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ORIGINAL ARTICLE

Tc-99m PMT scintigraphy in the diagnosis of pediatric biliary atresia

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Abstract

Purpose Hepatobiliary scintigraphy plays an important role in the differentiation of biliary atresia (BA) and non-BA. The usefulness of ^{99m}Tc-iminodiacetic acid (IDA) derivatives in BA diagnosis is reported in several papers. In contrast, there are no comprehensive data on differentiating BA from non-BA using ^{99m}Tc-*N*-pyridoxyl-5-methyl-tryptophan (PMT). Our objective was to evaluate the usefulness of ^{99m}Tc-PMT scintigraphy in the diagnosis of BA.

Materials and methods 52 infants who received ^{99m}Tc-PMT scintigraphy for suspected BA were retrospectively evaluated. Preoperative cholangiograms or follow-ups were used as the gold standard for diagnosis of BA. We analyzed the utility of ^{99m}Tc-PMT scintigraphy, various clinical and investigational parameters in the diagnosis of BA.

Results The final diagnoses in this group were BA (67.3%) and non-BA (32.7%). ^{99m}Tc-PMT scintigraphy, stool color change, total bilirubin, direct bilirubin, aspartate aminotransferase (AST) and γ-glutamyl transferase (γ-GTP) led to distinguishing between BA and non-BA in univariate analysis. Subsequent multivariate logistic regression analysis indicated that ^{99m}Tc-PMT scintigraphy and γ-GTP were independent predictors of BA. The diagnostic accuracy of ^{99m}Tc-PMT scintigraphy was 94.2%.

Conclusions ^{99m}Tc-PMT scintigraphy is more accurate in the diagnosis of BA than other conventional examinations. In addition, false positives of ^{99m}Tc-PMT scintigraphy could be reduced by combining γ-GTP level monitoring.

Keywords ^{99m}Tc-*N*-Pyridoxyl-5-methyl-tryptophan (PMT) · Biliary atresia (BA) · γ-Glutamyl transferase (γ-GTP)

Abbreviations

BA	Biliary atresia
PMT	*N*-Pyridoxyl-5-methyl-tryptophan
IDA	Iminodiacetic acid
LEHR	Low-energy high resolution
LMEGP	Low-medium energy general purpose
ROC	Receiver-operating characteristic
AST	Aspartate aminotransferase
ALT	Alanine aminotransferase
γ-GTP	γ-Glutamyl transferase
ALP	Alkaline phosphatase
AUC	Area under the receiver-operating characteristic curve

Introduction

Biliary atresia (BA) is one of the causes of persistent neonatal jaundice [1]. The early diagnosis of BA and differentiation from other causes of persistent neonatal jaundice hold the key to the survival of neonates [2, 3]. However, the distinction of BA from other causes of persistent neonatal jaundice may be clinically difficult, and clinical parameters or biochemical tests are usually inconclusive.

Hepatobiliary scintigraphy plays an important role in the differentiation of BA from non-BA [4, 5]. ^{99m}Tc-compounds for hepatobiliary scintigraphy are divided into two groups: ^{99m}Tc-*N*-pyridoxyl-5-methyl-tryptophan (PMT) is mainly used in Japan, while ^{99m}Tc-iminodiacetic acid (IDA) derivatives are commonly used in Western countries. The intravenous injection of ^{99m}Tc-PMT has rapid blood clearance, fast hepatobiliary transit, low urinary excretion and no intestinal reabsorption [6, 7]. ^{99m}Tc-PMT and ^{99m}Tc-IDA derivatives have almost the same pharmacokinetics.

The usefulness of ^{99m}Tc-IDA derivatives in BA diagnosis is reported in several papers [8–13]. In contrast, there are no comprehensive data on differentiating BA from non-BA using ^{99m}Tc-PMT. Our objective was to evaluate the

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usefulness of ^{99m}Tc-PMT scintigraphy in comparison with various clinical and investigational parameters in the diagnosis of BA.

Materials and methods

Study population

This study was approved by our institutional ethics board. All study procedures were in accordance with the Statement of Human and Animal Rights. Prior informed consent for inclusion in the study was obtained from all patients by their legal representatives.

A total of 52 infants who received ^{99m}Tc-PMT scintigraphy between August 2001 and October 2018 for suspected BA in our hospital were retrospectively evaluated. All patients were diagnosed BA or non-BA with preoperative cholangiogram or follow-up as the gold standard. Additionally, clinical factors (male, age, jaundice and stool color change), biochemical tests [albumin, total bilirubin, direct bilirubin, indirect bilirubin total bile acid, aspartate aminotransferase (AST), alanine aminotransferase (ALT), γ-glutamyl transferase (γ-GTP) and alkaline phosphatase (ALP)] and ultrasonography of gallbladder recorded in electronic medical charts were the parameters used for analysis.

