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RESEARCH ARTICLE

The value of radionuclide hepatobiliary scintigraphy in combination with determination of bilirubin from duodenal drainage in differential diagnosis of infantile persistent jaundice

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Abstract The aim of this study was to investigate the value of technetium etifenin injection (^{99m}Tc-EHIDA) hepatobiliary scintigraphy in combination with determination of bilirubin from duodenal drainage in differential diagnosis between infantile hepatitis syndrome and biliary atresia. ^{99m}Tc-EHIDA hepatobiliary scintigraphy in combination with duodenal fluid examination was used for evaluation in 84 infants with persistent infantile jaundice. For diagnosing biliary atresia, the sensitivity and specificity of scintigraphy were 100% and 74.5%, respectively; the sensitivity and specificity of scintigraphy in combination with duodenal fluid examination were 100% and 100%, respectively. In conclusion, hepatobiliary scintigraphy, which is a noninvasive, safe, valuable examination method, in combination with examination of duodenal fluid, is of value for the differential diagnosis between infantile hepatitis syndrome and biliary atresia.

Keywords jaundice; radionuclide hepatobiliary scintigraphy; duodenal drainage

1 Introduction

Congenital extrahepatic biliary atresia (EHBA) and infantile hepatitis syndrome (IHS) are two major causes of infantile persistent obstructive jaundice, but the treatment plans are completely different. Therefore, early diagnosis plays an important role in guiding treatment and recovery process. Since October 2004, we have conducted technetium etifenin injection (^{99m}Tc-EHIDA) hepatobiliary scintigraphy in combination with duodenal fluid examination in 84 infants with persistent infantile jaundice, followed by surgical pathology and clinical follow-up confirmation. The purpose of analyzing diagnostic results is to further explore the combined value of ^{99m}Tc-EHIDA hepatobiliary scintigraphy and duodenal fluid examination in infants with persistent infantile jaundice.

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2 Materials and methods

2.1 Clinical data

Between Oct. 2004 and Oct. 2008, 84 infants with persistent infantile jaundice underwent ^{99m}Tc-EHIDA hepatobiliary scintigraphy and duodenal fluid examination. Among them, 54 were male and 30 were female. Their ages varied from 15 to 90 days. Twenty-two cases were between 15 and 28 days old, 42 cases between 29 and 60 days, and 20 cases between 61 and 90 days. All infants have the following in common: (1) jaundice appeared, persisted and progressed during the first two months after birth; (2) total serum bilirubin value increased and dominated by the increase of direct bilirubin; (3) symptoms of liver pathology (hepatomegaly, abnormal hepatic texture); (4) light yellow or white stool; (5) congenital genetic metabolic diseases, sepsis, or choledochal cyst was excluded after screening. Before hepatobiliary scintigraphy, a detailed medical record was prepared, and laboratory examination was performed.

2.2 Methods

2.2.1 Hepatobiliary scintigraphy

Food and drink were forbidden to the patients 4–6 h prior to the hepatobiliary scintigraphy. After liquid intravenous

injection, if the patients kept crying, 10% chloral hydrate was given. The patients lied down on an even surface and were injected with ^{99m}Tc-EHIDA 74MBq. Hepatobiliary scintigraphy was performed with single photon emission computed tomography (SPECT) (GE-Starcam XR/T 4000) (60 s per frame, 30 frames totally). The matrix size was 128 × 128, and magnification 1.33. Static imaging was performed for 1 h. If no intestinal radioactivity was observed after one hour, further delayed static imaging would be done at the 2nd, 4th, 8th, 12th and 24th h. Hepatobiliary appearance and intestinal excretion of radionuclides were observed. If intestinal radioactivity appeared, stop imaging. In order to eliminate urine contamination, imaging of lateral and posterior sides could be added according to the circumstances.

2.2.2 Dynamic duodenal drainage

Infantile duodenal drainage tube (ZL. 97241165. 8) was applied following the procedures as described previously [1]: (1) food and drink were forbidden for 4 h before duodenal drainage. Intravenous infusion was then done; (2) if patients kept crying during the intubation, 10% chloral hydrate was given to them; and (3) the patients lied on their right side, and their heads maintained fixed posture helped by assistants. The operator needed to prepare one-off duodenal drainage tube. A little liquid paraffin was applied on the head, and the plug at the end of the drainage tube was opened. The drainage tube was slowly inserted from the right side of the head into the nasal cavity, through the nasopharynx and esophagus into the stomach. The depth was 30–35 cm. Gastric juice could be seen automatically outflowing from the tube. And then the drainage tube was inserted through the pylorus into the duodenum, with a depth being 40–45 cm. The color of the duodenal fluid in the drainage tube was observed. If the duodenal juice was yellow, or through fluoroscopy, it was found that the head of the drainage tube was in the lower portion of the duodenum, the intubation was successful. If no bile was found, the drainage tube would be kept for 24 h. If there was still no bile, intermittent drainage would be performed for another 48–72 h. During the process of drainage, breast-feeding was still on schedule. Following treatment was needed, if still no bile was found.

