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MRI Findings in the Liver in Biliary Atresia Patients after the Kasai Operation

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TAKAHASHI, A., HATAKEYAMA, S., SUZUKI, N., KUROIWA, M., IKEDA, H., MURAKAMI, J., SAKURAI, M., MATSUYAMA, S. and TSUCHIDA, Y. *MRI Findings in the Liver in Biliary Atresia Patients after the Kasai Operation.* Tohoku J. Exp. Med., 1997, **181** (1), 193-202 —— To evaluate liver function in biliary atresia (BA) patients after the Kasai operation, magnetic resonance imaging (MRI) was carried out 28 times in 19 BA patients. Sixteen of these were divided into three groups on the basis of the serum level of total bilirubin (t-bil), glutamic pyruvic transaminase (GPT) and γ-glutamyltransferase (γ-GTP) in the postoperative follow-up period (2-11 years). In group 1 ($n=7$) the t-bil was continuously kept under 1 mg/100 ml. In group 2 ($n=4$) the t-bil was continuously kept under 1 mg/100 ml, but GPT and γ-GTP remained high (GPT$>$100 IU/liter, γ-GTP$>$200 IU/liter) for more than 2 years. In group 3 ($n=5$) an increase in the t-bil level reappeared (1-2 mg/100 ml; $n=4$, $>$2 mg/100 ml; $n=1$). The differences between MRI finding in the 3 groups, and the correlation between MRI findings and laboratory data (t-bil, cholinesterase; ChE, GPT and γ-GTP), which were taken around the time of MRI examinations, were studied. The results were as follows: (1) All 19 patients had normal or high signl areas of various sizes on T1 weighted images (WI). (2) Eighteen of 19 patients had high signal areas of various sizes on T2 WI in the portal system areas and/or liver parenchyma, and these areas were enhanced by gadolinium-DTPA in about half of the patients. (3) Ten of 16 patients had atrophic change over one liver lobe. (4) MRI findings for group 1 and the other groups were significantly different, and MRI findings, except for atrophic change, were correlated with the increase or decrease in laboratory data taken around the time of MRI examinations ($p<0.05$). These results indicate that a normal or high signal area on T1 WI shows functional tissue, and that a high signal area on T2 WI shows tissue damaged by inflammation and/or progressive fibrosis. MRI is useful for evaluating liver function, especially in terms of morphological features, in BA patients after the Kasai operation, and will be one method for establishing their prognosis. —— biliary atresia; cirrhosis; magnetic resonance imaging

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It is known that biliary atresia (BA) patients can obtain a decrease in their jaundice by portoenterostomy, the Kasai operation (Ohi and Ibrahim 1992; Toyosaka et al. 1994), but some of them showed a deterioration of various degrees in liver function, finally resulting in liver failure (Ohi et al. 1986; Saeki et al. 1987). It is therefore necessary to evaluate the liver function of BA patients after the Kasai operation. It is also known that magnetic resonance imaging (MRI) has the potential to show morphological features in liver function associated with deteriorative or cirrhotic liver (Matsui et al. 1989; Marti-Bonmati et al. 1993; Ohtomo et al. 1993). We applied MRI to evaluate the liver function of BA patients in the postoperative follow-up period.

In this research, MRI was carried out in BA patients being followed up in our institution, and we studied whether MRI was useful for valuation of the liver function of these BA patients. To determine the usefulness of MRI, we examined the relationship between the MRI findings and the time course change in the serum level of total bilirubin (t-bil), cholinesterase (ChE), glutamic pyruvic transaminase (GPT) and γ-glutamyltransferase (γ-GTP) in postoperative BA patients, and also examined the correlation between MRI findings and these laboratory data taken around the time of MRI examinations.

Material and Methods

Thirty BA patients were admitted to our institution between 1983 and 1994, and were operated on using the Kasai procedure. Seven of them had no decrease in jaundice after the operation, and died due to liver failure within 1.5 years. The other 23 patients decreased their serum level of t-bil to under 1.0 mg/100 ml either consistently or at one point. Four of them could not be followed up in detail, and MRI examination was therefore carried out in the other 19 patients.