^{99m}Tc-PMT scintigraphy

The preparation included cessation of breastfeeding for at least 4 h before the test. Imaging was carried out on a Single Head Gamma Camera using a low-energy high-resolution (LEHR) collimator or low-medium energy general purpose (LMEGP) collimator with the patient in a supine position. The instruments used were GCA-7200A (Toshiba, between August 2001 and May 2002), GCA-90B (Toshiba, between August 2001 and May 2002), Millennium VG (GE Healthcare, between February 2002 and February 2013), Skylight (Philips Healthcare, between March 2002 and December 2013), Symbia T16 (Siemens Healthcare, between March 2010 and August 2018) and Discovery NM/CT 670 (GE Healthcare, between March 2013 and August 2018). The dose of ^{99m}Tc-PMT was intravenously injected based on age or body weight according to "Subcommittee for Standardization of Radionuclide Imaging, Medical and Pharmaceutical Committee, Japan Radioisotope Association" from 2001 to 2013 (administered activity = 48.1 MBq) [14] and "Japanese consensus guidelines for pediatric nuclear medicine" from 2014 to 2018 [administered activity (MBq) = 10.5 × weight-dependent multiple] [15]. Anterior view hepatic phase dynamic images were obtained for 60 min and followed by anterior static images at least once during 2–7 h. If no radiotracer was detected in the bowel until then, a delayed scan was taken at 24 h. Normally, most of the tracer is accumulated in the liver within 5 min after injection. The tracer appears in the proximal small bowel within 30 min. Cases were regarded as positive for BA, if the scans showed good liver uptake with no intestinal excretion till 24 h (Figs. 1, 2)

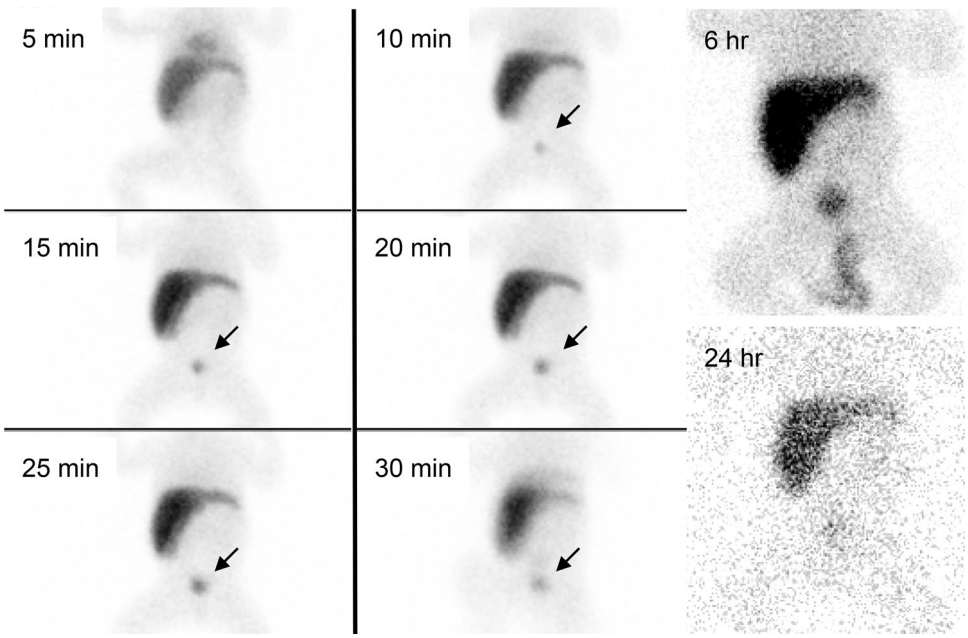

Fig. 1 True positive case. BA in a 63-day-old infant. ^{99m}Tc-PMT tracer showed normal uptake in the liver within 5 min after injection. Then no intestinal excretion was visualized till 24 h. On the other hand, the bladder was seen at an early stage due to increased renal excretion (black arrows represents bladder). *BA* biliary atresia, *PMT N*-pyridoxyl-5-methyl-tryptophan

