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New Diagnostic Approach in Biliary Atresia with Emphasis on Ultrasonographic "Triangular Cord" Sign

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INTRODUCTION

Infantile cholestatic jaundice, characterized by persistent conjugated hyperbilirubinemia, has remained a major diagnostic challenge despite continual improvement of diagnostic tests and increasing knowledge regarding its pathogenesis. It is important that the infants with biliary atresia(BA) should be identified early, as the success of the Kasai procedure is inversely related to age and is greatest if performed during the first two months of life(Kasai *et al*, 1968; Karrer *et al*, 1990; Ohi & Ibrahim, 1995). No single test or imaging modality can reliably define the causes of infantile cholestasis. Ultrasonography has played a role in screening infantile cholestasis, mainly focusing on shape and/or contractility of the gall bladder (Abramson *et al*, 1982; Kirks *et al*, 1984; Altman & Abramson, 1985; Brun *et al*, 1985; Green & Carroll *et al*, 1986; Weinberger *et al*, 1987; Ikeda *et al*, 1989). Lately the authors reported that ultrasonographic triangular code(TC) which represents a cone-shaped fibrotic mass cranial to the bifurcation of the portal vein in BA infants, was very useful in the diagnosis of BA(Choi *et al*, 1996; Choi *et al*, 1997).

The aim of this paper is to reassess the role of ultrasonography(US), hepatobiliary scintigraphy(HS), and liver needle biopsy(NBx) with particular emphasis on ultrasonographic TC in differentiating BA from other causes of intrahepatic cholestasis and to propose a new diagnostic approach in the evaluation of infantile cholestasis.

ROLES AND LIMITATIONS OF EACH DIAGNOSTIC MODALITIES

Infantile cholestasis occurs in a number of disorders such as infections, metabolic or genetic disorders, and anatomic abnormalities. Cholestasis is diagnosed when the conjugated bilirubin fraction comprises more than 20% of total bilirubin or more than 2mg%(Balistreri, 1985). Among the many causes of infantile cholestasis, investigation leads to a diagnosis of BA or idiopathic NH in 70%-80% of infants(Balistreri, 1985). It is well established that the success of the Kasai procedure is time-dependent. The success of the Kasai procedrue is greatest if performed during the first two months of life(Kasai *et al*, 1968; Karrer *et al*, 1990; Ohi & Ibrahim, 1995).

Clinical features and standard laboratory tests of liver function frequently cannot distinguish BA from NH or other causes of

cholestasis. A large number of diagnostic tests have been attempted to distinguish BA from NH or other causes of cholestasis. Despite continual improvements and changes in the diagnostic accuracy of these tests, none has been constantly reliable. Therefore, a multidisciplinary approach to the evaluation of infantile cholestasis is required.

Ultrasonography

Ultrasonography is a simple and noninvasive procedure which has been used in all cases with infantile cholestasis as a first step in the work-up of these patients. An abdominal US is useful in the detection of a choledochal cyst, but it is not so helpful in differentiating BA from NH or other causes of intrahepatic cholestasis. Most investigators have forcused on the shape and/or change in size of the gall bladder(Abramson *et al*, 1982; Kirks *et al*, 1984; Altman & Abramson, 1985; Brun *et al*, 1985; Green & Carroll *et al*, 1986; Weinberger *et al*, 1987; Ikeda *et al*, 1989). Nonvisualization of the normal gall bladder was thought to suggest BA(Abramson et al, 1982; Kirks et al, 1984; Altman & Abramson, 1985; Brun et al, 1985; Green & Carroll *et al*, 1986; Weinberger *et al*, 1987; Ikeda *et al*, 1989), but this may occur in association with both BA and severe intrahepatic cholestasis(Abramson *et al*, 1982; Altman & Abramson, 1985). Furthermore, several investigators(Kirks *et al*, 1984; Altman & Abramson, 1985; Weinberger *et al*, 1987; Choi *et al*, 1996) have documented BA cases with a normal gall bladder. Although the gall bladder is usually small or nonvisible in BA, a normal gall bladder does not exclude the diagnosis of BA. Conversely, nonvisualization of the gall bladder does not exclude the diagnosis of NH or other intrahepatic cholestatic disorders.

