Cranial ultrasonographic findings in healthy full-term neonates: A retrospective review

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Abstract

Background: Ultrasonography is a non-invasive diagnostic technique, and it has been used to detect intracranial lesions in neonates for a long time. Correspondingly, screening tests using cranial ultrasonography have been applied for early detection of intracranial lesions in full-term neonates during the past decade.

Methods: We retrospectively reviewed the findings of cranial ultrasonographic screening tests in healthy full-term neonates between September 2004 and August 2009. The ultrasonographic findings were divided into the following categories: (a) nonsignificant (NS) group, including normal and normal variations, (b) minor anomaly group, including tiny cystic lesions, mild hemorrhage, or mild ventricular anomaly, and (c) major anomaly group, including significant anomaly of any intracranial pathology. The participants with major anomalies were further reviewed, and the following medical records of all enrolled patients were reviewed until they were 24 months of age.

Results: There were a total of 3186 neonates who received cranial ultrasonographic screening examination during the 5-year period, and most of them (2982 cases, 93.6%) were assigned to the NS group. The most common normal variation was the presence of cavum septum pellucidum (1979 cases, 62.1%). Minor anomalies were found in 202 (6.3%) neonates, including 119 (3.7%) neonates with tiny cysts, and 59 (1.9%) neonates with mild intraventricular hemorrhage. Major anomalies were found in two (0.06%) neonates, including obstructive hydrocephalus and agenesis of the corpus callosum. Two other infants (0.06%) initially presented with minor anomaly or normal variation, but they were diagnosed as Moyamoya disease and neonatal seizure some months later.

Conclusion: The incidence of minor and major anomalies detected by cranial ultrasonographic screening examinations in healthy full-term neonates is 6.3% and 0.06%, respectively. Thus, cranial ultrasonographic screening testing may play a role in the early diagnosis of intracranial anomalies of otherwise healthy neonates. However, this examination cannot exclude or detect all cranial abnormalities, including many potential neurologic diseases of neonates, so continuing clinical diligence is still important for all infants.

Keywords: brain; neonate; newborn screening; ultrasonography

1. Introduction

Ultrasonography is a non-invasive technique of deep tissue structure image study that has proven useful in detecting cranial abnormalities in neonates for many years. Because the anterior fontanelles of neonates remain open for a certain period of time, ultrasonography has been effectively used to detect intracranial lesions in neonates.1–11 Most neonatal patients requiring cranial ultrasonography are premature babies or sick full-term infants because they are at a high risk of having intracranial lesions.11,12 In addition, brain ultrasonography can be performed in special care units because it is easy to move the necessary equipment bedside to survey
patient intracranial lesions. Therefore, cranial ultrasonography is generally a safe and convenient way to rapidly evaluate intracranial conditions in neonates.

In addition to high-risk neonates, some full-term neonates may have asymptomatic intracranial lesions at birth, and some of the lesions may cause long-term neurologic deficits in infants. Early screening for intracranial lesions in newborn babies has been used for early evaluation and diagnosis in some medical centers, and investigators have reported finding different intracranial lesions on the cranial ultrasonographic screening examinations. Therefore, cranial ultrasonography has been determined to be a useful tool for early diagnosis of neonatal intracranial pathologies.

Cranial ultrasonographic screening has been performed for more than 10 years in many tertiary hospitals in Taiwan. A detailed analysis of these ultrasonographic findings is important to elucidate the effectiveness and clinical significance of cranial ultrasonography in healthy full-term neonates. Therefore, we designed this retrospective analysis to review and analyze the findings of cranial ultrasonography in healthy full-term neonates during the past 5 years.

2. Methods

We retrospectively reviewed all cranial ultrasonographic screening tests in healthy neonates who were born in Taipei Veterans General Hospital in Taipei, Taiwan, R.O.C., between September 2004 and August 2009. All basic characteristics of the patients and the cranial ultrasonography reports were reviewed. This retrospective study has been approved by the Institutional Review Board of Taipei Veterans General Hospital, protocol number: 2012-04-013A.