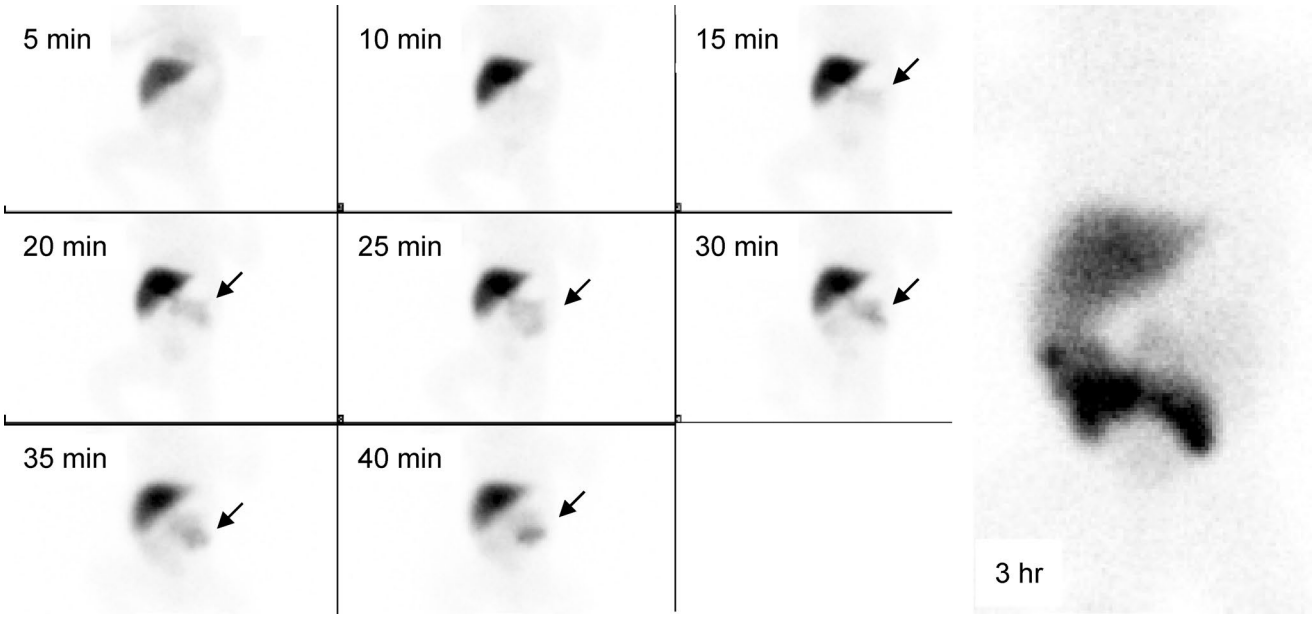

Fig. 2 True negative case of non-BA. ^{99m}Tc-PMT scan in a 30-day-old infant. The extrahepatic ducts and proximal jejunum are well visualized within 40 min after injection (black arrows represents proximal jejunum). *BA* biliary atresia, *PMT N*-pyridoxyl-5-methyl-tryptophan

[4]. Two nuclear medicine physicians visually analyzed the images. If the two readers' interpretations were conflicting, a third nuclear medicine physician reviewed the study.

Other examinations

Stool color change was defined as positive for BA if the stool color card screening resembled the numbers 1–3 (white, clay-colored, or light yellowish). About ultrasonography of gallbladder, when a normal-sized gallbladder could not be detected, it was regarded as confirmed BA.

Statistical analysis

Continuous variables were presented as the median (interquartile range). Categorical variables were the number of patients followed by the percentage in parentheses. Data were analyzed using the Fisher's exact probability test for categorical variables and Mann–Whitney *U* test for continuous variables; p values < 0.05 were considered statistically significant in diagnosis between BA and non-BA. For statistically significant factors, logistic regression analysis was used for multivariate analysis. Then, diagnostic accuracy was evaluated by calculating sensitivity, specificity, positive and negative predictive value (PPV, NPV) and accuracy. The cutoff values of the continuous variables were based on the receiver-operating characteristic (ROC) curve to show the highest accuracy for the differentiation between BA and non-BA. Statistical analyses were done using SPSS (version 25; IBM SPSS, Chicago, IL, USA).

Results

A total of 52 infants (24 male and 28 female) were included in this study. Age at investigation ranged from 17 to 145 days. The final diagnoses in this group were BA (67.3%), neonatal hepatitis (23.1%), infectious diseases (3.8%), hepatitis with unknown origin (1.9%), citrullinemia (1.9%) and genetic diseases (1.9%).

The results of patient profiles and examination parameters between BA and non-BA infants are presented in Table 1. In univariate analysis, stool color change, total bilirubin, direct bilirubin, AST, γ-GTP and ^{99m}Tc-PMT scintigraphy were useful instruments to distinguish between BA and non-BA. (The method of measuring albumin was changed from bromocresol green to bromocresol purple in October 2008. There was no significant difference between BA and non-BA in the albumin level of any groups "that were for albumin before October 2008 and after 2008". The method of other biochemical tests was not changed during our research period). Subsequent multivariate logistic regression analysis indicated that ^{99m}Tc-PMT scintigraphy and γ-GTP were independent predictors of BA (^{99m}Tc-PMT scintigraphy; $p < 0.0001$, γ-GTP; $p = 0.001$).

The sensitivity, specificity, accuracy, PPV and NPV of significant factors in univariate analysis for detection of BA (stool color change, total bilirubin, direct bilirubin, AST, γ-GTP and ^{99m}Tc-PMT scintigraphy) were summarized in Table 2. ^{99m}Tc-PMT scintigraphy had the highest sensitivity and it was the most accurate method (sensitivity; 100%, specificity; 82.4%, accuracy; 94.2%).

Table 1 Patient profiles and examination parameter results

	Univariate analysis			Multivariate analysis
	BA ($n=35$)	Non-BA ($n=17$)	p*	p*
Male	13 (37.1%)	11 (64.7%)	NS	–
Age (day)	59.0 (41.0–69.0)	55.0 (37.5–73.5)	NS	–
Jaundice	35 (100%)	17 (100%)	NS	–
Stool color change	33 (94.3%)	11 (64.7%)	0.0107	NS
Albumin	4.0 (3.7–4.3)	3.7 (3.5–4.3)	NS	–
Total bilirubin	8.9 (8.1–10.0)	6.2 (5.1–7.6)	0.0007	NS
Direct bilirubin	5.6 (4.6–6.5)	3.5 (2.8–4.2)	0.0001	NS
Indirect bilirubin	3.1 (2.5–3.9)	3.2 (2.0–4.0)	NS	–
Total bile acid	113.3 (88.3–141.3)	121.2 (93.9–207.3)	NS	–
AST	168.0 (85.0–224.0)	103.0 (52.0–148.0)	0.0203	NS
ALT	109.0 (46.0–168.0)	59.0 (27.5–114.5)	NS	–
γ-GTP	449.0 (305.0–801.0)	169.0 (86.5–261.0)	< 0.0001	0.001
ALP	1833.0 (1415.0–2650.0)	1862.0 (1403.5–2729.5)	NS	–
Ultrasonography	28 (80.0%)	9 (52.9%)	NS	–
^{99m}Tc-PMT scintigraphy	35 (100%)	3 (17.7%)	< 0.0001	< 0.0001