Green & Carroll(1986), and Ikeda *et al*(1989) have suggested that BA can be excluded when the change in the gall bladder size is observed after feeding on serial US examinations. Although in infants with BA, the gall bladder is usually small and difficult to identify, it is not surprising to demonstrate the contractility of the gall baldder after feeding, because a patent bile duct from the gall bladder to the duodenum can be seen in 19-22% of cases(Brun *et al*, 1985; Karrer *et al*, 1990; Ohi & Ibrahim, 1995). Three of 25 BA infants demonstrated contractility of the gall bladder after feeding in our study(Park, et al, 1997). We believe that ultrasonographic evaluation of the gall bladder shape, size and contractility is not such a reliable test for the differentiation of BA from intrahepatic cholestasis.

With the development of high resolution gray-scale recording and real-time imaging technique with 7.0 MHz or 10 MHz transducer, the authors recently reported the sonographic feature of a fibrous cone at the porta hepatis as a triangular or tubular echogenic density just cranial to the portal vein bifurcation on transverse or longitudinal scan(Fig 1)(Choi *et al*, 1996; Park *et al*, 1997; Choi *et al*, 1997). The echogenic density was confirmed to represent the fibrous remnant in the porta hepatis of BA cases at surgery. We named this echogenic density "the triangular cord"(TC). The TC appears to be a very specific ultrasonographic finding representing the fibrous cone in BA cases, showing overall diagnostic accuracy of 95% with 85% sensitivity and 100% specificity on the basis of our study(Park *et al*, 1997).

In the light of our experience, there can be pitfalls with this proposal. False negative TC may occur in some BA infants because

