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Evaluation of the Triangular Cord Sign in the Diagnosis of Biliary Atresia

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ABSTRACT. *Background.* **Infantile cholestasis continues to represent a diagnostic challenge. It is very important to diagnose surgically correctable disorders, such as biliary atresia, in a timely manner to prevent progressive damage to the liver. It has been recently suggested that the triangular cord (TC) sign is a simple and useful tool in the diagnosis of biliary atresia.**

Methods. **We prospectively studied 65 infants presenting with conjugated hyperbilirubinemia (age range: 32–161 days). All patients underwent ultrasonographic examination with a 7.0-MHz transducer (Acuson, Mountain View, CA). The TC was defined as a triangular, or tubular, echogenic density seen immediately cranial to the portal vein bifurcation.**

Results. **The TC sign was identified in 25 infants, and all of them had histologic features suggestive of biliary atresia; the diagnosis was confirmed at surgery by gross morphology of hepatobiliary system, and liver biopsy, with or without intraoperative cholangiogram. Among the 40 patients who did not have the TC sign, 6 had paucity of the intrahepatic bile ducts. Three had alph-1-antitrypsin deficiency, and 31 had neonatal hepatitis. None of the 40 patients who did not have the TC sign developed acholic stools. Seven patients with biliary atresia were followed by ultrasonographic examination for 6 months after the Kasai procedure. The TC sign disappeared in all patients after the surgery; however, the TC sign reappeared in 3 patients who developed progressive cholestasis after the procedure.**

Conclusion. **The TC sign is a simple, timesaving, and reliable diagnostic tool in the evaluation of infants with infantile cholestasis. The TC sign may also prove to be helpful in following patients after hepatoportoenterostomy. We suggest a new diagnostic strategy for patients suspected to have biliary atresia. When the TC sign is visualized, the patient should undergo intraoperative cholangiogram to confirm the diagnosis of biliary atresia, reserving percutaneous liver biopsy for those patients in whom the TC sign could not be detected. *Pediatrics* 2001; 108:416–420; *biliary atresia, neonatal cholestasis, ultrasonography, triangular cord sign.***

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ABBREVIATIONS. NH, neonatal hepatitis; BA, biliary atresia; US, ultrasonographic; TC, triangular cord.

Infantile cholestasis continues to represent a diagnostic challenge. The evaluation of the infant with cholestasis is a multistep process that should follow a logical, cost-effective sequence. It is important to recognize disorders for which specific treatment is available, which, if instituted early, may prevent progressive hepatic damage. However, in 70% of the cases, the nature of the aberration is difficult to pinpoint; idiopathic neonatal hepatitis (NH) and biliary atresia (BA) will be the working diagnosis.[1]

BA is an idiopathic, localized, complete obliteration, or discontinuation, of the hepatic or common bile ducts at any point from the porta hepatis to the duodenum.[2] Patients suspected to have BA usually undergo percutaneous liver biopsy. If the liver biopsy suggests the presence of BA, exploratory laparotomy is conducted to confirm the diagnosis, and the Kasai procedure is done to provide biliary drainage.[3,4] The success of the Kasai procedure is much higher if it is performed before 2 months of age.[1]

Ultrasonography has played a role in screening patients with infantile cholestasis, mainly focusing on the shape or contractility of the gall bladder.[5–7] It has been recently reported that ultrasonographic (US) triangular cord (TC) sign, which represents a cone-shaped fibrotic mass cranial to the bifurcation of the portal vein in BA patients, was very useful in the diagnosis of BA.[8–10]

The aim of our study was to reassess the accuracy of the TC sign in the diagnosis of BA.

MATERIAL AND METHODS

Sixty-five consecutive infants who presented with prolonged conjugated hyperbilirubinemia were evaluated using standardized protocol.[1,11] All patients had US examination and percutaneous liver biopsy. Tc-99 m-DISIDA hepatobiliary scintigraphy was done in 27 infants. The patients undergoing the study ranged in age from 32 to 161 days. Patients with choledochal cysts were excluded from the study.