During that period of time, all of the examinations were performed and reported by one of 3 well-trained attending physicians (including two neonatologists and one pediatric neurologist). In addition, the same portable ultrasound system (Acuson Cypress, Model No. 08267219, Siemens Medical Solutions USA, Inc., Mountain Views, CA, USA) with the same transducer probe (Acuson 7V3C ultrasound probe, Siemens Medical Solutions USA, Inc.) was used to perform cranial ultrasonography. The settings and the scanning procedures, including at least six coronary (orbital roofs, pentagon view, third ventricle, fourth ventricle, trigones, and over the top) and seven sagittal (midline, parasagittal-right, steep parasagittal-right, sylvian fissure-right, parasagittal-left, steep parasagittal-left, sylvian fissure-left) views, were all kept consistent.

The criteria for enrollment of subjects into our study were defined as follows: (a) healthy full-term neonates with gestational age between 37–42 weeks, and uneventful birth that did not require neonate admission for management or treatment except for neonatal jaundice requiring phototherapy, (b) the screening examination was requested by the family, and not at the behest of the medical staff for disease check-up, and (c) the examination was performed during the first 7 days of age.

The reports of the cranial ultrasonography of all enrolled subjects were reviewed, and findings were grouped into the following three categories: (1) nonsignificant (NS) group, which included normal and normal variations, (2) minor anomaly group, which included cystic lesions, mild hemorrhage, or mild ventricular dilatation, and (3) major anomaly group, which included significant anomaly of the corpus callosum, significant ventricular dilatation, or other major anomalies of the brain. For grouping of the findings in ventricular size, the following definitions were used: (a) frontal horn prominence: solitary finding of frontal horn width 3–5 mm, (b) lateral ventricular body prominence: solitary finding of ventricular body width 3–5 mm, (c) occipital horn prominence: solitary finding of thalamo-occipital distance 15–20 mm, (d) mild ventricular dilatation: ventricular body width > 5 mm and ≤10 mm, and/or thalamo-occipital distance > 20 mm, and (e) significant ventricular dilatation: ventricular body width > 10 mm and thalamo-occipital distance > 20 mm.

The width of the lateral ventricular body was measured at the midway position in-between frontal and occipital horn on the parasagittal view.

If the reports revealed positive findings that might be grouped into minor or major anomaly groups, then another neonatologist to confirm the diagnosis and measurement would review the recorded images.

The medical records of enrolled infants were also reviewed, extending through 24 months of age, to evaluate if any late onset of neurological disease occurred in the first 2 years of life. Any information regarding to neurologic image studies, or neurologic/developmental problems were recorded.

3. Results

During the study period, there were a total of 6875 neonates born in Taipei Veterans General Hospital, and 3186 (1664 boys and 1522 girls, male-to-female ratio: 1.09) of them underwent cranial ultrasonographic screening testing. The birth body weight of enrolled patients was 3161 ± 387 g (range: 2062–4486 g), and the gestational age was 39 ± 1 weeks (range: 37–42 weeks).

3.1. NS group

There were 2982 (93.60%) neonates grouped into the NS, group, including 817 cases of normal cranial structures and 2165 cases with one or more normal cranial variations. There was no significant difference between male and female infants. The most common finding within the normal cranial variations was the presence of cavum septum pellucidum, which was found in 1979 neonates (62.12% of total cases). Other variations included the presence of ventricular variations, prominence of choroid plexus or cisterna magna, cavum vergae, mild periventricular echogenicity, benign mild extracerebral fluid accumulation, and corpus calosum variations [thin (11 cases) or atypical (3 cases) appearance]. These are detailed in Table 1.
3.2. Minor anomalies

There were 202 neonates (6.34%) reported with the following minor anomalies in the cranial ultrasonographic examinations, including tiny cystic lesions, mild hemorrhage, and mild ventricular anomalies. Generally, there was no significant difference between male and female infants.

