Neonatal Choroid Plexus Cysts and Early Childhood Developmental Outcome

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Background and Purpose: Choroid plexus cysts (CPCs) are incidental findings on sonograms of the neonatal head. The incidence of CPCs and their association with childhood neurodevelopmental outcome remains unclear. The purpose of this study was to determine the incidence of neonatal CPCs and their association with early childhood neurodevelopmental outcome.

Methods: Between July 1997 and June 1998, routine brain sonographic examinations were performed on 2,111 normal newborns. All neonates in whom CPCs were detected were followed up with serial sonograms at 1, 2, 4, and 6 months of age. Developmental milestones were subsequently evaluated at follow-up, with assessments performed according to the Denver II Developmental Screening Test.

Results: CPCs were identified in 186 neonates (8.8%), 14 (7.5%) of which were bilateral. The mean (± standard deviation) cyst diameter was 2.6 ± 0.8 mm (range, 1.1–8.6 mm), with five cysts of more than 5 mm. Physical examinations were otherwise normal for all 186 neonates with a CPC. Follow-up ultrasonographic studies were completed for 155 children, with cysts regressing spontaneously in 137. By 6 months of age, residual cysts were visible in only 18 children (11.6%). Developmental outcome was normal for all 179 children who completed the scheduled follow-up ranging from 30 to 42 months (mean, 35 mo).

Conclusions: CPCs were detected in 8.8% of neonates. Most of the cysts resolved spontaneously. The existence of isolated CPCs in the newborn was not associated with abnormal physical findings or with any delay in early childhood development.

The choroid plexus is a region of the secretory epithelium, located in the brain ventricles, which produces cerebrospinal fluid (CSF). It can be visualized on fetal ultrasound as an echogenic mass as early as the ninth week of gestation [1]. During the second trimester, cysts may develop from entanglement of the rapidly growing choroidal villi, which appear as hypoechoic regions filled with CSF [2, 3]. Choroid plexus cysts (CPCs) can be detected in 0.18 to 3.6% of all second-trimester fetal sonograms [2, 3]. In 1984, Chudleigh et al first described these cysts as a benign anatomic variant that resolved spontaneously in utero [4]. Since then, disagreement has continued regarding the associated risk of chromosomal abnormalities, such as aneuploidy, with this ultrasonic finding [5–8]. Most studies have described the significance of CPCs detected from second-trimester fetal ultrasonogram, and there have been few studies that have investigated CPCs detected in neonates [9, 10] and their influence on later development [11]. The incidence of CPCs in normal newborns has not been reported. The present study was designed to determine the incidence and associated early neurodevelopmental outcome in children who had neonatal CPCs.

Subjects and Methods

During a 1-year period from July 1997 to June 1998, a total of 2,111 normal newborns at our department underwent brain ultrasonographic examinations in the first 3 days of life for routine neonatal screening. All
neonates with CPCs were followed up with serial sonograms at 1, 2, 4, and 6 months of age, with some followed up for longer durations depending on availability. The characteristics of the cysts and associated sonographic abnormalities were initially evaluated by three well-trained technicians, and subsequently confirmed by either of the authors. The diagnosis of CPC was sonographically established based on identification in both coronal and sagittal planes as a thin-walled, fluid-filled, hypoechoic lesion within or projecting from the choroid plexus.

Achievement of developmental milestones was evaluated by either of the authors during clinical follow-up. Developmental status was assessed using the Denver II Developmental Screening Test, a screening test covering the major developmental aspects for children from birth through 6 years, including gross and fine-motor, social, cognitive, and language skills [12]. A modification of the Denver II Developmental Screening Test, performed by one of two examiners through telephone survey, was used for those parents who were not able to visit our clinic regularly.

Cranial ultrasound was performed using a Hewlett-Packard M2410A (Andover, MA, USA) at the neonatal stage and then using an Acuson 128XP (Mountain View, CA, USA) for follow-up studies; each of the machines was equipped with a 5.0-MHz sector transducer.

Results

CPCs were detected in 186 (8.8%) of the 2,111 newborns. Among them, 113 were male and 73 were female, with gestational ages ranging from 36 to 41 weeks (mean, 39.1 wk) and birth weight from 2,220 to 4,600 g (mean, 3,231 g). The mean Apgar scores at 1 and 5 minutes were 8.5 and 9.0, with no scores below 6 and 8, respectively. No lesions or CPCs were revealed during maternal ultrasound examinations. The mean maternal age was 31 years (range, 21–40 yr). Maternal age was advanced (> 35 yr) in 23 subjects. Of these, prenatal amniocentesis for cytogenetic study was performed in 18 women, with all revealing normal fetal karyotypes. Physical findings were normal at birth for the other five neonates without prenatal karyotyping.

Among the 1,925 neonates without CPCs, the mean gestational age was 38.9 weeks and mean birth weight was 3,254 g. No significant difference was found in the neonates with or without CPCs in terms of gestational age and birth weight (p = 0.055 and 0.445, respectively).

Of the 186 neonates with CPCs, 14 (7.5%) had bilateral cysts. The mean (± standard deviation) diameter of the cysts was 2.6 ± 0.8 mm (range, 1.1–8.6 mm). Five subjects (2.7%) had cysts larger than 5 mm, and one such case is shown in Fig. 1. All 186 neonates showed normal physical examinations with uneventful postnatal courses, except for transient cyanosis (2), transient tachypnea (3), transient hypoglycemia (2), and neonatal hyperbilirubinemia requiring phototherapy (3). Additional findings from brain ultrasound included subependymal cysts (7), lenticulostriate vascular echogenicity (1), and mild subdural effusion (4).