All infants had the US examination after at least 4 hours fasting using Acuson XP-10 (Acuson, Mountain View, CA) equipped with 7-MHz convex linear transducer (Acuson, Mountain View, CA). The US examination focused on the presence, or absence, of

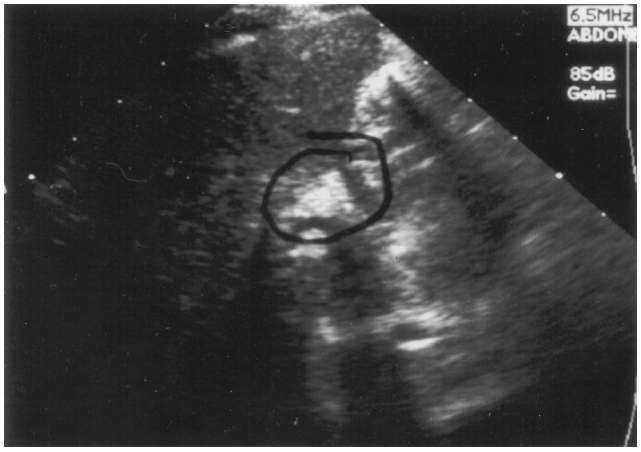

Fig 1. Longitudinal ultrasonogram showing the TC sign (circled) cranial to the portal vein in a patient with biliary atresia.

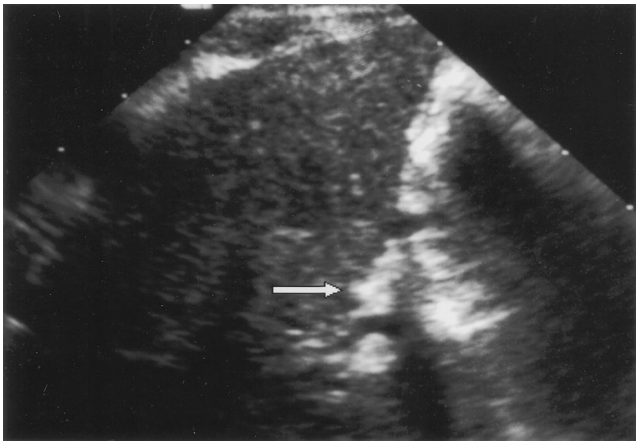

Fig 3. Longitudinal ultrasonogram showing reappearance of the TC sign (arrow) after disappearance following the Kasai procedure.

fibrous tissue at the porta hepatis. As reported earlier, the TC sign was defined as a triangular or tubular echogenic density just cranial to the portal vein bifurcation.[8,9] The presence of the TC sign was interpreted as having BA, whereas its absence was interpreted as having NH, or other causes of conjugated hyperbilirubinemia.

Tc-99 m-DISIDA hepatobiliary scintigraphy was performed after a 5-day course of phenobarbital pretreatment (5 mg/kg/d). Images were obtained at 3, 5, 10, 15, 30, 45, 60, 120, and 240 minutes. As needed, images were obtained up to 24 hours after the injection. Lack of excretion of the tracer was suggestive of having BA, whereas excretion of the tracer in 24 hours was suggestive of NH, or other causes of conjugated hyperbilirubinemia.

Percutaneous liver biopsy was performed in all patients with local anesthesia. The diagnosis of BA was suggested by the presence of bile duct proliferation, or other features suggestive of extrahepatic obstruction (bile plugs, portal tract expansion, or fibrosis). All patients suspected of having BA underwent exploratory laparotomy.

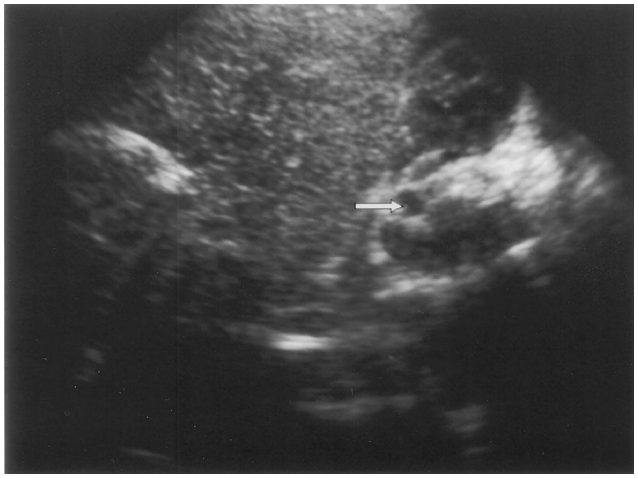

Fig 2. Transverse ultrasonogram showing disappearance of the TC sign after the Kasai procedure. No echogenicity seen cranial to the portal vein (arrow).

