MR Cholangiography and Dynamic Examination of Duodenal Fluid in the Differential Diagnosis between Extrahepatic Biliary Atresia and Infantile Hepatitis Syndrome

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Summary: In order to evaluate the value of magnetic resonance cholangiography (MRC) and dynamic examination of duodenal fluid in the differential diagnosis between extrahepatic biliary atresia (EHBA) and infantile hepatitis syndrome (IHS), 52 patients with infantile cholestatic jaundice were examined by MRC and duodenal fluid examination. Original interpretations were compared with clinical outcome. Calculated sensitivity of duodenal fluid examination in diagnosis of EHBA was 100 %, and specificity was 91.1 %. Sensitivity of MRC in the diagnosis of EHBA was 94.4 % and specificity 88.24 %. The sensitivity of MRC and examination of duodenal fluid combined in diagnosis of EHBA was 94.4 % and specificity 97.06 %. We are led to conclude that MRC and dynamic examination of duodenal fluid are useful in the differential diagnosis between IHS and EHBA and the combined use of the two techniques yield better resutls.

Key words: magnetic resonance cholangiography; duodenal fluid examination; infant; biliary atresia
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The common causes of infantile persistent cholestatic jaundice are infantile hepatitis syndrome (IHS) and extrahepatic biliary atresia (EHBA)[1]. The differential diagnosis between IHS and EHBA is very difficult because there is considerable clinical, biochemical, and histopathologic overlaps between them. Magnetic resonance cholangiography (MRC) is a newly-established non-invasive modality used for the diagnosis of EHBA in infants. Their results varied on the accuracy, sensitivity and specificity of MRC in the diagnosis of EHBA[2–4]. The examination of duodenal fluid can show whether there is bile directly coming from the biliary duct, but the result may be affected by intubation technique and the severity of liver lesions and cholestasis. In order to evaluate the value of MRC and dynamic examination of duodenal fluid in the differential diagnosis between EHBA and IHS, we analyzed 52 infants with persistent cholestatic jaundice who had undergone MRC and dynamic examination of duodenal fluid.

1 MATERIALS AND METHODS

1.1 Patients

Included in the study were 52 patients with infantile cholestatic jaundice (29 males, 23 females, with age ranging from 15 to 90 days). Clinically, these patients had light or acholic stools, hepatomegaly with or without the increase in firmness, prolonged or progressive conjugated hyperbilirubinemia that occurred in the first 2 months after birth. In this study, prolonged conjugated hyperbilirubinemia was defined as a total serum bilirubin level of more than 51 μmol/L with direct form more than 40 % of the total (normal values: 3.4–17.1 μmol/L and 0–3.4 μmol/L, respectively). The patients were excluded from this study if laboratory tests and abdominal ultrasonography brought up the likelihood of diagnosis of organic aciduria, glycogen storage disease, galactosemia, α_1-antitrypsin deficiency, and choledochal cysts.

1.2 MRC

The patients were fasted for 6 h before MRC. All MRCs were performed after sedation by oral administration of chloral hydrate at 50–60 mg/kg body weight. Examinations were then performed with a 1.5T MR imaging unit (Signal CVi; GE Medical Systems, USA). Images were obtained in axial plane and MR imaging sequences included a T_1-weighted, SE sequence (400/8 ms, TR/TE); a T2-weighted, FSE sequence (3000/80 ms, TR/TE) and fat-suppressed sequence (slice thickness: 5 mm; slice gap: 0 mm; FOV: 180 mm; matrix: 256×256; NEX: 4; scan time: 5 min). MRC was performed with a T_2-weighted single-shot fast SE sequence (2049/1146, TR/TE; slice thickness: 50 or 30 mm; slice gap: 0 mm; FOV: 340 mm; matrix: 384×256; NEX: 0.5; scan time: 2 s) both in axial plane and oblique-coronal plane. Any finding was taken as EHBA if either common hepatic duct or common bile duct could not be delineated (fig. 1). A finding was taken IHS if common hepatic duct and common bile duct could be clearly displayed (fig. 2).