Of the 186 neonates with a diagnosis of CPC, follow-up ultrasonic studies were completed for 155. Cyst resolution was determined in 38 of the 155 subjects (24.5%) by 1 month of age, by 2 months of age in an additional 45 subjects (21.4%), and by 4 months in an additional 29 subjects (Fig. 2A and B). Residual cysts were still visible in 18 subjects (11.6%) at 6 months of age. Of these, follow-up ultrasonic examinations at 9 months of age showed complete resolution in 6 subjects (3.8%); 4 of these were male and 2 were female. Fig. 1. Large single cyst (7.3 mm) of the right choroid plexus in a neonate. A) coronal section, B) sagittal section.
Neonatal Choroid Plexus Cyst

**Discussion**

While often detected from prenatal ultrasound during routine second-trimester examinations [1–8], most CPCs are asymptomatic, and generally regarded as a benign variant [1]. Several reports, however, have proposed their predominance in aneuploid fetuses, especially trisomy 18 [6–8, 13]. Therefore, the detection of CPCs in the second trimester of pregnancy is an indication for ultrasound targeted specifically for signs of aneuploidy [1, 13]. Controversy still exists, however, over the need for routine amniocentesis when the presence of isolated CPCs is detected with no associated structural anomalies [5–8, 13–15]. Several recent studies have recommended karyotypic survey when some risk factors are present: advanced maternal age [16, 17], additional structural anomalies [18, 19], abnormal biochemical screening results in the mother [20, 21], and large (>10 mm) bilateral cysts [22].

Postnatally, cysts of the choroid plexus are commonly found and rarely symptomatic [1, 10]. Incidental CPCs were detected in more than 50% of neonatal autopsy specimens [9]. In one postmortem study [23], CPCs with an epithelial lining were found in 25% of fetuses and infants, and in 50%, 48%, and 35% of persons who died between 1 and 30, 31 and 60, and 61 and 91 years of age, respectively. The incidence of CPCs detected on routine neonatal ultrasound (8.8%) in the present study was higher than has been reported from studies in utero (0.4%–3.6%) [2, 3]. This difference is explained by the properties of the maternal abdominal cavity, which present an effective anatomical barrier to prenatal ultrasonic examination. Better resolution is obtained through the open fontanel after delivery. Previous studies reported that the minimum size of a detectable CPC was 2 mm in utero [6, 14], while the minimum detectable size of CPC in the neonates in this study was 1.1 mm. Another study found that the prevalence of CPCs was 3% in neonates admitted for various indications during a study period of 2.5 years [10]. A study from Taiwan revealed 18 cases of CPCs among 3,307 pediatric neurosonographic examinations due to various clinical complaints within a period.
of 5 years [24]. The present study is the first to describe the incidence of CPCs determined through routine ultrasonic screening in a newborn population.

In this study, CPC size ranged from 1.1 to 8.6 mm, confirming findings from previous reports that the majority of CPCs in newborns are less than 1 cm in size [1, 25]. Symptomatic CPCs are larger, ranging from 1.5 to 9 cm in diameter [25, 26]. CPCs usually remain static in size or regress spontaneously [25]. Chudleigh et al first reported five transient CPC cases that resolved spontaneously in utero [4]. Several prenatal studies have demonstrated that the majority of CPCs develop before 20 weeks of gestation and subside before 24 weeks [4, 5]. However, the late disappearance or persistence of CPCs has also been demonstrated for the normal fetus [27]. In this study, the prenatal origin of neonatal CPCs could not be confirmed since such ultrasonic lesions were not identified in maternal prenatal examinations. It is clear, however, that isolated neonatal CPCs are not uncommon, and are not usually associated with neurologic diseases.

There are comparatively few data on the postnatal ultrasound characteristics of CPCs [9, 10, 24] and follow-up study of the sonographic changes has been reported solely by Riebel et al [10]. In that study, complete disappearance of CPCs was found in only seven of 32 (22%) patients during follow-up periods ranging from 3.5 to 13 months. By contrast, ultrasound evidence of resolution of CPCs was demonstrated in about 88% of our normal subjects by 6 months of age. This difference may be explained by the fact that Riebel et al’s subjects consisted not of normal infants as in our series, but of infants admitted with various indications. From prenatal observations [1, 11], it has been theorized that CPCs regress as the loose supporting stroma decreases with growth of the fetus. The resolution mechanism for neonatal CPCs is probably similar. A possible association between CPC persistence and increased prevalence of chromosomal aberration has been proposed in some prenatal investigations [27, 28]. Further, as demonstrated from this study, the size of the cyst is another important factor affecting resolution. Nevertheless, the finding that most neonatally detected CPCs resolve with age corresponds with what occurs in utero, with resolution increasing with age [4, 26]. Large-scale follow-up studies are necessary to more clearly determine the natural course of CPCs detected at the neonatal stage.

Our literature review identified only one report of developmental follow-up for children with prenatally diagnosed CPCs [11] and no previous study attempting to determine the overall outcome for normal neonates with CPCs. Although Riebel et al found no association between CPCs and chromosomal aberration or neurologic disease in their patient group [10], the present study provides the first data regarding early neurodevelopmental outcome for normal neonates with CPCs. In the present study, the Denver II Developmental Screening Test was chosen to evaluate developmental status since it is used worldwide and is a reliable test for the identification of developmental delay from birth through 6 years of age [12]. Providing an overall evaluation of gross- and fine-motor, social and cognitive skills, and expressive and receptive language, the test can detect developmental delay as early as 3 to 6 months of age [29]. In recent years, a policy of early intervention for developmental delay has been proposed in many countries, based on the presumption that detection and intervention before 2 years of age may have a significant influence on the future of these children [30]. The findings of this study suggest that isolated CPCs in neonates do not affect infant or early childhood development and may provide useful information for counseling parents of infants with a diagnosis of CPC.

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References