The number of patients is followed by the percentage in parentheses. Continuous variables are presented as the median (inter-quartile range). *NS* not significant ($p \geqq 0.05$); $p < 0.05$ (significant)

BA biliary atresia, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *γ-GTP* = γ-glutamyl transferase, *ALP* alkaline phosphatase, *PMT* = *N*-pyridoxyl-5-methyl-tryptophan

*Fisher's exact test or Mann–Whitney *U* test

Table 2 Diagnostic performance of significant factors in univariate analysis

	Cutoff AUC	Sensitivity	Specificity	Accuracy	PPV	NPV
Stool color change		94.3% (33/35)	35.3% (6/17)	75.0% (39/52)	75.0% (33/44)	75.0% (6/8)
Total bilirubin	≧ 8.1 0.79	80.0% (28/35)	82.4% (14/17)	80.8% (42/52)	90.3% (28//31)	66.7% (14/21)
Direct bilirubin	≧ 4.4 0.83	80.0% (28/35)	82.4% (14/17)	80.8% (42/52)	90.3% (28//31)	66.7% (14/21)
AST	≧ 146 0.70	65.7% (23/35)	76.5% (13/17)	69.2% (36/52)	85.2% (23/27)	52.0% (13/25)
γ-GTP	≧ 305 0.86	77.1% (27/35)	88.2% (15/17)	80.8% (42/52)	93.1% (27/29)	65.2% (15/23)
^{99m}Tc-PMT scintigraphy		100% (35/35)	82.4% (14/17)	94.2% (49/52)	92.1% (35/38)	100% (14/14)

AUC area under the receiver-operating characteristic curve, *PMT N*-pyridoxyl-5-methyl-tryptophan, *BA* biliary atresia, *PPV* positive predictive value, *NPV* negative predictive value

In ^{99m}Tc-PMT scintigraphy, there were no cases of false negatives. By contrast, 3 infants proved to be false positives. In all cases, the ^{99m}Tc-PMT tracer showed normal uptake in the liver within 5 min after injection, then no intestinal excretion were visualized till 24 h (Fig. 3). BA could not be excluded on the basis of the ^{99m}Tc-PMT scan alone. Two infants of them were diagnosed with neonatal hepatitis and improved over time. One of them was diagnosed with hepatitis of unknown cause and he needed a liver transplant later. Their bilirubin levels took more time to normalize than other true negatives of ^{99m}Tc-PMT scintigraphy (Fig. 4). Other examination results of them were presented in Table 3. Stool color change also regarded them as BA. In contrast, their bilirubin levels and γ-GTP were surely not as high as suspected BA. Incorporating optimal thresholds using ^{99m}Tc-PMT scintigraphy and γ-GTP were visualized on a 2-dimensional plot (Fig. 5). In all cases of negative ^{99m}Tc-PMT scintigraphy, BA could be denied. BA was diagnosed in infants with positive ^{99m}Tc-PMT scintigraphy, only when γ-GTP was high (≧ 305 U/L). When γ-GTP was low (< 305 U/L) and ^{99m}Tc-PMT scintigraphy was positive, most of the cases were BA with a few non-BA exceptions. Criteria for