Sixteen of them were followed up for over 2 years, so their short-term prognosis is thought to be clear. These 16 patients were divided into three groups on the basis of the time course change in the serum level of t-bil, GPT and γ-GTP. In group 1 ($n=7$), t-bil was decreased and continuously kept under 1.0 mg/100 ml, and GPT and γ-GTP were decreased and kept within the normal range. In group 2($n=4$), t-bil was continuously kept under 1.0 mg/100 ml, but GPT and γ-GTP remained high (GPT $>$ 100 IU/liter, γ-GTP $>$ 200 IU/liter) for more than 2 years. In group 3 ($n=5$), an increase in t-bil (1.0–2.0 mg/100 ml; $n=5$, $>$2.0 mg/100 ml; $n=1$) reappeared. T-bil, ChE, GPT and γ-GTP were measured every one or two months during the follow-up period.

From 1994, MRI was carried out on 19 patients, for a total of 28 times. Three images, T1 weighted image (WI), T2 WI and T1 WI with an administration of gadolinium-DTPA (Gd-DTPA) were taken in each examination. Two values were adopted as an indicator of MRI findings. The values were estimated as follows: Three films of the cross section, a middle film including the porta hepatis and other films at 2 cm aboue and below the middle film, were selected. In these

films, the area of the abdominal cavity (A-AC), the area with a normal or high signal of T1 WI (A-T1) and the area with a high signal of T2 WI (A-T2) were measured. Then, A-T1/A-AC and A-T2/A-AC were calculated in each film. The final value for each indicator was expressed by the sum total of three values in each film. The differences in A-AC and the area of liver/A-AC in 3 groups were not significant. In addition, the degree of the atrophic change in liver was divided into 3 grades on the basis of the extent of atrophic change ($n=16$). In grade 0, no atrophic change is found. In grade 1, an atrophic change is partially found in one liver lobe. In grade 2, atrophic change extend to one or more liver lobes.

The differences between MRI findings in 3 groups were calculated by the Student's t-test ($n=16$). Correlation analyses were performed for MRI findings and laboratory data taken around the time of MRI examinations ($n=19$). The level of significance was accepted as $p<0.05$.

Results

A high or normal signal area on T1 WI

The MRI films showing a normal or high signal area on T1 WI are shown in Fig. 1. The patient presented is a 7-year-old boy, and is classified in group 1. Most of his liver parenchyma consists of a normal or high T1 WI signal. A high signal area on T2 WI, which is enhanced by Gd-DTPA, is found in the portal system areas, but its extent is limited.

All patients had normal or high signal areas of various sizes on T1 WI. The differences between group 1 and other groups were statistically significant ($p<0.05$). The coefficients of correlation between the extent of the area and the serum levels of ChE, GPT and γ-GTP were statistically significant ($p<0.05$). These results are shown in Tables 1 and 2.

A high signal area on T2 WI

The MRI films showing a high signal area on T2 WI are shown in Fig. 2. The patients presented is a 5-year-old girl, and is classified in group 3 ($1<$t-bil<2). Her left lobe is atrophic, and consists of a high signal area on T2 WI, which is slighty enhanced by Gd-DTPA. The area extends both in the portal system areas and liver parenchyma. Inside her right lobe consists of a normal or high signal area on T1 WI.

Eighteen of 19 patients had high signal areas of various sizes on T2 WI in the portal system area and/or liver parenchyma. The dfferences between group 1 and other groups were statistically significant ($p<0.05$). The coefficient of correlation between the extent of the area and the serum levels of t-bil, ChE, GPT and γ-GTP were statistically significant ($p<0.05$). These results are shown in Tables 1 and 2.