1.3 Duodenal Intubation and Collection of Duodenal Fluid

A special duodenal drainage catheter for infants (Patent no. ZL97241165.8) was inserted via the nostril to

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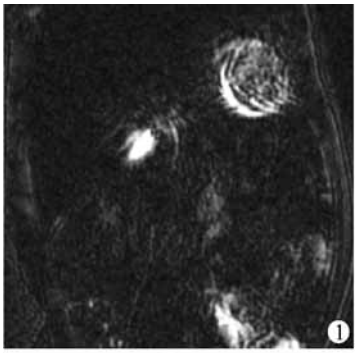

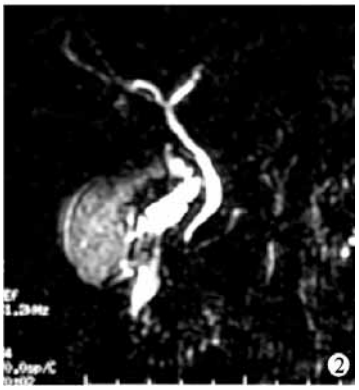

Fig. 1 MR cholangiogram in an infant with EHBA
No bile ducts were visualized

Fig. 2 MR cholangiogram in a male infant with IHS
All bile ducts were visualized

the duodenum of the patients. Before duodenum drainage, the patients were fasted for 4 h and were under intravenous support with a 5 % dextrose-saline solution (120 mL/kg per day). Chloral hydrate at 50–60 mg/ kg body weight was administered orally or diazepam at 0.5–1 mg/kg body weight was given intravenously if the patients cried when intubation was performed. The catheter, with its end open, was slowly introduced into the third portion of the duodenum through nostril, pharynx, esophagus and stomach. When the catheter went into stomach (the depth is about 30–35 cm), gastric juice came out of the tube. When the tube reached duodenum (the depth was about 40–45 cm), a yellow duodenal fluid came out. Correct positioning was verified by the change of the color of the fluid or by abdominal radiography. In all patients the visual evaluation of the duodenal fluid flow was performed by one of the clinicians involved. The duodenal fluid was collected by gravity drainage. Specimens were separated into two-hour aliquots. Two milliliters of duodenal fluid was sent for biochemical examination. If no drainage fluid was constantly of white color, 2–3 more specimens were collected for the biochemical examination depending on the changes of the color of duodenal fluid. The bile was considered to be positive when a yellow biliary duodenal fluid was observed and the examination of duodenal fluid showed total bilirubin is beyond 8.5 μmol/L. When no yellow biliary duodenal fluid was observed, the fluid was collected intermittently for another 24 h and, if it was negative, the result was taken as negative. Breast feeding was given to the patients every 3 h. IHS diagnosis could be established if patient's duodenal fluid contained bile while EHBA diagnosis could be made if the fluid contained no bile.

1.4 The Diagnostic Criteria of EHBA and IHS with Above Two Methods Combined

The diagnosis of IHS can be established if both common bile duct and common hepatic duct are visualized, and duodenal fluid contains bile. Diagnosis of EH BA can be made if either common bile duct or common hepatic duct is not visualized and duodenal fluid contains no bile. The gold standard for EHBA diagnosis is obstruction of the biliary tract as confirmed by surgery and the gold standard for IHS diagnosis was jaundice resolution as confirmed by clinical follow-up.

2 RESULTS

2.1 MRC

In the 18 patients with EHBA, common hepatic duct or common bile duct were not display by MRC. Among those patients, 12 had a small gallbladder, and 1 had a big gallbladder. In 30 of the 34 patients with IHS, MRC clearly showed common hepatic duct and common bile duct. In 2 patients with IHS, neither common bile duct nor common hepatic duct were visualized, only smaller gallbladder was depicted. In the other 2 patients, either common bile duct or common hepatic duct was not depicted.

2.2 Examination of Duodenal Fluid

In 16 of the 18 patients with EHBA, the duodenal fluid contained no bile, and in the remaining 2 cases, their duodenal fluid contained only minimal bilirubin (TB: 0.4 μmol/L and 0.6 μmol/L, respectively) and their bile acid was negative. In 31 of 34 IHS patients, their duodenal fluid contained bilirubin (22.2–223 μmol/L) and bile acid. Minimal bilirubin (0.6–1.2 μmol/L) was detected in the duodenal fluid in 3 of the 34 patients with IHS, and their duodenal fluid contained no bile acid and the fluid was of white color. After treatment for 1 to 2 weeks, another duodenal drainage was performed in these 3 patients and examination of duodenal fluid showed that their duodenal fluid contained bilirubin (>46 μmol/L) and bile acid, and the duodenal fluid turned yellow.

2.3 Comparison among MRC, Duodenal Fluid Examination and MRC in Combination with Duodenal Fluid Examination for the Diagnosis of EHBA

Fourfold table analysis showed that the sensitivity of MRC was 94.4 % and specificity was 88.24 %. The sensitivity of duodenal fluid examination was 100 % and specificity was 91.1 %. The sensitivity of MRC in combination with duodenal fluid examination for the diagnosis of EHBA was 97.06 % and the specificity was 94.4 %.

