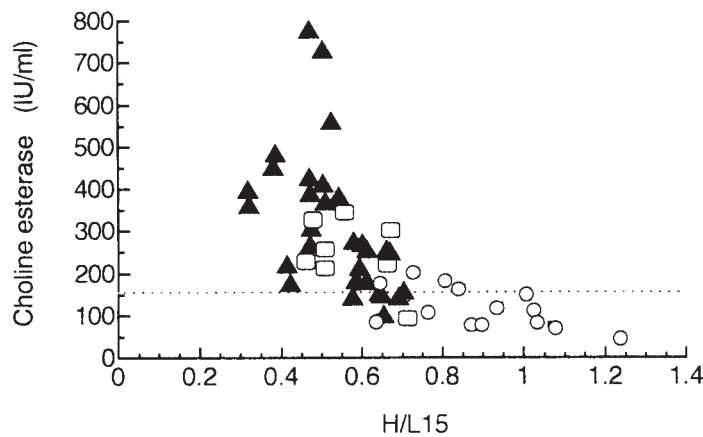


Fig. 6. The relationship between H/L15 and choline esterase.

$$y = 573.5 - 498.5x \quad CC; 0.640$$

▲, almost normal liver function group; □, severe portal hypertension group;
○, indication for liver transplantation.

line. In this case H/L15 reflected severity of the liver dysfunction and clinical status. This scintigram was useful as an index for the evaluation of liver transplantation.

DISCUSSION

Reports on the long term survivors of biliary atresia after Kasai operation are increasing and it becomes more important to predict the prognosis and clinical outcome of BA patients (Ohi et al. 1990). Many investigators are trying to precisely predict the clinical status and prognosis of BA patients (Endo et al. 1995). In some studies the level of serum bilirubin (Hitch et al. 1979; Vazquez-Estevez et al. 1989) and urine excretion of D-glucaric acid (Fujimoto et al. 1994) have been investigated in an attempt to predict the clinical outcome in BA

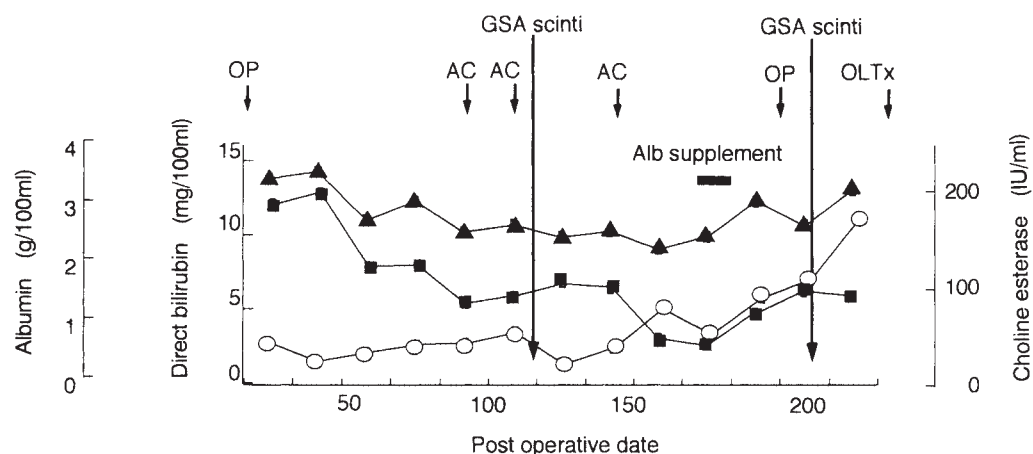


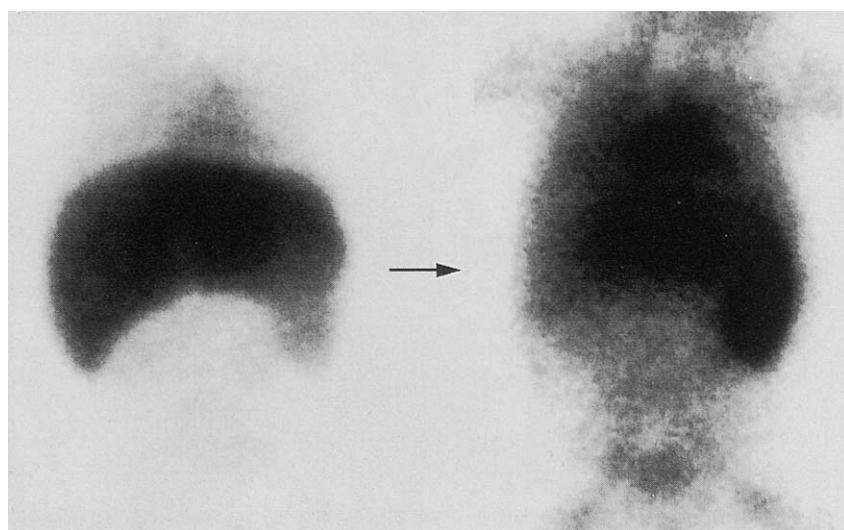
Fig. 7. Clinical course of a representative case.