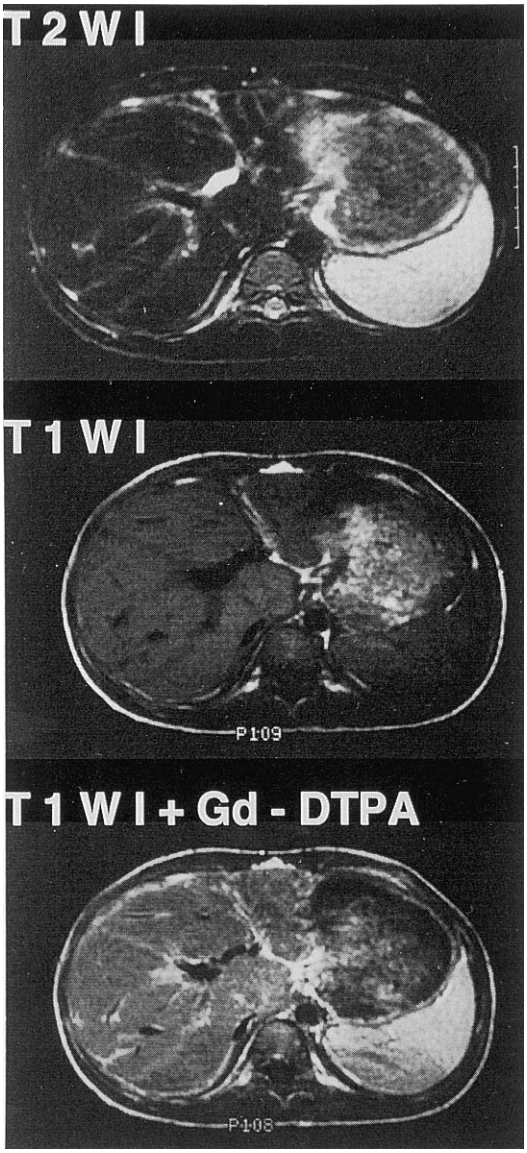

Fig. 1. Typical MRI films showing a normal or high signal area on T1 WI. T2 WI; T2 weighted image. T1 WI; T1 weighted image. T1 WI+Gd-DTPA; T1 weighted image enhanced by gadolinium-DTPA.

Atrophic change in liver

The MRI films showing the atropic change are shown in Fig. 3. The patients presented is an 11-year-old boy, and is classified in group 2. 5 years ago, he had a large cyst in the left lobe, and internal drainage between the cyst and the Roux-ex-Y intestine was performed. His left lobe is small and consists of a high signal area on T2 WI without the enhancement of Gd-DTPA. On the other hand, his right lobe is enlarged and consists of a normal or high signal on T1 WI.

An atrophic change of grade 2 was found in 10 of 16 patients (2 of 7 patients in group 1, all 4 patients in group 2 and 4 of 5 patients in group 3). The differences between group 1 and other groups were statistically significant ($p < 0.05$). The coefficient of correlation between the degree of the atrophic change

TABLE 1. *The differences between groups in MRI findings*

	Group 1	Group 2	Group 3
A-T1/A-AC	12.38	9.43	8.97
		*	
			*
A-T2/A-AC	0.59	2.65	3.69
		*	
			*
Atrophic change	0.86 (1)	2.00 (2)	1.80 (2)
		*	
			*

A-T1; Area with a normal or high T1 WI signal.
A-T2; Area with a high T2 WI signal.
A-AC; Area of abdominal cavity.
Values are the mean (median) and expressed in arbitrary units.
$^*p<0.05$.

TABLE 2. *The correlation between MRI findings and laboratory data*

	Bilirubin	Cholinesterase	GPT	γ-GTP
A-T1/A-AC	−0.359	0.829	−0.404	−0.451
A-T2/A-AC	0.533	−0.765	0.566	0.571
Atrophic change	0.069	−0.551	0.244	0.224

A-T1; Area with a normal or high T1 WI signal.
A-T2; Area with a high T2 WI signal.
A-AC; Area of abdominal cavity.
Values are coefficients of correlation, and values underlined are $p<0.05$.

and the serum levels of t-bil, GPT and γ-GTP were not significant statistically.

Enhancement of Gd-DTPA

The area with a high T2 WI signal was enhanced by Gd-DTPA in about half of the patients. The enhancement was found in 4 of 7 patients in group 1, 3 of 4 patients in group 2 and 3 of 5 patients in group 3. The degree of enhancement was not statistically different between groups.

DISCUSSION

The short-term prognosis in BA patients after the Kasai operation has recently been improved. Ohi et al. reported that operative results have improved since 1972, and that the disappearance rate for jaundice during the years 1987–1991 was 81% (Ohi and Ibrahim 1992). Toyosaka et al. reported that jaundice in BA patients cleared up in 93.7% cases since 1984 after introducing the extensive dissection at the porta hepatis (Toyosaka et al. 1994). Despite recent improve-

