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Original article

Neurodevelopmental outcomes in children with prenatally diagnosed corpus callosal abnormalities

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Abstract

Objective: Although corpus callosal abnormalities are among the most common brain malformations detected prenatally, few previous studies have described the neurodevelopmental outcomes of children with this condition. The aim of our study was to evaluate the neurodevelopmental outcomes and associated clinical features of children with corpus callosal abnormalities diagnosed by prenatal ultrasonography.

Methods: Between July 2011 and July 2016, forty-nine children with corpus callosal abnormalities were born in Asan Medical Center Children's Hospital. Neurodevelopmental assessments were conducted in 40 patients at a median age of 24.8 months using the Bayley Scales of Infant Development II or the Korean Infant and Child Development Test. Patients were categorized according to their postnatal magnetic resonance imaging (MRI) findings and accompanying anomalies. Baseline characteristics and developmental outcomes of each group were compared.

Results: Isolated agenesis or hypoplasia of the corpus callosum was found in 16 (32.7%) patients, other associated central nervous system (CNS) abnormalities were found in 28 (57.1%) patients, and non-CNS abnormalities were found in 11 (22.4%) patients. Among the 40 patients who underwent developmental assessment, 18 (45.0%) showed normal development and 10 (25.0%) showed moderate-to-severe global developmental delay. Seven of the twelve (58.3%) patients with isolated corpus callosal abnormalities showed normal development. The combination of corpus callosal abnormalities with non-CNS anomalies was significantly associated with developmental delay (odds ratio 2.5, 95% confidence interval 1.6–3.9, $p = 0.001$). Conversely, children with isolated corpus callosal abnormalities showed relatively favorable neurodevelopmental outcomes.

Conclusion: Appropriate evaluation and comprehensive therapeutic approaches are strongly recommended for neonates who present with corpus callosal abnormalities combined with additional anomalies.

Keywords: Corpus callosal abnormality; Ultrasonography; Isolated agenesis of corpus callosum; Neurodevelopmental outcome; Prenatal diagnosis

1. Introduction

The corpus callosum comprises about 200 million axons that connect the right and left cerebral hemispheres [1]. These interhemispheric connections facilitate the integration of complex motor and sensory informa-

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tion from both sides of the body and influence higher cognition associated with abstract reasoning, executive functioning, social interaction, and language [2]. Corpus callosal abnormalities (CCAs) have an estimated prevalence of 0.3–0.7% of patients undergoing neuroimaging in the general population and 2–3% in the developmentally challenged population [3]. Improvements in neuroimaging techniques have improved the ability to detect CCAs in the general population, and a recent study in southeastern Hungary found an estimated birth prevalence of 2.05 per 10,000 live births [4]. In humans, the development of the corpus callosum begins at about 8 weeks of fetal life. Recent molecular analyses have revealed a large number of genes associated with CCAs, including transcription factors, guidance molecules and their receptors, intracellular signaling molecules, growth factors, and patterning molecules [5].

Prenatal diagnosis of CCAs has been reported since the 1980s, and typical sonographic signs have been described as either direct (complete or partial absence of the corpus callosum in the midsagittal plane) or indirect (obliteration of the cavum septum pellucidum, colpocephaly, elevation and dilatation of the third ventricle, and an abnormal course of the pericallosal artery) [6,7]. Although advances in prenatal imaging techniques have led to an increased detection rate of CCAs, clinical outcomes in patients with a CCA are variable and unpredictable, ranging from asymptomatic cases to mild or severe neurodevelopmental disabilities. The variable presence of other associated anomalies could explain the heterogenous clinical symptoms and neurological outcomes in children with a CCA. A CCA can present as an isolated anomaly or in association with somatic anomalies and/or other central nervous system (CNS) malformations, such as abnormal development of the cerebellum or brainstem and malformation of cortical development (polymicrogyria, subependymal heterotopia, or cortical dysplasia).

Previous postnatal studies have been biased toward patients with other associated anomalies, in whom overestimation of functional impairment was unavoidable [8–10]. A recent meta-analysis of prenatal studies revealed that about two-thirds of children with isolated agenesis of the corpus callosum showed a normal neurodevelopmental outcome, although some presented with varying degrees of impairment in fine and gross motor control, coordination, language, and cognition [11]. However, in light of the paucity of data regarding the neurodevelopmental outcome in children with prenatally diagnosed CCA, further studies are needed to appropriately counsel prospective parents.

Hence, the aim of this study was to evaluate the structural neurodevelopmental outcomes and associated clinical features in patients with a prenatally diagnosed CCA. This study was designed as a retrospective evaluation of neurodevelopmental outcomes and risk factors of poor neurological outcome in children with a CCA diagnosed by prenatal ultrasonography.

2. Subjects

We reviewed the medical records of 52 cases with a prenatal diagnosis of CCA who were referred to the Asan Medical Center Children's Hospital, a tertiary care center, from July 2011 to July 2016. The study was approved by the appropriate ethics review board, and informed consent was waived due to the retrospective design.

3. Methods

Ultrasonographic examinations were carried out using an Accuvix XQ or A30 machine (Samsung Medison Co, Ltd, Seoul, Korea) equipped with a 2–6-MHz transabdominal transducer by experts in prenatal ultrasonography (JY Shim, MY Lee, and HS Won). The diagnosis of CCA was made at a median gestational age of 29 weeks (range, 18.7–37). Ultrasonographic reports and pregnancy outcomes were reviewed for the 52 cases with a prenatally diagnosed CCA and the prenatal sonographic findings were divided into complete and partial ACC (including hypoplastic corpus callosum). Prenatal diagnoses were verified postnatally by magnetic resonance imaging (MRI). We divided the CCA cases into three groups based on the postnatal neuroimaging findings as follows [12]: Complete agenesis of the corpus callosum (ACC) defined as complete absence of all callosal fibers, partial ACC defined as either anterior (the rostrum, genu, and body) or posterior (the splenium) agenesis, and hypoplasia defined as complete thinning of the corpus callosum. We also categorized CCA cases into those with isolated CCA and those with non-isolated CCA. Isolated CCA was defined by the absence of associated CNS or non-CNS abnormalities. As CCAs are usually associated with ventriculomegaly, enlarged bilateral posterior horns of the cerebral ventricles was not included as an associated CNS anomaly.

For each patient, we collected the following data: gestational age at birth, gender, birth weight, mode of delivery, Apgar score at birth, prenatal and postnatal diagnoses, and other associated anomalies. Follow-up examinations were conducted at a median age of 24.8 months (range, 10–60), which included neurodevelopmental assessment by a neonatologist or pediatric neurologist. To score neurodevelopmental outcomes, the Bayley Scales of Infant Development (BSID-II) [13] or the Korean Infant and Child Development Test (KICDT) [14–17] was chosen in 40 patients at the time of the last follow-up visit. These scales are used to estimate neurodevelopment in the areas of gross motor control, fine motor control, personal-social skills, cognitive functioning, and language. Normal development was

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