RESULTS

US examinations of the 65 infants were performed. The TC sign was identified in the 25 infants in whom the diagnosis of BA was made based on liver biopsy and the intraoperative cholangiogram at the time of the Kasai procedure (Fig 1).

Seven infants with BA were followed by US examination after hepatoportoenterostomy. The TC sign disappeared in all of them (Fig 2). However, repeated US done in 7 patients 6 months after hepatoportoenterostomy denoted the reappearance of the TC sign in 3 patients (Fig 3). The 3 patients who redeveloped the TC sign had conjugated hyperbilirubinemia, despite normalization of their bilirubin after hepatoportoenterostomy. The 4 patients who did not redevelop TC sign had normal serum bilirubin levels.

Among the 40 patients who did not have the TC sign, 6 had paucity of the intrahepatic bile ducts, 3 had alph-1-antitrypsin deficiency, and 31 had NH. None of the 40 patients who did not have the TC sign developed acholic stools (Table 1).

In 25 infants with BA, the gall bladder was invisible in 11, small in 12, and normal (>1.5 cm in length) in 2 infants. Contractility was seen in 2 infants. On the other hand, in the 40 infants with NH, or other causes of cholestasis, the gall bladder was invisible in 10 and normal in 30 infants.

Twenty-seven infants underwent Tc-99 m-DISIDA hepatobiliary scintigraphy. Eleven of 12 patients with BA, and 6 of the 15 infants with NH or other causes of cholestasis, had no gut excretion, denoting 94% sensitivity and 40% specificity (Table 2). The mean serum bilirubin level of the infants with intrahepatic cholestasis was 4.9 mg/dL for those with no

TABLE 1. Diagnostic Accuracy of Ultrasonography (Using the TC Sign)

	Interpretation by Ultrasonography	
	BA	NH/Other
BA (n = 25)	25	0
NH/other (n = 40)	0	40

Sensitivity 100% and specificity 100%.

TABLE 2. Diagnostic Accuracy of Hepatobiliary Scintigraphy

	Interpretation by Hepatobiliary Scintigraphy	
	BA	NH/Other
BA (n = 12)	11	1
NH/other (n = 15)	9	6

Sensitivity 93% and specificity 40%.

tracer gut excretion, and 4.2 mg/dL for those who had gut excretion.

Sixty-five infants underwent percutaneous liver biopsy. In 25 biopsies from the 25 infants with BA, the histopathologic findings were suggestive of extrahepatic biliary obstruction showing 100% sensitivity. However, in 2 infants an initial liver biopsy, done at 32 and 37 days of age, respectively, features of NH were seen. But, a follow-up biopsy, done at 53 and 60 days of age, respectively, showed the features of BA.

On the other hand, features of NH, or other causes of cholestasis, were seen in 37 of the 40 infants who had either NH or other causes of cholestasis showing 95% specificity (Table 3).

DISCUSSION

The initial evaluation and management of infants presenting with conjugated hyperbilirubinemia must be rapid and decisive. It is very important to diagnose surgically correctable disorders, such as BA, in a timely manner to prevent progressive damage to the liver. The success rate for establishing good bile flow after hepatoportoenterostomy is much higher (90%) if the procedure is done before 2 months of age; the chances of obtaining adequate flow are much lower (~20%) when the procedure is performed in infants older than 90 days.[4,12–14]

Hepatobiliary scintigraphy with technetium-labeled iminodiacetic acid derivatives has been used to differentiate BA from nonobstructive causes of cholestasis.[15–17] In BA, the hepatic uptake of the agent is unimpaired, but excretion into the intestine is absent. However, the uptake may be impaired in NH, although excretion into the bowel will eventually occur. Therefore, obtaining a follow-up scan may be of value in determining the patency of the extrahepatic biliary tree. The administration of phenobarbital (5 mg/kg/d) for 5 days before the scan may enhance biliary excretion of the isotope. Hepatobiliary scintigraphy has been found to be a sensitive, but not specific, test for BA.[16,17] It also fails to identify other structural abnormalities of the biliary tree or vascular anomalies. In our study, 6 of the 15 patients who had either NH or other causes on intrahepatic cholestasis had excretion of the tracer into the bowel, denoting specificity of 40%. The need to wait for 5 days and the lack of the specificity of the test makes this procedure less practical and its usefulness limited for most children suspected to have BA.