2.2.3 Comprehensive analysis of the two examination results

If intestinal radioactivity appeared, bile outflowed by duodenal drainage, and jaundice faded away, IHS was confirmed; while EHBA was confirmed by no intestinal radioactivity or no bile in duodenal drainage examination, the final diagnosis was made after switching to surgery. Twenty-nine cases were diagnosed of EHBA by surgery, and 55 cases diagnosed of IHS by jaundice extinction afterwards.

3 Results

3.1 Radionuclide hepatobiliary scintigraphy

Examination results were achieved by co-diagnosis of two doctors. Among 84 infants with persistent jaundice, 29 cases were EHBA positive, and no intestinal radiological imaging appeared (Fig. 1). Among 55 infants with IHS, 41 cases were EHBA negative, and hepatobiliary scintigraphy showed radioactive imaging in gallbladder and intestine (Fig. 2). Fourteen cases were false positive, and no radioactive imaging in gallbladder and intestine appeared.

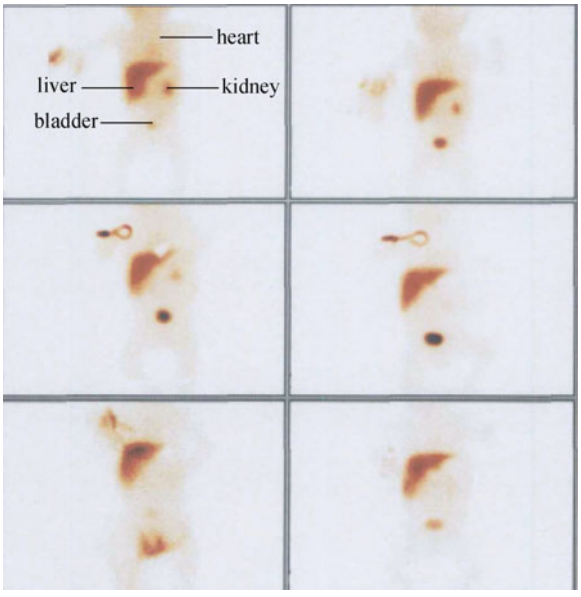

Fig. 1 Images of extrahepatic biliary atresia. It shows radiological imaging in liver, heart and kidney but no radiological imaging in gallbladder or intestine.

3.2 The results of dynamic duodenal drainage

Among 29 infants with EHBA, 26 of them have white duodenal fluid and no bilirubin. In the other three cases, the color of duodenal fluid was light yellow alternating with white, and the bilirubin was less than 8.5 μmol/ L. Among 55 infants with IHS, 41 cases with negative results in hepatobiliary scintigraphy had yellow or light yellow duodenal fluid, and the bilirubin was greater than 30 μmol/L; 14 cases with a false-positive result had light yellow or white duodenal fluid, and the bilirubin was between 8.5 μmol/L and 30 μmol/ L.

3.3 Diagnosis performance

The sensitivity of diagnosing EHBA with ^{99m}Tc-EHIDA hepatobiliary scintigraphy was 100% (29/29), the diagnostic specificity 74.5% (41/55), and the accuracy 83.3%

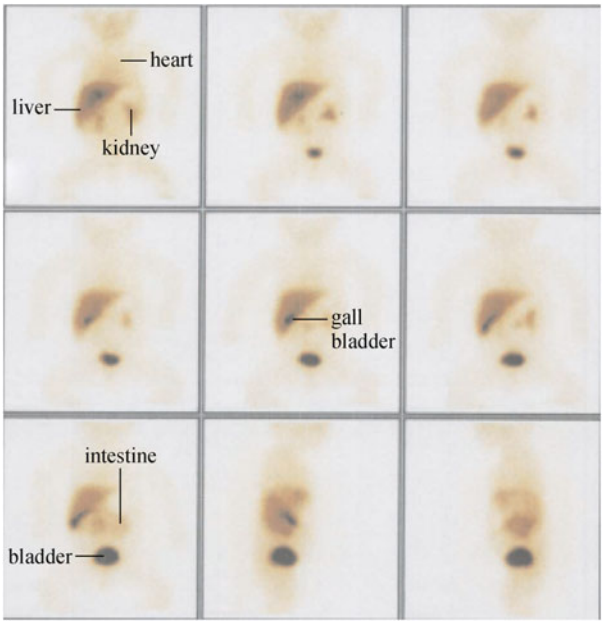

Fig. 2 Images of infantile hepatitis syndrome. It shows radiological imaging in liver, heart, kidney, gallbladder and intestine.

(70/84). The sensitivity of diagnosing EHBA through determination of bilirubin from duodenal drainage was 89.7% (26/29), the diagnostic specificity 100% (55/55), and the accuracy 96.4% (81/84). The sensitivity of diagnosing EHBA through radionuclide hepatobiliary scintigraphy in combination with determination of bilirubin from duodenal drainage was 100% (29/29), the diagnostic specificity 100% (55/55), and the accuracy 100% (84/84).

