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Hepatic tumours in children with biliary atresia: Single-centre experience in 13 cases and review of the literature

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AIM: To establish the risks of developing of hepatic tumours and to investigate their clinical and imaging findings in children with biliary atresia (BA) after Kasai portoenterostomy (Kasai).

MATERIALS AND METHODS: Among 157 children who had undergone Kasai for BA over an 18 year period, patients who had newly developed hepatic tumours were identified. Patient demographics, clinical features, and imaging findings were retrospectively reviewed.

RESULTS: Three male and 10 female patients (mean age 3.9 years) all (8%, of 157) had single hepatic tumours, which were confirmed in 10 explanted and three non-explanted livers. Ten (77%) were benign and three (23%) were malignant. Of the benign hepatic tumours, focal nodular hyperplasia (FNH; $n = 6$) was the most common, followed by regenerative nodules ($n = 3$) and adenoma ($n = 1$). All FNH appeared in young children <1 year of age and showed a subcapsular location, bulging contour, and lack of central scar. Malignant tumours included two hepatocellular carcinomas and one cholangiocarcinoma.

CONCLUSION: Hepatic tumours developed in approximately 8% of children with BA after Kasai. Although benign tumours, including FNHs and regenerative nodules, were more common than malignant tumours, screening with alpha-foetoprotein (AFP) levels and regular imaging studies are the mainstay of malignant tumour detection.

Introduction

Biliary atresia (BA) is a progressive fibro-obliterative cholangiopathy of neonates that affects both the intrahepatic and extrahepatic bile duct.[1] Although Kasai portoenterostomy (Kasai) has been accepted as the primary therapeutic option for establishing biliary drainage, subsequent liver transplantation (LT) is indicated for children in whom clearance of jaundice is inadequate or when complications of chronic liver disease appear.[2,3]

Children with BA inevitably progress to cirrhosis and also have a risk of hepatic tumour development.[4,5] Malignant transformation is a well-recognized complication of cirrhotic liver from whatever cause. A variety of hepatic tumours has been reported in patients with long-standing BA. Regenerative nodules and hepatocellular carcinoma (HCC) may be associated with cirrhosis.[4–9] Other tumours that are rarely encountered in the cirrhotic liver, such as focal nodular

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hyperplasia (FNH), hepatoblastoma, and cholangiocarcinoma have also been described.[5,10–14] Differentiating a benign entity from malignant tumours may be challenging; however, it is very important for BA survivors awaiting LT.

The purpose of the present study was to establish the risks of development of hepatic tumours and to investigate their clinical and imaging findings in children with BA after Kasai. A review of the literature was also undertaken regarding hepatic tumours associated with BA.

Materials and methods

Patients

This retrospective study was approved by the institutional review board, and requirement to obtain informed consent was waived. Between 1997 and 2012, a search of the medical records on the electronic database of the Department of Pediatric Surgery at Samsung Medical Center revealed 180 consecutive patients diagnosed with BA who underwent Kasai. Among them, 157 patients ($n = 110$, Kasai followed by LT; $n = 47$, Kasai alone) had follow-up visits after Kasai at the outpatient clinic and received hepatobiliary ultrasound or computed tomography (CT) examinations. Review of the radiological and histopathological results for these 157 patients identified 13 patients (13/157, 8.2%) who had a newly developed hepatic tumour after Kasai; one of these was previously reported in the literature.[15] The patients included three male and 10 female patients with a mean age at the initial detection of the hepatic tumour of 2.1 years (range 4.6 months to 16 years) during a median follow-up period of 14.4 months (range 4 months to 15.8 years) after Kasai. Of these 13 patients, 10 patients underwent subsequent LT (mean age 2.9 years, range 7.3 months to 13.6 years) as a result of underlying biliary cirrhosis ($n = 9$) and newly developed malignant hepatic tumour ($n = 1$, case 13) and three patients received Kasai alone. Eleven tumours were confirmed at histopathology ($n = 10$, explanted liver; $n = 1$, percutaneous biopsy) and the remaining two were considered to be FNH (case 6) and HCC (case 12), based on imaging findings compatible with each diagnosis. Patient demographics and clinical features were determined by chart review.