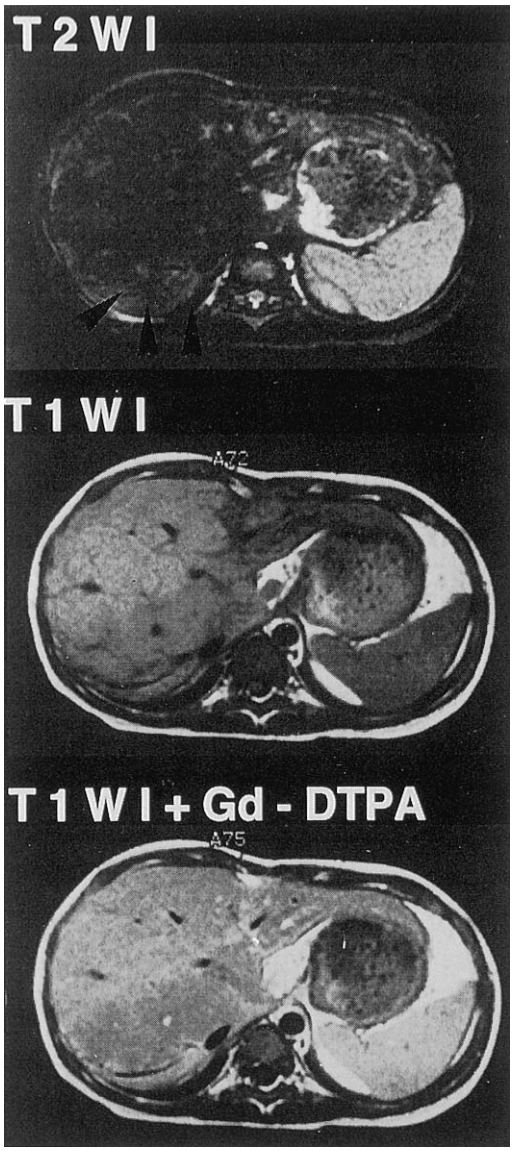

Fig. 2. Typical MRI films showing a high signal area on T2 WI.
Arrows show the high signal area on T2 WI. Abbreviations are the same as those in Fig. 1.

ments in surgical technique and postoperative management which have brought a decrease in serum level of t-bil to the normal range either consistently or at one point in the majority of BA patients, Akiyama et al. and Ohi et al. reported that the percentage of long-term survivors in BA exceeding 10 years was 39.2% and 48%, respectively (Akiyama et al. 1986; Ohi et al. 1990). The deterioration of long-term survivors is considered to be caused by post-operative complications such as cholangitis, portal hypertension and/or hypersplenism, which sometimes occur after a successful Kasai operation (Ohi et al. 1986; Saeki et al. 1987; Ohi and Ibraham 1992).

Gautier et al. histologically studied the liver specimens obtained from 20 patients at least 5 years after the operation, and reported that biliary cirrhosis was definitely seen in most of the patients (Gautier et al. 1984). Kimura et al.

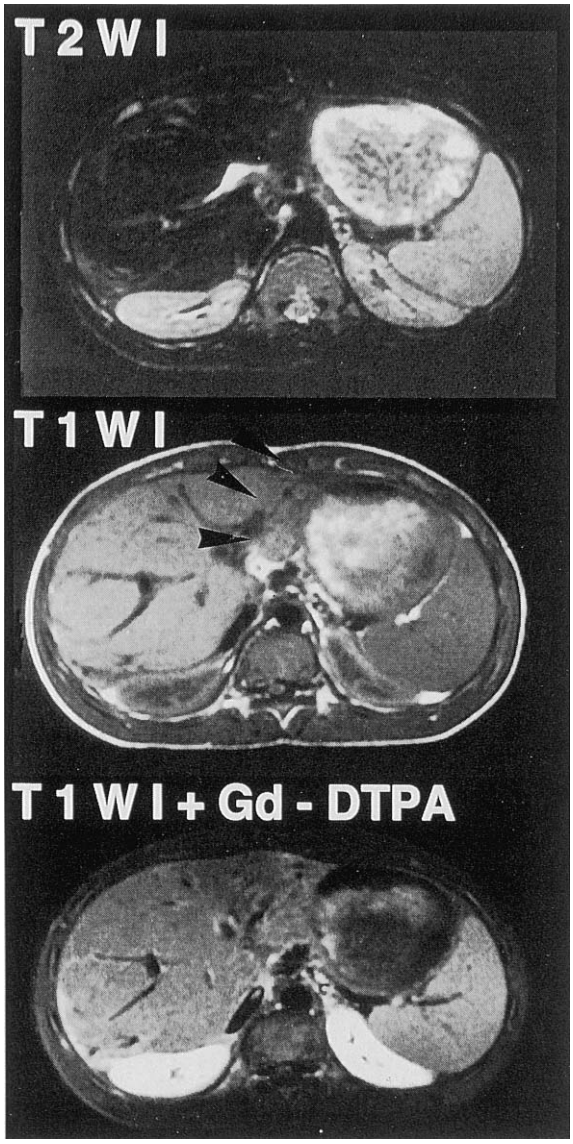

Fig. 3. Typical MRI films showing atrophic change.
Arrows show atrophic change in the left lobe. Abbreviations are the same as those in Fig. 1.