3 DISCUSSION

The accurate and prompt differentiation between IHS and EHBA is a challenge for pediatrician and pediatric gastroenterologist. For IHS patients, the early accurate diagnosis can help avoid unnecessary surgery and for EHBA patients, prompt surgical treatment can start as soon as possible. A number of diagnostic techniques, including hepatobiliary ultrasonography (US)[5], ^{99}Tcm-EHIDA hepatobiliary scintigraphy[6], and endoscopic retrograde cholangiopancreatography[7] have been

used for the diagnosis of infantile cholestatic jaundice. Hepatobiliary US is the earliest non-invasive imageologic investigation for cholestatic jaundice in the infants but cannot reliably identify all causes. Hepatobilairy scintigraphy has very high sensitivity for the diagnosis of EHBA, but it has low specificity and requires cautious interpretation. ERCP has very high sensitivity and specificity in the differential diagnosis of infantile cholestatic jaundice. But it is invasive and sometimes can cause severe complications such as hemorrhage, retrograde infection, pancreatitis and perforation. These limit it application in clinical practice. So some less or non-invasive modalities should be used in the differential diagnosis of EHBA and IHS.

It has been known that bile is of yellow color because of bilirubin in it. The duodenal fluid becomes yellow when bilirubin is secreted into duodenum through the patent biliary tree. Therefore, we can differentiate EHBA and IHS by the presence of bile in duodenal fluid by using conventional duodenal drainage[8, 9]. Duodenal fluid may assume one of the three colors: yellow, light yellow, and white. The presence of yellow and light yellow bile found in duodenal fluid examination can directly confirm the patency of the biliary ducts. The white bile indicates either severe intrahepatic cholestasis or extrahepatic biliary atresia. In our series, the duodenal fluid of the 18 patients with EHBA contained no bile. On the other hand, the duodenal fluid of 31 of the 34 IHS patients were bile-positive and those of the other three were bile-negative. The sensitivity of duodenal fluid examination for the diagnosis of EHBA was 100 % and specificity was 91.1 %. These demonstrated the examination of duodenal fluid could be used in the diagnosis of EHBA. But with this technique, severe cholestatic IHS might be mistaken for EHBA in some cases. In 3 IHS patients with severe cholestatic jaundice, the first-time duodenal fluid examination revealed no bile. After 1–2 week treatment, the second examination showed presence of bile in duodenal fluid. So we are led to conclude that the color and the concentration of bilirubin of the duodenal fluid in IHS are parallel to the degree of liver damage and cholestasis and that the color of the duodenal fluid became yellow gradually with the recovery of liver damage. Dynamic examination of duodenal fluid can help to minimize possibility of misdiagnosis of EHBA.

MRC is imaging technique in which strongly T2-weighted images are used to depict the bile, which is identified by means of its high-intensity signal. The typical MRC image of IHS is the partial visualization of intrahepatic ducts and visualization of the whole extrahepatic ducts including gallbladder, common bile duct and common hepatic duct and the typical MRC image of EHBA is the failure of visualization of either common bile duct or common hepatic duct. Our present study demonstrated that either common bile duct or common hepatic duct was visualized in all of the 18 patients with EHBA, but one had a big gallbladder. The diagnostic sensitivity of MRC for EHBA was 94.4 % and the specificity was 88.24 %. Jaw *et al* found that EHBA was usually accompanied by an atrophic gallbladder while IHS was usually accompanied by a big gallbladder[2]. But one patient in our series only showed a big gallbladder on MRC and was erroneously diagnosed as having IHS, which turned out to be EHBA as confirmed surgery. These results suggest if only a big gallbladder is visualized, other examinations, such as duodenal fluid examination, should be performed for the differention between IHS and EHBA. In the present study, the reason of non-visualision of the extrahepatic biliary ducts of 4 IHS patients might had something to do with severe liver damage and decreased bile secretion.

Examination of duodenal fluid is simple and inexpensive and can directly confirm the patency of biliary tracts. But it can not depict the structure of extrahepatic and intrahepatic biliary ducts. The liver damage and cholestasis can lead to false-negative results and make it difficult to distinguish between EHBA and severe cholestatic IHS. MRC can depict the extrahepatic biliary ducts in infants, provide the images of biliary ducts similar to those of ERCP and is very safe even if it is used in young infants. But it can give false-negative results when severe liver damage and cholestasis cause substantial decrease of bile flow, and it may cause false-positive results when an EHBA patient has a big gallbladder. Then, we recommend that the patients with infantile cholestatic jaundice should undergo duodenal fluid examination first. If the fluid is found to contain bile, the diagnosis of IHS is suggested. If no bile is found in the fluid, MRC should be performed for differentialtion between IHS and EHBA. The examination of duodenal fluid in combination with MRC allow us to directly observe whether bile is present in the duodenal fluid and depict the extrahepatic biliary ducts clearly. It has a relative high sensitivity and specificity (97.06 %, 94.4 % respectively) for the diagnosis of EHBA.

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