Cystic lesions (119 neonates, 3.74%) were the most common findings, and the caudothalamic groove was the most common site (Table 1). In addition, most cases were found to have cystic lesions at the left caudothalamic junction, or bilaterally, and less commonly found only at the right side (Table 2).

Mild intraventricular hemorrhage was the second common finding (59 cases, 1.85%), and most of those cases were found
to have mild germinal matrix hemorrhage (58 neonates, 1.82%). These results are shown in Table 1. Bilateral germinal matrix hemorrhage was commonly found at more than just one site (Table 2).

In the 24 cases of mild ventricular anomalies, most of them were reported as mild ventricular dilatation (20 cases, 0.63%). These results are shown in Table 1. Among those cases, six infants had bilateral dilatation, 12 infants had left side dilatation, and only two infants had dilatation only on the right side. In addition, there were four infants noted to have some intraventricular septums in bilateral lateral ventricles.

### 3.3. Major anomalies

There were two neonates grouped into major anomalies, including one infant with significant ventricular dilatation and the other one noted with agenesis of corpus callosum (Table 1).

The first major anomaly neonate was found to have significant ventricular dilatations in the initial cranial ultrasonography. Brain magnetic resonance imaging (MRI) revealed marked obstructive hydrocephalus with significant dilatation of bilateral lateral ventricles and the third ventricle, and the presence of a retrocerebellar arachnoid cyst with a diameter larger than 5 cm (Fig. 1). An endoscopic ventriculostomy of the third ventricle was performed when the child was 2.5 months of age. Follow-up cranial ultrasonography revealed much improvement and the presence of a small cyst (0.5 cm in diameter) at retrocerebellar region 10 months later. Tracing back to the child’s prenatal reports, there was no record of any anomaly on fetal ultrasonography.

The second infant in the major anomaly group was found to have agenesis of corpus callosum, a choroid plexus cyst at the left lateral ventricle and right colpocephaly at the initial cranial ultrasonography (Fig. 2). Subsequent auditory hearing test and electroencephalography (EEG) both showed no abnormality, and there was no record regarding any neurologic problem of the child during the first 2 years. After tracing back to the child’s maternal history, dilatation of subarachnoid cisterns had been noted when the pregnancy gestation period was 32 weeks.

### 3.4. Cases with late onset of neurologic problems

After review of the enrolled cases of NS and minor anomaly groups, there were two additional neonates later admitted due to neurologic disease within 2 years after birth, the first case involved neonatal seizure and the second case a diagnosis of Moyamoya disease.

In the case of neonatal seizure, the child had been found to have prominence of bilateral frontal horns in the initial cranial ultrasonography after birth, and seizure attacks began on Day 6 after the child was born. MRI and EEG did not show any abnormality. Phenobarbital was used to control the seizure. However, the patient’s mother stopped the medication on her own initiative 3 weeks later, and then there were no more seizure attacks or presence of any other new neurologic problems recorded.

In the neonate case with Moyamoya disease, the child was observed to have bilateral germinal matrix hemorrhage on cranial ultrasonography after birth. However, she was unable to be located or follow-up by our hospital. Approximately 2 years later, the child was admitted to another hospital after she suffered right limbs weakness and seizure attack; Moyamoya disease was diagnosed following cranial angiography. After two neurosurgical procedures, the right limb weakness continued to progress. The child returned to our hospital when she was 2.5 years of age, and MRI and EEG revealed multiple cranial infarctions with diffuse cortical dysfunction. After her last visit to our hospital, she had ongoing challenges and had limb disabilities and mild mental retardation; she was in need of long-term rehabilitation.