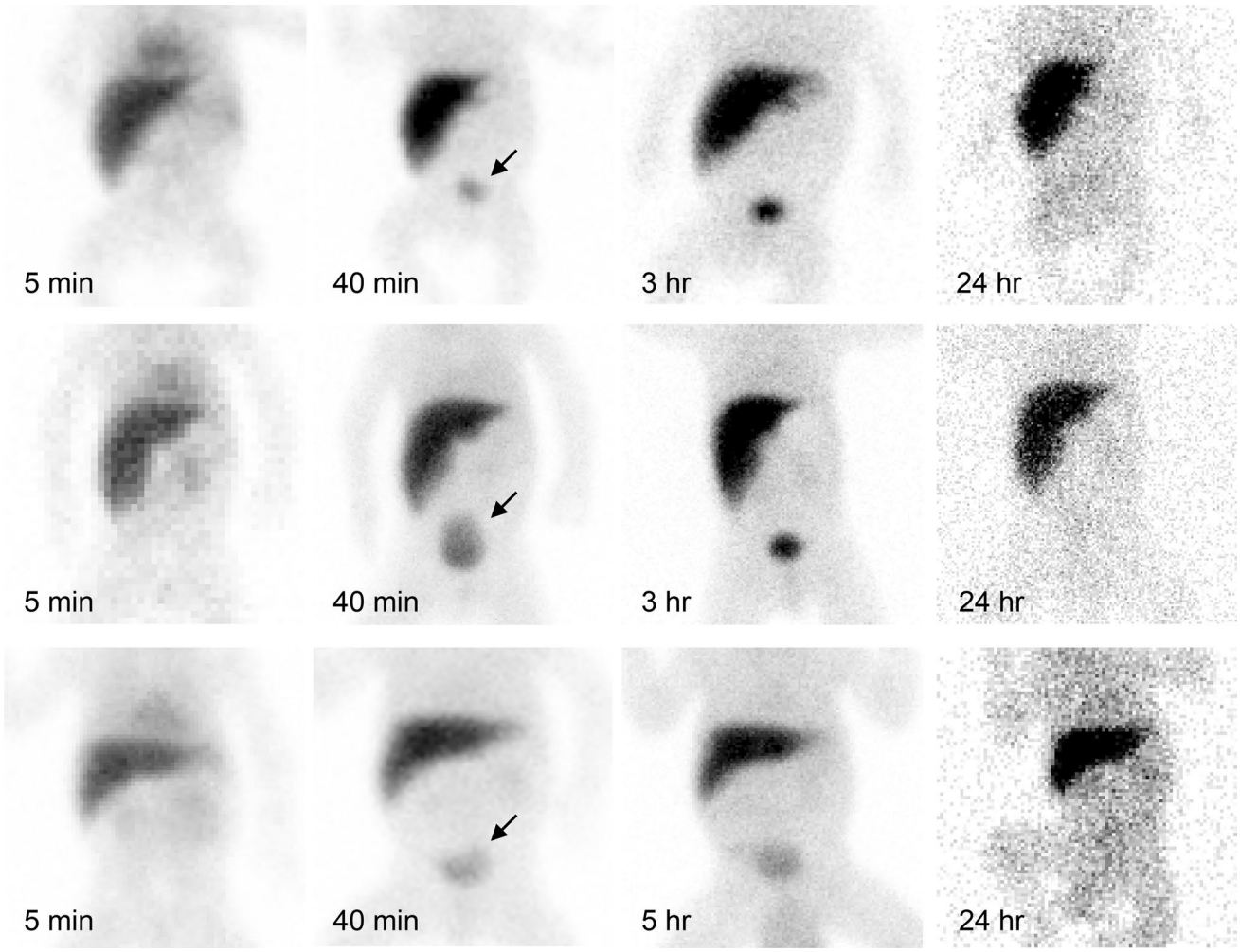

Fig. 3 False-positive cases of ^{99m}Tc-PMT scintigraphy. Patient 1 is a 140-day-old infant (top). Patient 2 is a 97-day-old infant (middle). Patient 3 is a 40-day-old infant (bottom). In all cases, ^{99m}Tc-PMT tracer showed normal uptake in the liver within 5 min after injection, then no intestinal excretion were visualized till 24 h. By contrast, ^{99m}Tc-PMT tracer was excreted in the bladder at an early stage (black arrows represents bladders). *PMT N*-pyridoxyl-5-methyl-tryptophan

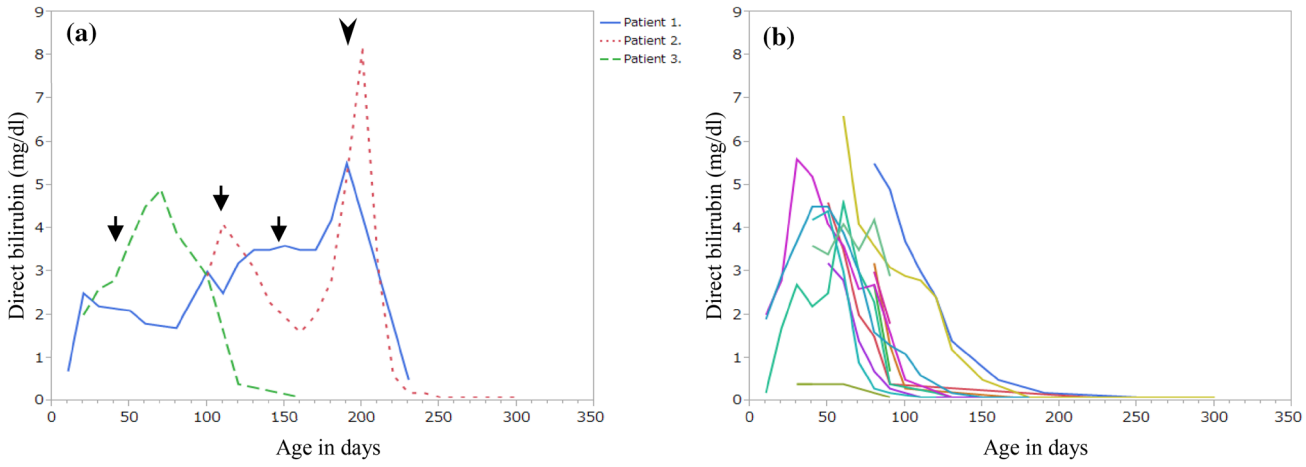

Fig. 4 Direct bilirubin levels of non-BA infants. **a** 3 infants with false positives of ^{99m}Tc-PMT scintigraphy, **b** 14 infants with true negatives of ^{99m}Tc-PMT scintigraphy. Black arrows indicate the days when infants were performed ^{99m}Tc-PMT scintigraphy. The arrowhead represents the day when patient 2 was operated with liver transplantation. *BA* biliary atresia, *PMT N*-pyridoxyl-5-methyl-tryptophan