4 Discussion

Early differential diagnosis of IHS and EHBA is very important [2]. For IHS, surgical trauma can be avoided. Early operation for EHBA can reconstruct biliary passage, restore bile flow and promote recovery. Although a large number of examination methods have been applied to differential diagnosis of IHS and EHBA, with the limitations of laboratory equipment and inspection technology, the high cost and traumatic nature, sometimes, examination results overlap. Low accuracy and large variation limit wide clinical application. Therefore, it is very necessary to search for a simple, practical, non-invasive and economical method.

A lot of comparative studies showed that hepatobiliary dynamic imaging was an easy and non-invasive dynamic examination method in a physiological state. It has a great advantage in clinical application for persistent jaundice, especially in diagnosis and differential diagnosis of IHS and EHBA [3]. The principle of radionuclide hepatobiliary imaging is that the ^{99m}Tc-IDA derivative compounds can be taken from blood by liver cells and then released into capillary bile ducts and exported to intestine through the biliary system together with the bile. As a tracer, it enables biliary system imaging. Because an imaging agent cannot enter into the intestine through the biliary system in the case of biliary atresia, the gallbladder and intestine show no radioactivity. EHIDA is the most commonly used IDA imaging agent compound. It clears fast from blood, excretes less through kidney and is less affected by the serum bilirubin concentration. Nadel [4], Charearnrad [5], and Esmaili [6] reported that the accuracy of ^{99m}Tc-EHIDA hepatobiliary imaging can be higher than 95%. The current study showed that the sensitivity, specificity, and accuracy of ^{99m}Tc-EHIDA hepatobiliary imaging in diagnosing biliary atresia were 100%, 74.5%, and 83.3%, respectively. Compared with literature reports, the sensitivity in this study is the same, but the specificity and accuracy are lower [7]. In our results, among 55 infants with IHS diagnosed by ^{99m}Tc-EHIDA hepatobiliary imaging, 14 cases had no sign of biliary tract imaging. These infants shared the following characteristics in common: (1) concentration of bilirubin in blood $>$ 102 μmol/ L; (2) severe liver damage and cholestasis; (3) low bilirubin concentration in duodenal fluid; (4) the pathogen consists primarily of cytomegalovirus (CMV); and (5) swelling liver with obvious change in texture. From the above analysis, the main limitations of hepatobiliary imaging are as follows: (1) in some cholestatic IHS, the intake function of liver cells is good, but bile duct has severe inflammation and even obstruction. The excretion of the imaging agent with bile is little, and it is difficult to distinguish images. (2) In IHS, especially in CMV hepatitis [8,9], the high concentration of serum bilirubin and severe damage of liver cells result in poor intake function of liver cells and lead to blurred liver imaging. Furthermore, it is easier for imaging agents to excrete through the urinary system, and intestinal radioactive excretion is little. All these lead to the degradation of the capability of intestinal radioactive imaging and the false negative of IHS. In order to enhance the differential diagnosis value of ^{99m}Tc-EHIDA hepatobiliary imaging, bile excretion was promoted through taking phenobarbital orally, which is called the phenobarbital trial. One week later, hepatobiliary imaging was reexamined to exclude IHS. This method can improve the diagnostic specificity; however, it prolongs the time of diagnosis and treatment [4]. Researchers also proposed to use an imaging agent with high anti-bilirubin ability (e.g. ^{99m}Tc-mebrofenin), as one of the methods to optimize the quality of the image [10].

The value of observing the color of duodenal juice has been proven in differential diagnosis of EHBA and IHS [11,12]. This study demonstrated that dynamic observation of the color of duodenal fluid and quantitative determination of bilirubin could better reflect bile secretion of liver cells and patency of the biliary tract. The first two colors (yellow and light yellow) confirmed the patency of the

biliary tract; light yellow and white colors showed that the degree of swelling, degeneration, and necrosis in liver cells were severe, and cholestasis occurred in cholangioles of intra-liver, which obstructed bile excretion and reduced bile flow, resulting in light yellow or white stool. When lesions of liver cells improved, bile flow increased, and duodenal fluid and stool turned yellow. It was observed during the drainage process that duodenal fluid maintained white for a long period of time in some cholestatic IHS. After several days or weeks, duodenal fluid changed from white to yellow. Based on this, the color of duodenal fluid, bilirubin level and stool color were correlated to lesions of liver cells and severity of cholestasis. Therefore, dynamic and persistent examination of duodenal fluid is very important.

This study showed that ^{99m}Tc-EHIDA hepatobiliary imaging was a non-invasive, safe and effective method. It was of high clinical value to the differential diagnosis of IHS and EHBA. But due to its own limitations, some infants with IHS and severe cholestasis were likely to be misdiagnosed with EHBA. Therefore, we believe that ^{99m}Tc-EHIDA hepatobiliary imaging combined with dynamic duodenal fluid examination for the early differential diagnosis of IHS and EHBA has a significant clinical value.

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