### 4. Discussion

The present study revealed that 93.6% (2892/3186) of healthy neonates undergoing cranial ultrasonographic
screening tests had no obvious abnormal findings. Of that number, 72.6% (2165/2982) of them had different kinds of normal variations. Some neonates (6.3%, 202/3186) had different minor abnormal findings; tiny cystic lesions were the most common (63.9%, 129/202), especially at the caudothalamic grooves. There were only two (0.06%, 2/3186) neonates who were found to have significant cranial anomalies by the screening cranial ultrasonographic examinations.

There have been significant advances in the technology of cranial ultrasonography in recent years. In cranial ultrasonography, it is not difficult to examine the developing cerebral surface, assess sulcal-gyral maturation, and even investigate the subtle changes in cerebral blood flow and parenchymal perfusion by using Doppler ultrasonography. Furthermore, there is no risk of any radiation exposure or invasive procedure to the frail neonatal brain while performing this examination. Therefore, the clinical role ofcranial ultrasonography will become more important in future neonatal care. Using cranial ultrasonography for early identification of significant intracranial lesions in healthy full-term neonates may help clinicians to perform early and effective management to improve their patients’ neurodevelopmental outcomes.

In the NS group of our present study, cavum septum pel- lucidum (91.4%, 1979/2165) was the most common normal variation, with a prevalence of 62.1% (1979/3186) in all examined neonates. Of course cavum septum pellucidum is typically present in all fetuses, so it is commonly seen in preterm infants. More than 85% of them may fuse by 3–6 months after birth in full-term neonates, so cavum septum pellucidum can be classified as a normal variation in full-term neonates. However, neurodevelopmental abnormalities involving midline structures had been considered, possibly having psychopathologic consequences. Although the persistent presence of cavum septum pellucidum had even been reported to be loosely associated with schizophrenia, chronic brain trauma, limbic epileptogenesis, or chromosomal anomaly, there was still no strong evidence that might establish such a relationship. Long-term follow-up of cases with the persistent presence of cavum septum pellucidum may be necessary in the future to better understand any connection with potential neurodevelopmental anomalies.

Subependymal cysts and choroid plexus cysts had been reported as common findings in neonatal cranial ultrasound scans, and reported in 1%–5% of the neonatal population. The presence of an isolated subependymal cyst or a choroid plexus cyst usually resolves after a variable period of time, and no serious neurodevelopmental complications occur in most cases. However, in the meta-analysis of Alvarez and colleagues, they found that one in four to five infants with bilateral multiple subependymal cysts or choroid plexus cysts may have a congenital infection or genetic anomaly. Therefore, newborn infants with multiple or bilateral cranial cystic lesions should be carefully examined for the potential underlying diseases. In the present study, 3.7% (119/3186) of all examined neonates were found to have cystic lesions, which is similar to other reports (Table 1). Of those cystic lesions found, we found that 31.1% (37/119) presented as bilateral intracranial cysts (Table 2). However, we did not find any abnormal neurodevelopmental record in the following 18–24 months after discharge. A further follow-up may be necessary to identify and assess any neurodevelopmental anomalies of these neonates that may occur in the future.

Intraventricular hemorrhage is common in premature infants or those of very low birth weight. However, it is also can be seen in full-term neonates. When the hemorrhage is restricted to grades I or II, there are often no further complications. Clinically significant intraventricular hemorrhage, such as grades III or IV, are considered to have a strong correlation with poor neurodevelopmental outcomes in neonates. Long-term neurologic sequelae, including epileptic disorder, perceptual difficulties, cognitive deficiencies, and mental and other neurologic handicaps, have been reported in these survivors. In the present study, the prevalence of asymptomatic intraventricular hemorrhage, including germinal matrix and choroid plexus hemorrhage, was less than 2% in healthy full-term neonates. Although all of these neonates exhibited no neurological deficit during the studied follow-up period, long-term observation and neuro- logical follow-up for these infants may be necessary.