Image acquisition

All the ultrasound examinations ($n = 13$) were performed by one of three paediatric radiologists. The equipment used was an ultrasound systems (HDI 5000, Philips Medical Systems, Best, The Netherlands; Sequoia, Siemens Healthcare, Erlangen, German) with a high-resolution 5–12 MHz linear-array transducer and a 5–10 MHz curved-array transducer.

All CT examinations ($n = 13$) were obtained using multidetector CT machines (LightSpeed 16 or LightSpeed VCT XT, GE Medical Systems, Milwaukee, WI, USA) with a low-dose technique based on patient weight and automatic exposure control. The three-phase (arterial, portal, and venous phase, $n = 4$), two-phase (arterial and portal-venous phase, $n = 1$), or single portal phase ($n = 8$) were obtained after injection of intravenous contrast material [2 ml/kg (maximum 120 ml) iomeprol, 300 mg iodine/ml; Iomeron 300, Bracco, Milan, Italy]. Imaging parameters were 80–120 kV and 50–150 mA with a 3.75–5 mm section thickness. The mean interval between ultrasound examination and contrast-enhanced CT was 14.7 days (range 0–52 days; median 2 days).

Magnetic resonance imaging (MRI; $n = 1$) was performed using a 3 T MRI system (Intera Achieva 3 T; Philips Medical Systems). The protocol included T1-weighted three-dimensional turbo-field-echo images (T1 high-resolution isotropic volume examination, THRIVE), breath-hold multi-shot T2-weighted images, and respiratory-triggered single-shot T2-weighted images. Contrast-enhanced dynamic images included arterial (20–35 s), portal (60–70 s), venous (3 min), and hepatobiliary phase (20 min) after administration of gadoxetic acid (Primovist, Bayer-Schering Pharma, Berlin, Germany) at a dose of 0.1 ml/kg.

Image analysis

Two paediatric radiologists retrospectively reviewed all of the images in consensus. Although the reviewers knew that all patients had hepatic tumours after Kasai, they were unaware of the histopathological diagnoses and clinical findings. The imaging findings were evaluated with emphasis on the location, size, margin, internal architecture, and pattern of enhancement of the lesion. The size of the lesion was measured at its greatest diameter. The margin of the lesion was classified as well-defined or ill-defined. The internal architecture of the lesion was determined by echogenicity and vascularity at ultrasound, attenuation on portal-phase CT images, and signal intensity on T1- and T2-weighted MRI images. The presence, if any, of calcification or central scar within the lesion was recorded. The pattern of enhancement of the lesion was evaluated on three or two phases. Hepatic parenchymal changes and the presence of intrahepatic biliary cysts were also evaluated.

Results

The clinical and imaging findings of hepatic tumours in 13 patients with BA after Kasai are summarized in Table 1. All patients had a single hepatic tumour, ranging in diameter from 0.6–5.7 cm (mean 2.5 cm). Ten patients (of 13, 77%) had a benign hepatic tumour, with FNH being the most common ($n = 6$), followed by large regenerative nodule ($n = 3$), and adenoma ($n = 1$). Three patients (of 13, 23%) developed a malignant hepatic tumour including HCC ($n = 2$) and cholangiocarcinoma ($n = 1$). All 13 patients had hepatic parenchymal changes including surface nodularity in 13 and left lobe hypertrophy in nine. Intrahepatic biliary cysts were found in seven patients: these were solitary and simple cysts ($n = 3$) or multiple and complicated cysts ($n = 4$).

All six FNHs appeared in young children <1 year of age (mean 6.8 months) with female predilection (female:male ratio = 2). All lesions were located at the subcapsular area with bulging contours, and were well-defined, ovoid