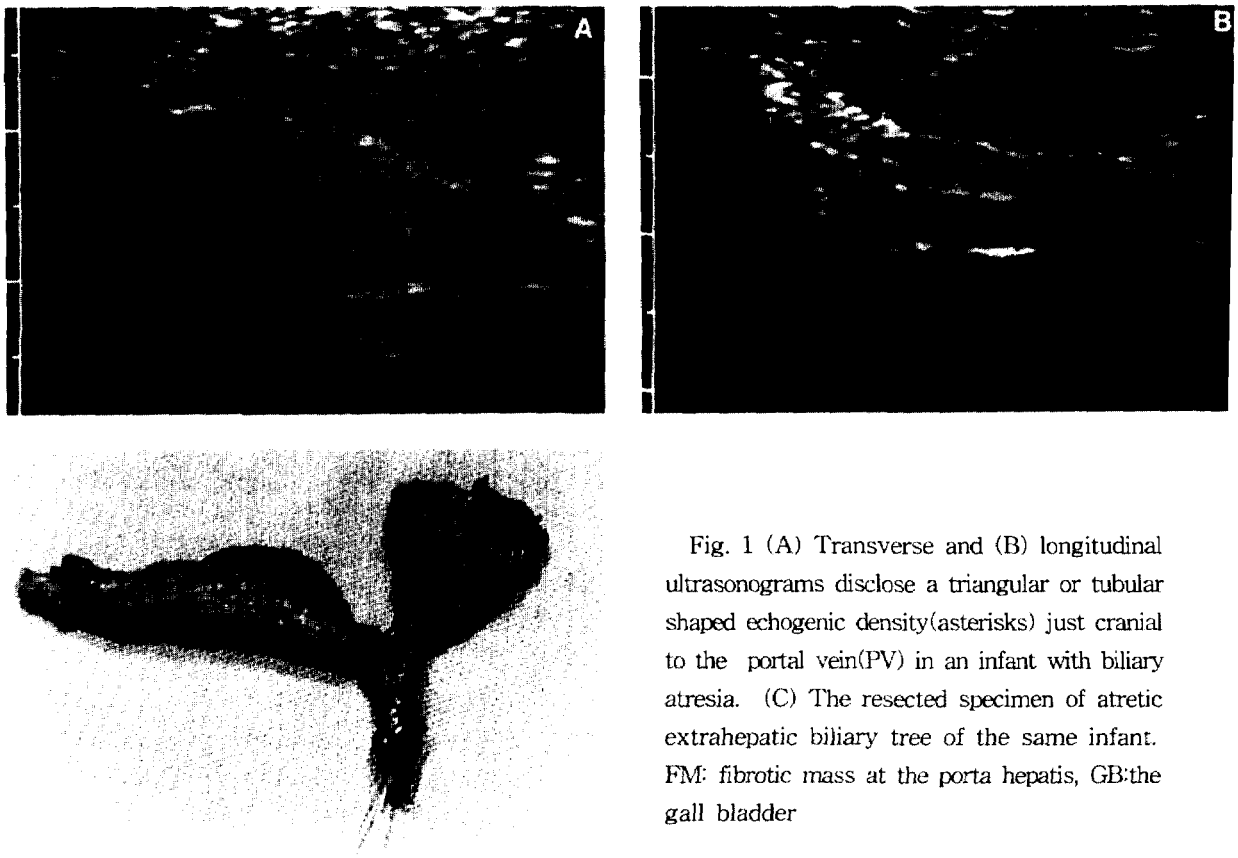

Fig. 1 (A) Transverse and (B) longitudinal ultrasonograms disclose a triangular or tubular shaped echogenic density(asterisks) just cranial to the portal vein(PV) in an infant with biliary atresia. (C) The resected specimen of atretic extrahepatic biliary tree of the same infant. FM: fibrotic mass at the porta hepatis, GB:the gall bladder

of the patterns of unusual hepatic radicles such as hypoplastic, aplastic, or fibrous hepatic ducts(Ohi & Ibrahim, 1995), and in the early stage of some BA cases. The fibrotic remnant at the porta hepatis may be inconspicuous at the early stage of the disease but it can be recognizable with time as seen in our two cases(Park, *et al*, 1997). A false negative TC due to a large right hepatic artery running over the relatively small fibrotic mass at the porta hepatis as seen in our one BA case, may also occur (Park, *et al*, 1997).

Tc-99m-IDA Hepatobiliary Scintigraphy

Tc-99m-IDA hepatobiliary scintigraphy can be used to evaluate the degree of hepatocyte dysfunction using hepatocyte clearance and bile duct patency using excretion of tracer into the small bowel. The majority of the infants with BA are expected to have no excretion of tracer into the small bowel. The diagnosis of infantile cholestasis is mostly dependent upon presence or absence of tracer excretion rather than degree of hepatocyte clearance(Majd *et al*, 1981; Gerhold *et al*, 1983; Manolaki *et al*, 1983; Tolia *et al*, 1986; 김우석 외, 1997). The majority of the literature report that the sensitiviy of the Tc-99m-IDA hepatobiliary scintigraphy for the diagnosis of BA is as high as 97-100%, while the specificity varied

from the reports, ranging from 33%-91% (Majd *et al*, 1981; Gerhold *et al*, 1983; Manolaki *et al*, 1983; Tolia *et al*, 1986; 김우석 외, 1997). This discrepancy in specificity is thought to be attributable to the different age, diagnosis, and the severity of diseases in the study population. Thus, excretion of tracer can exclude BA but no excretion of tracer requires further investigation such as percutaneous needle biopsy because of its low specificity. Infants with low birth weight less than 2200 gram, premature infants, infants with TPN, infants with severe NH are prone to have no gut excretion of tracer(Spivak *et al*, 1987; 김우석 외, 1997).

Percutaneous Liver Needle Biopsy

In our institution, percutaneous liver needle biopsy is usually performed to confirm BA before exploratory laparotomy when there is no excretion of tracer on hepatobiliary scintigraphy. Several portal areas should be included in the specimen for proper diagnosis (Altman & Abramson, 1985; Desmet, 1992). Although there are some histologic similarities between BA and NH, most investigators agree that the most reliable criteria for the diagnosis of extrahepatic biliary obstruction is ductal proliferation, portal fibrosis, and canalicular bile stasis(Brough & Bernstein, 1974; Altman & Stolar, 1985; Lai *et al*, 1994; Shah & Spivak, 1994; Park *et al*, 1996). Recognition of the degree of ductal proliferation requires quantification of the bile duct to portal space ratio in the liver biopsy specimen. Watkins(1993) defines that bile duct to portal space ratio in normal infants is between 0.9-1.8. Bile duct proliferation of more than average 5 per one portal area with portal fibrosis was interpreted as having BA, and average 3-4 ducts /one portal area as having probable BA(Majd *et al*, 1981; Gerhold *et al*, 1983; Manolaki *et al*, 1983; Tolia *et al*, 1986; Park *et al*, 1997; 김우석 외, 1997). No ductal proliferation (average 1-2 ducts/one portal area) with hepatocellular degeneration was interpreted as having NH or other causes of cholestasis and less than 0.5 duct/one portal area was interpreted as having paucity of intraheaptic bile duct(Watkins, 1993; Park *et al*, 1996; Park *et al*, 1997; 김우석 외, 1997).