Table 3 Other examination results of infants with false positive by ^{99m}Tc-PMT scintigraphy

	Patient 1	Patient 2	Patient 3
Age	140 days	97 days	40 days
Final diagnosis	Neonatal hepatitis	Hepatitis of unknown origin	Neonatal hepatitis
Stool color change	Positive	Positive	Positive
Total bilirubin	5.0	6.2	7.3
Direct bilirubin	3.6	2.9	3.7
AST	71	103	201
γ-GTP	95	62	38

PMT N-pyridoxyl-5-methyl-tryptophan

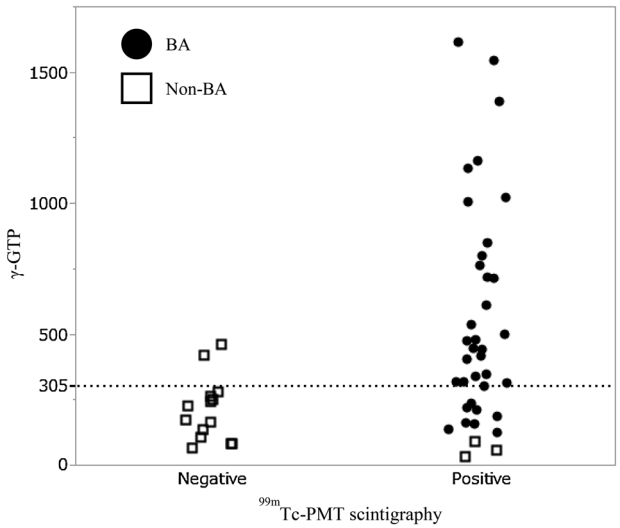

Fig. 5 ^{99m}Tc-PMT scintigraphy and γ-GTP visualized on a 2-dimensional plot. Each dot represents a single patient, color coded as BA or non-BA. The single horizontal dashed line on *y*-axis (305 U/L) corresponds to γ-GTP's cutoff value based on the ROC curve to show the highest accuracy for the differentiation between BA and non-BA. *PMT N*-pyridoxyl-5-methyl-tryptophan, *BA* biliary atresia, *ROC* receiver-operating characteristic

diagnosis of BA using ^{99m}Tc-PMT scintigraphy and γ-GTP is shown in Fig. 6.

Discussion

Hepatobiliary scintigraphy performs well in differentiating BA from non-BA. The usage of ^{99m}Tc-IDA derivatives scintigraphy in diagnosing BA was previously reported [8, 9]. In contrast, diagnosing BA in infants using ^{99m}Tc-PMT scintigraphy has not been reported. Thus, we attempted to clarify the usefulness of ^{99m}Tc-PMT scintigraphy in the diagnosis of BA.

In our study including 52 infants, univariate analysis identified 6 features (stool color change, total bilirubin, direct bilirubin, AST, γ-GTP and ^{99m}Tc-PMT scintigraphy) that were significantly different between BA and non-BA. Multivariate logistic regression analysis indicated that ^{99m}Tc-PMT scintigraphy and γ-GTP were independent predictors of BA.

Γ-GTP is localized to the bile canaliculi near portal areas [16]. Γ-GTP is released into the circulation if the bile duct is damaged [17]. Liu et al. [18] reported that γ-GTP > 300 U/L had an accuracy of 85% for the diagnosis of BA. El-Guindi et al. [19] found that γ-GTP at a cutoff of > 286 U/L has 76.7% sensitivity and 80% specificity for the discrimination of BA. In our study, γ-GTP at a cutoff ≧ 305 U/L had a sensitivity of 77.1%, a specificity of 88.2% and accuracy of 80.8%, respectively. Chen et al. reported that the area under the ROC curve (AUC) of total bilirubin, direct bilirubin and γ-GTP was 0.584, 0.614 and 0.843, respectively [20]. Γ-GTP had a highest AUC than other biochemical tests. Our results also indicated that γ-GTP had a higher AUC than total bilirubin, direct bilirubin and AST (γ-GTP; 0.86, total bilirubin; 0.79, direct bilirubin; 0.83, AST; 0.70). Γ-GTP is a non-invasive and helpful diagnostic marker for the diagnosis of BA. In particular, γ-GTP has a few false positives. In other words, there are few infants with high γ-GTP among non-BA.

In our study, ^{99m}Tc-PMT scintigraphy had a high sensitivity (100%), a high specificity (82.4%) and a high accuracy (94.2%). It had a higher accuracy than other clinical and investigational parameters in the diagnosis of BA. The diagnostic rate of ^{99m}Tc-diethyl-IDA or ^{99m}Tc-diisopropyl-IDA scintigraphy for BA was reported by Gerhold et al. [4] as 91% accuracy, 97% sensitivity and 82% specificity. Lin et al. also [21] reported a high sensitivity (100%), specificity (87.5%) and accuracy (90.5%) of ^{99m}Tc-diisopropyl-IDA scintigraphy in differentiating BA from other forms of neonatal jaundice, very similar to our current study results. It is expected that ^{99m}Tc-PMT and ^{99m}Tc-IDA derivatives have almost the same pharmacokinetics: rapid blood clearance, fast hepatobiliary transit, low urinary excretion and no intestinal reabsorption. Additionally, ^{99m}Tc-PMT has the advantage that it is much more resistant to high bilirubin levels (close to 20 mg/dl) than ^{99m}Tc-IDA derivatives [6]. Several studies, however, did not find hepatobiliary scintigraphy to be a very specific test. In a large meta-analysis, Kianifar et al. [9] reported a sensitivity of hepatobiliary scintigraphy for the diagnosis of BA between 98.1 and 99.2% and the specificity from 68.5 to 77.2% in ^{99m}Tc-IDA derivatives. Park et al. [22] reported a sensitivity (96.0%), the specificity (35.0%) and the accuracy (56.0%) of ^{99m}Tc-diisopropyl-IDA scintigraphy in differentiating BA from other forms of neonatal jaundice. The majority of these studies did not utilize