AC, ascending cholangitis; OP, operation.

○—○, DB (direct bilirubin); ▲—▲, Alb (albumin); ■—■, ChE (choline esterase).

108 POD

206 POD



HH15:0.597, LHL15:0.932
H/L15 : 0.6451

HH15:0.74, LHL15:0.72
H/L15 : 1.0277

Fig. 8. ^{99m}Tc-GSA on 108 and 206 POD in a representative case.

patients. Other investigators have focused on the histological analysis of actin and myosin deposits around the bile canaliculi (Segawa et al. 1993), the immunohistochemical study (Hossain et al. 1995) and the morphological typing (Tan et al. 1994) as predictors of the clinical outcome after Kasai operation.

In the follow up of BA patients in our institute, we generally check the liver function tests by blood draw, the episodes of ascending cholangitis, the severity of portal hypertension and weight and height for the nutritional status (Nio et al. 1996). To know the severity of portal hypertension, we perform endoscopy to check for esophageal varices, congestive gastropathy and hypersplenism. The

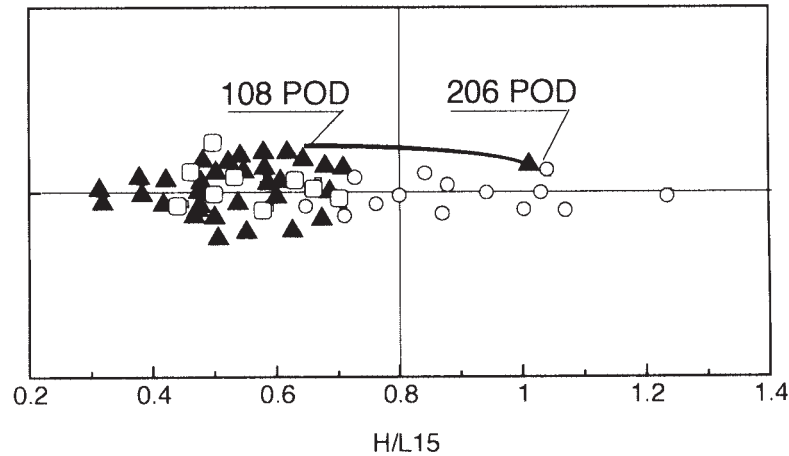


Fig. 9. Deterioration of H/L15.

▲, almost normal liver function group; □, severe portal hypertension group;
○, indication for liver transplantation.

scintigram using ^{99m}Tc -GSA which binds selectively to the asialoglycoprotein receptors on hepatocytes is a good index of hepatocyte function in various liver diseases in adult patients (Sawamura et al. 1985; Torizuka et al. 1991, 1992 a, b; Koizumi et al. 1992; Ohno et al. 1993). Some authors (Marshall et al. 1978; Sawamura et al. 1981, 1984) have reported that serum asialoglycoprotein increases in various liver diseases, and have given the reason for the increase of serum asialoglycoprotein as the decrease in the number of asialoglycoprotein receptor on hepatocyte in those conditions. It means that the number of asialoglycoprotein receptors reflects the reserve of the functional parenchymal hepatocytes. Accordingly the results of the imaging of asialoglycoprotein receptors indicate the clinical status and the prognosis of the patients in various liver diseases (Stadalnik et al. 1985; Bossuyt et al. 1990). And asialoglycoprotein is resolved soon after its intake into hepatocytes (Price and Ashwell 1971) and not secreted to the bile flow, so ^{99m}Tc -GSA scintigram can reflect the reserve value of liver function even in the patients with severe cholestasis (Sawamura et al. 1985).

From this point of view, we performed 53 series of ^{99m}Tc -GSA scintigram in our 43 BA patients and also checked laboratory data of blood draw, the clinical status and the presence of portal hypertension to examine whether this scintigram reflects the clinical status and liver functions and it is a good index to predict the clinical status in BA patients. We examined the relationship between H/L15 and liver function tests and found that the value of H/L15 correlated strongly with total bilirubin, direct bilirubin, albumin and choline esterase in the serum.

One patient underwent ^{99m}Tc -GSA scintigram twice before liver transplantation. As shown in this case, the result of H/L15 on the 206th POD deteriorated compared with that on the 108th POD, i.e., proportionally to the deteriorating of the liver function tests, the clinical status and the portal venous flow, indicating that the results of H/L15 reflected severity of the liver dysfunction and clinical

status and this scintigram was an useful index for the evaluation of liver transplantation. The ^{99m}Tc -GSA scintigram is not only an useful index of clinical status and hepatic function but also shows change of the hepatic parenchymal reserve in BA patients especially for the evaluation of liver transplant indication.

We conclude that 1) The deterioration of the liver functions and clinical status correlates proportionally with H/L15, 2) the results of ^{99m}Tc -GSA scintigram correlate with several liver function tests, especially direct bilirubin, albumin and choline esterase, 3) The ^{99m}Tc -GSA scintigram is an useful index of clinical status and hepatic function as well as the change of the hepatic parenchymal reserve in BA patients, especially for the evaluation of liver transplantation.

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