Heibel and others had reported 3.5% (35/1000) of healthy full-term neonates had different grades of intracranial hemorrhage, and four of them developed hemipareses or infantile spasm within 1 year of birth. Wang and coauthors
also had reported 0.26% (6/2309) of healthy full-term neonates had major brain lesions, including intracranial hemorrhage, corpus callosum agenesis, and lacunar infarct, and four of them had significant developmental delay at the mean age of 24 months. The prevalence of intracranial major anomaly (0.06%) or intraventricular hemorrhage (1.85%) in our study were lower than described in previous reports. One possible explanation for this difference is the popularization and advancement of ultrasonographic devices and techniques. Recently, pregnant women can receive regular obstetric ultrasound follow-up before delivery, so most major lesions can be detected after 20 weeks of gestational age. Any neonates known to have any concern of significant intracranial anomalies or hemorrhage before delivery would be admitted and examined soon after birth. In our survey, only 0.03% of all cases had mild ventricular dilatation. Although none of those patients reported neurologic problems during the following 2 years of life, long-term follow-up is still suggested.

Ultrasound imaging is a sensitive diagnostic tool, and can frequently detect significant ventricular dilatation and midline brain lesions. In our study cases, there was one patient with obstructive hydrocephalus that presented as marked ventricular dilatation in the initial cranial ultrasonography. After adequate surgical interventions, there was no further neurological problem reported during the following 2 years of life. In this case, definite benefits were obtained from cranial screening ultrasonographic examination. In addition, we also found that 20 infants (0.63% of all cases) had mild ventricular dilatation. Although none of those patients reported neurologic problems during the following 2 years, follow-up is still suggested.

Agenesis of the corpus callosum is a rare midline brain congenital abnormality, with a reported prevalence of 0.03%—0.7% in the general population and 2.3% among developmentally disabled individuals. In our study, only one case involved a diagnosis of agenesis of the corpus callosum, so its incidence was also only 0.03% in healthy full-term infants, which is similar to other reports. When agenesis of the corpus callosum is diagnosed, many neurological problems, such as mental retardation or developmental delay, seizure, cerebral palsy, borderline intelligence, and other abnormalities had been reported. In addition, it is considered to be a component of many different syndromes. Although our diagnosed infant did not show any sign of neurological problem during the first 2 years of life, long-term follow-up is still necessary.

Although cranial ultrasonography is a convenient technology used to detect intracranial lesions, it has some limitations, especially in minute parenchymal problems or vascular diseases such as cerebral infarction, minor vascular anomalies or small hemangiomas. We did find two cases (0.06% of all neonates) with late onset of neurologic problems even with normal or minor anomaly in the initial cranial ultrasonographic examination, so the cranial ultrasonography could not expose all neurologic pathology in neonates. Clinical alertness to any sign of neurologic deficit is important for all infants even if they have been examined with cranial ultrasonography in the early neonatal period.

The retrospective study design has a benefit that we could conclude more than 3000 infants who had previously received the cranial ultrasonography at birth. However, the retrospective design is also the major limitation of the present study, so there was no well designed neurologic/developmental follow-up. Furthermore, not all enrolled infants kept visiting our hospital during the following 24 months. The incidence of late onset neurologic problems might be higher than we have found in the medical charts. A future study with prospective design for a longer period of time should be done in the future for elucidating the residual questions on the diagnostic value of neonatal cranial ultrasonographic screening test.

In conclusion, the incidence of minor and major anomalies detected by cranial ultrasonographic screening examinations in healthy full-term neonates is 6.3% and 0.06%, respectively. Thus, cranial ultrasonographic screening may play a role in the early diagnosis of intracranial anomalies of healthy full-term neonates. However, this examination cannot exclude all neurologic diseases of neonates, so it is important for practitioners to remain clinically alert for all infants.

References


27. Fernandez Alvarez JR, Amess PN, Gandhi RS, Rabe H. Diagnostic value of subependymal pseudocysts and choroid plexus cysts on neonatal