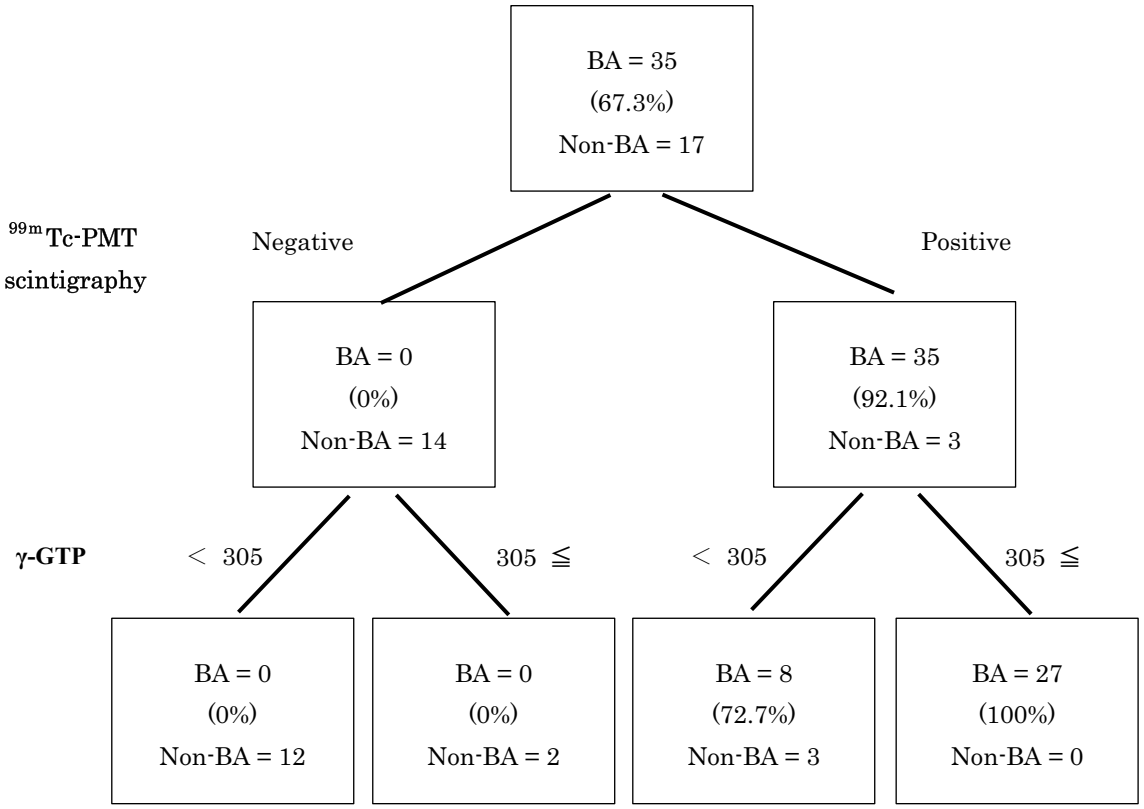

Fig. 6 Criteria for diagnosis of BA using ^{99m}Tc-PMT scintigraphy and γ-GTP. BA could be rejected in infants regardless of γ-GTP level if ^{99m}Tc-PMT scintigraphy was negative. BA was diagnosed in infants with positive ^{99m}Tc-PMT scintigraphy, only when γ-GTP was high (≧ 305 U/L). When γ-GTP was low (< 305 U/L) and ^{99m}Tc-PMT scintigraphy was positive, most of the cases were BA with a few non-BA exceptions. *BA* biliary atresia, *PMT N*-pyridoxyl-5-methyl-tryptophan

hepatic uptake as a parameter in interpretation and calculation of results, although some of them did record the uptake. In some of these studies, the variability in results could also be related to differences in the patient group selection.