TABLE 3. Diagnostic Accuracy of Percutaneous Liver Biopsy

	Interpretation by Liver Biopsy	
	BA	NH/Other
BA (n = 25)	25	0
NH/other (n = 40)	2	38

Sensitivity 100% and specificity 95%.

Percutaneous liver biopsy is a valuable procedure in the evaluation of neonatal hepatobiliary diseases.[18] The characteristic histopathologic features suggesting obstructive forms of neonatal cholestasis include portal tract expansion and bile duct proliferation; canalicular and cellular bile stasis may be also observed.[4] Portal inflammation and giant cells may be also seen, confusing the picture and making differentiation from NH difficult. Although liver biopsy is safe, even in small children,[19] it is still an invasive procedure and it will be advantageous to the patient if it can be replaced with a simple and noninvasive procedure such as ultrasonography.

Abdominal ultrasound is a useful diagnostic tool in the evaluation of neonatal hepatobiliary disease because it will identify choledocholithiasis, perforation of the bile duct, or other structural abnormalities of the biliary tree, such as a choledochal cyst.[5,20] In addition, in those children with BA and associated anomalies, abdominal ultrasound will detect polysplenia and vascular malformations, such as interruption of the inferior vena cava.[21] In BA, the gallbladder is either not visualized or a microgallbladder is seen. However, children with intrahepatic cholestasis caused by idiopathic NH, cystic fibrosis, or total parenteral nutrition-associated liver disease may have similar ultrasonographic findings. As a result, the sensitivity of abdominal ultrasound for BA exceeds 85%, whereas the specificity of the ultrasound findings is slightly <80%.[21]

It has been suggested that the diagnosis of BA can be excluded if a change in the gall bladder size is seen after eating on serial ultrasound examination.[22] In our study, change in the size of the gall bladder was observed in 3 patients who were found to have BA as suggested by the liver biopsy and confirmed by intraoperative cholangiogram. This can be explained by the fact that a patent bile duct from the gall bladder to the duodenum can be found in up to 22% of the patients with BA.[4,23,24] Therefore, ultrasonographic evaluation of the size, or contractility, of the gall bladder is not a reliable test in the evaluation of patients with possible BA.

Choi et al[8] have recently reported the sonographic feature of a fibrous cone at the porta hepatis as a triangular-shaped or tubular-shaped echogenic density, just cranial to the bifurcation of the portal vein on transverse or longitudinal scan. The echogenic density was shown to represent the fibrous remnants at the porta hepatis of BA cases at surgery. The echogenic density was named the TC sign by the authors who concluded that the TC sign appears to be a very specific ultrasonographic finding in patients with BA.

Seven of our BA patients were followed for up to 6 months after the Kasai procedure. Initially, all 7 patients had a good bile flow with clearing of their jaundice. However, 3 of the 7 patients developed progressive jaundice. It is interesting that these 3 patients redeveloped an echogenic density seen im-