demonstrated in a morphological study of the liver of long-term survivors of the Kasai operation that biliary cirrhosis and portal fibrosis had developed in a non-homogeneous pattern. Parts of the liver may appear normal, whereas other parts may show signs of advanced cirrhotic or fibrotic changes (Kimura et al. 1987). Yeung et al. studied the morphological structure of livers taken during liver transplantation after a successful Kasai operation, reporting that a well-circumscribed central zone of normal hepatic parenchyma was surrounded and encased by a peripheral zone of fibrotic, cirrhotic tissue, and that the peripheral fibrotic tissue might have prevented the normal growth of the draining central segment, leading to hepatic decompensation at a later age (Yeung et al. 1993). In view of these findings, early identification of liver failure is essential, and it is necessary to evaluate the morphological and pathological features in the liver of BA patients for a long time.

In this study, we used MRI to evaluate liver function, especially from the standpoint of the analysis of morphological features, in BA patients during the postoperative period. As a result, MRI findings were found to be significantly different in group 1 than those in the other groups. The extent of the normal or high signal area on T1 WI was correlated with the decrease in GPT and γ-GTP, and the increase in ChE. The extent of the high signal area on T2 WI was correlated with the increase in t-bil, GPT and γ-GTP, and the decrease in ChE. These results indicate that MRI findings are related to the time course change in liver function during the postoperative follow-up period and the liver function taken around the time of MRI examinations.

In liver MRI, it is thought that a normal or high signal area on T1 WI may reflect almost normal liver tissue, and that a high signal area on T2 WI may reflect tissue with inflammation and/or progressive fibrosis (Matsui et al. 1989; Marti-Bonmati et al. 1993; Ohtomo et al. 1993). These reports and our results indicate that a normal or high signal area on T1 WI reflects the functional liver tissue, and the extent corresponds to good function of the liver in postoperative BA patients, and that a high signal area on T2 WI reflects damaged tissue, with inflammation and/or progressive fibrosis, and the extent corresponds to the deterioration in liver function in BA patients.

Atrophic change of various degrees was also found in the liver of many postoperative BA patients. Although the ratio of atrophic change to whole liver structure was correlated with the time course change in the liver function in postoperative BA patients, there was no correlation between the extent of atrophic change and the liver function taken around the time of MRI examinations. These results indicate that the extent of atrophic change itself does not reflect the total liver function of BA patients at MRI examination. The prognosis of postoperative BA patients may not be reflected by the volume of complete fibrosis of the liver, but by the volume of residual functional tissue.

The degree of Gd-DTPA enhancement was not correlated with the time course change in the liver function in postoperative BA patients. This enhancement was found in some patients in group 1, whose serum levels of GPT and γ-GTP were within the normal range. However in some patients in group 3, whose liver function was thought to have deteriorated, the enhancement was not found. It is reported that Gd-DTPA enhances inflammatory tissue and tissue with progressive fibrosis, but not the final stage of fibrosis (Ohtomo et al. 1993). Because of these properties of Gd-DTPA, inflammatory change or progressive fibrosis will remain in some group 1 patients, and fibrosis will be complete in some group 3 patients. In our study, it is thought that the degree of Gd-DTPA enhancement does not reflect the liver function at the time of MRI examination, but this area might have the potential to proceed to fibrosis and atrophy later.

It is reported that the serum type IV collagen level was significantly higher in patients who had undergone a liver transplantation and active and progressive

fibrosis was microscopically detected in specimens taken from portal system areas, and that the increase in the level of these products and the extent of fibrosis were correlated with the patient's age at the time of the liver transplantation (Oike et al. 1996). These results suggest that the state of progressive fibrosis in the liver is one factor regulating liver function, and that evaluation of the fibrosis is important in making a prognosis for postoperative BA patients. In our research, we grossly evaluate the extent of hepatic injury by MRI at one point. The functional areas, considered to be normal on MRI, could have an active and progressive fibrosis when observed microscopically, and these fibrosis will proceed later. We therefore need a further detailed study of hepatic injury and time course analysis by MRI to make a more precise prognosis of postoperative BA patients.

We conclude that MRI is useful for evaluating liver function and for estimating the prognosis of BA patients after the Kasai operation.

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