In this study, there were no cases of false negatives (excretion of the tracer into the bowel despite BA). Kianifar et al. [9] also mention false-negative results are extremely rare. It is very probable that these false-negative results were misinterpretations of the scan. Verreault et al. [23] who reported two false-negative results that were caused by urine contamination interpreted as bowel excretion. In contrast, there were three cases of false positives for BA in our study. Two infants of them were diagnosed with neonatal hepatitis and improved over time. One of them was diagnosed with hepatitis of unknown cause and he needed a liver transplant later. In hepatobiliary scintigraphy, severe neonatal hepatitis causes no excretion of tracer and bowel non-visualization. This means that false-positive results are the major shortcoming of ^{99m}Tc-PMT scintigraphy. Γ-GTP monitoring may help to solve this problem. Normally, γ-GTP of BA infants was statistically higher than those of non-BA. The optimal cut-point values of γ-GTP in the diagnosis of BA were 305 U/L in our study. On the other hand, all infants with false positives in ^{99m}Tc-PMT scintigraphy had γ-GTP lower than the optimal cutoff levels for BA. However, the distinction between non-BA infants with false positive by ^{99m}Tc-PMT scintigraphy and BA infants with low γ-GTP (< 305) might be rather difficult to determine. The results of non-BA infants with false positive by ^{99m}Tc-PMT scintigraphy and BA infants with low γ-GTP (< 305) are presented in Table 4. Γ-GTP was significantly lower in non-BA infants with false positive than in BA infants with low γ-GTP. Bilirubin levels also tended to be lower in non-BA infants with false positive than in BA infants with low γ-GTP, although bilirubin levels were not statistically significantly different. The reason remains uncertain but total bile acid was higher in non-BA infants with false positive. In the cases with positive ^{99m}Tc-PMT scintigraphy and especially low γ-GTP, it may be better to follow-up clinical symptoms and biochemical tests without immediately conducting invasive tests to distinguish between BA and non-BA.

Among biochemical tests, only γ-GTP was useful in multivariate analysis of this study and bilirubin levels and AST were also useful instruments in distinguishing between BA and non-BA in univariate analysis. In contrast, albumin, total bile duct, ALT and ALP were not

Table 4 Patient characteristics of non-BA infants with false positive by ^{99m}Tc-PMT scintigraphy and BA infants with low γ-GTP (< 305)

	Non-BA infants with false positive of PMT ($n=3$)	BA infants with low γ-GTP (< 305) ($n=8$)	p*
Male	3 (100%)	2 (25.0%)	NS
Age (day)	97.0 (40.0–14.0)	55.0 (42.0–58.0)	NS
Jaundice	3 (100%)	8 (100%)	NS
Stool color change	3 (100%)	7 (87.5%)	NS
Albumin	3.7 (2.6–4.3)	4.1 (3.4–4.4)	NS
Total bilirubin	6.2 (5.0–7.3)	9.0 (8.3–10.9)	NS
Direct bilirubin	3.6 (2.9–3.7)	5.3 (3.6–7.5)	NS
Indirect bilirubin	3.3 (1.4–3.6)	3.5 (3.4–4.6)	NS
Total bile acid	182.9 (147.6–356.9)	110.4 (85.6–138.7)	0.0189
AST	103.0 (71.0–201.0)	153.5 (90.0–220.5)	NS
ALT	59.0 (33.0–108.0)	113.5 (56.5–175.5)	NS
γ-GTP	62.0 (38.0–95.0)	177.0 (144.8–220.5)	0.0189
ALP	2156.0 (1975.0–2807.0)	1782.5 (1619.0–2851.0)	NS
Ultrasonography	2 (66.7%)	8 (100.0%)	NS
^{99m}Tc-PMT scintigraphy	3 (100%)	8 (100.0%)	NS

The number of patients is followed by the percentage in parentheses. Continuous variables are presented as the median (inter-quartile range). *NS* not significant ($p \geqq 0.05$); $p < 0.05$ (significant)

BA biliary atresia, *PMT N*-pyridoxyl-5-methyl-tryptophan, *γ-GTP* γ-glutamyl transferase, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *ALP* alkaline phosphatase

*Fisher's exact test or Mann–Whitney *U* test

significantly different from BA and non-BA in univariate analysis. In previous studies, there are reports that albumin, total bile acid, ALT and ALP were both useful and unhelpful for the diagnosis of BA [20, 24–26]. The discrepancy in the results could be due to differences such as age or severity in the patient group selection. It might be better to combine some biochemical tests such as γ-GTP and bilirubin levels to diagnose BA correctly.

Our study has some limitations. First, it was retrospective. However, the lack of other prospective studies justify it. Second, the sample size was relatively small. However, the study period covered over 17 years. Third, we only used planar images and were not able to evaluate SPECT/CT images in this study. Although SPECT/CT images offers opportunity to add the more diagnostic information than planer images [27], radiation exposure is higher with SPECT/CT images than planar images. Considering patients age, we do not evaluate SPECT/CT to minimize radiation dose at our hospital. In cases without intestinal excretion of ^{99m}Tc-PMT, adding SPECT/CT images may reduce false positives of ^{99m}Tc-PMT since SPECT/CT has increased the detectability of intestinal activity. Quantitative methods of hepatobiliary scintigraphy such as hepatic clearance will add information to help differentiate BA, and it is useful for determining the degree of liver dysfunction semi-quantitatively [28]. Although we are unable to quantitatively evaluate ^{99m}Tc-PMT scintigraphy at our hospital, knowing the potential difference hepatic clearance in BA/non-BA cases is highly desirable. Further studies are required to answer this issue.

Conclusion

We showed that ^{99m}Tc-PMT scintigraphy was a more accurate method of BA diagnosis in infants than other conventional examinations. ^{99m}Tc-PMT scintigraphy should, therefore, be actively considered if BA is suspected. In addition, false positives of ^{99m}Tc-PMT scintigraphy could be reduced by combining γ-GTP level monitoring.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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