Although NBx is considered to be very valuable test with a diagnostic accuracy of over 93%(Altman & Stolar, 1985; Manolaki *et al*, 1983; Desmet, 1992), NBx biopsy is invasive and can be misleading in certain cases(Manolaki *et al*, 1983; Brough & Bernstein, 1974; Desmet, 1992; Lai *et al*, 1994; Shah & Spivak, 1994). If it is performed before 4-8 weeks of age in infants with BA, it may not show the characteristic ductal proliferation or portal fibrosis(Lai *et al*, 1994; Shah & Spivak, 1994) necessitating a second later biopsy as demonstrated in our two false negative cases. False positive results can occur in some cholestatic liver diseases such as bile plug syndrome, alpha-1-antitrypsin deficiency, and some neonatal hepatitis (Manolaki *et al*, 1983; Tolia *et al*, 1986; Spivak *et al*, 1987; Desmet, 1992; 김우석 외,1997). Park, et al(1997) also experienced one false positive case with TPN associated cholestasis who showed mild ductal proliferation (3-4 ducts/one portal area). In these cases, we have to evaluate infants with cholestatic jaundice in the context of clinical and laboratory data.

NEW DIAGNOSTIC APPROACH

In conclusion, since the introduction of the TC sign on US in the diagnosis of BA by our institution, we found that it seemed to

be a simple, time saving, highly reliable, and non-invasive tool in the diagnosis of BA from other causes of cholestasis. The authors would like to propose a new diagnostic strategy in the evaluation of infantile cholestasis. When the TC is visualized on US, prompt exploratory laparotomy is mandatory without further investigations. When the TC is not visualized, hepatobiliary scintigraphy is the next step. Excretion of tracer into the small bowel actually rules out BA. Liver needle biopsy can be reserved only for the infants without gut excretion of tracer. We believe that a correct decision regarding the need for surgery can be made in almost all cases of infants with cholestatic jaundice by this multidisciplinary approach(Fig. 2).

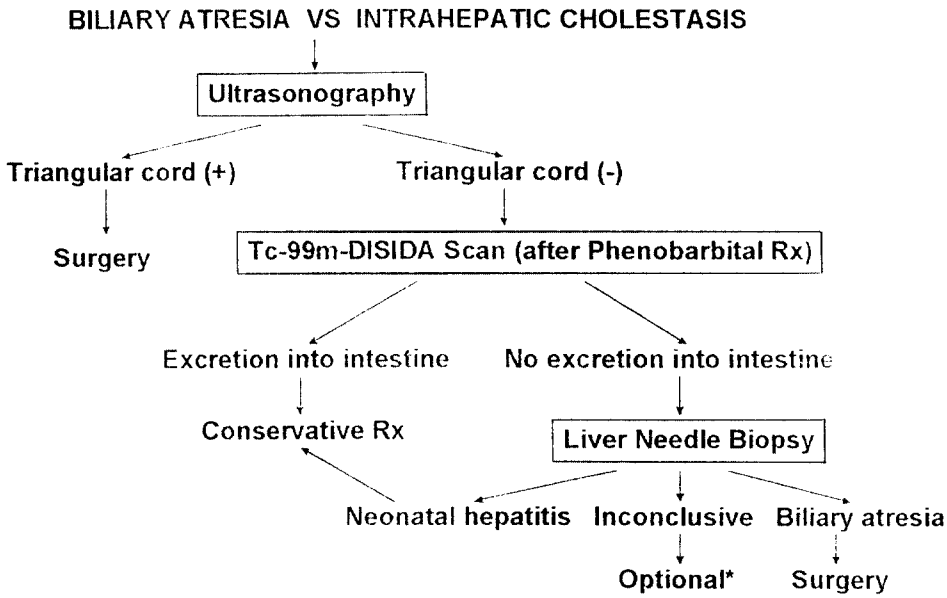

Fig. 2 Algorithm for workup of infantile cholestasis.
Optional : Minilaparotomy or laparoscopy is advised in older infants(more than 8 weeks) but repeat ultrasonography, liver biopsy, and/or hepatobiliary scan are mandatory in 2 weeks in younger infants(less than 8 weeks).

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