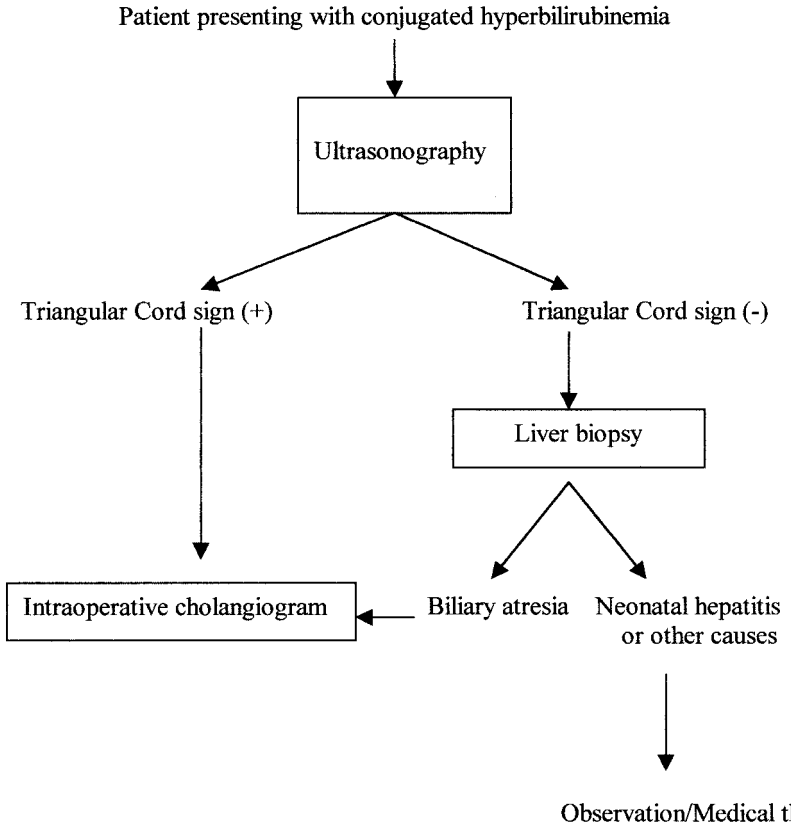

Fig 4. Suggested algorithm for evaluation of patients expected to have BA.

mediately cranial to the portal vein bifurcation (Fig 3). The echogenic density was not seen in the 4 patients who continued to be jaundice-free after the Kasai procedure. This shadow can be explained by the fact that patients with BA might continue to have ongoing fibrosis following the Kasai procedure. The TC sign seen before hepatoportoenterostomy might represent the fibrotic remnant of the obliterated cord in BA with surrounding fibrosis in the periportal connective tissue, because the fibrotic remnants of the bile duct cannot explain the whole TC sign. Therefore, following patients with BA after the Kasai procedure with ultrasonography might be beneficial. However, this needs to be further studied.

Our study shows that the TC sign is 100% sensitive and specific in the diagnosis of BA (Table 1), which is higher than what was reported by Park et al (85% sensitivity and 100% specificity)[10]. This can be explained by the fact that the mean age of their BA infants was lower than the mean age of our patients (60 vs 84 days, respectively). On the other hand, our results are similar to those reported by Choi et al,[8] who reported the presence of the TC sign in all of their BA patients and its absence in patients with NH or other causes of cholestasis. Other possible explanation of the false negative TC sign reported in some studies may be also explained by too small periportal fibrous mass seen on ultrasound, or unusual hepatic radicals such as hypoplastic, aplastic, or fibrous hepatic duct.[9,25]

Our study confirms the finding of Choi et al,[8] and reports for the first time the reappearance of the TC sign in the patients who redevelop cholestasis after hepatoportoenterostomy. Based on our study, we would like to propose a new diagnostic algorithm for the evaluation of patients presenting with conjugated hyperbilirubinemia (Fig 4). We recommend that the patient undergo intraoperative cholangiogram if the TC sign is visualized to confirm the diagnosis of BA. Park et al[11] have suggested that hepatobiliary scintigraphy should be the next step if the TC sign is not visualized, reserving percutaneous liver biopsy for patients without gut excretion of the tracer. However, we find that percutaneous liver biopsy, and not hepatobiliary scintigraphy, should be the most reasonable next step if the TC sign is not detected. The presence, or absence, of gut excretion of the tracer in patients undergoing hepatobiliary scintigraphy will not obviate the need to perform liver biopsy in these patients to establish the diagnosis. We believe that by following this algorithm, almost all cases of BA can be diagnosed in a simple, less invasive, and timely manner.

CONCLUSION

The TC sign is a simple, timesaving, and reliable diagnostic tool in the evaluation of infants with infantile cholestasis. The TC sign may also prove to be helpful for following patients after hepatoportoenterostomy.

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MOVING ONE MARBLE

No innovation comes without strings attached. The more technologically advanced an innovation is, the more likely its introduction is to produce many consequences—some of them unanticipated, but others unintended and hidden. A system is like a bowl of marbles: move any one of its elements and the position of all the others is inevitably changed also.

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Submitted by Student