Editorial
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Head circumference alone at birth, is it practical?

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Head circumference (HC) measurement is an important physical examination of infants because an abnormality of HC can indicate an underlying congenital, genetic, or acquired neurologic problem. An abnormality of HC is determined by brain size, including any malformations and space occupying lesions, cerebrospinal fluid and blood volume, presence of subdural fluid and thickness of skull bones and overlying tissue scalp. The HC measurement, herein referred to as the occipital frontal circumference (OFC), extends from the most prominent part of the glabella to the most prominent posterior area of the occiput. The OFC can be affected by thick hair and cranial bone deformations or hypertrophies. Ethnicity and growth stature must also be considered when evaluating the OFC.

Relative macrocephaly indicates that the OFC plots within 2.0 standard deviations (SDs) of the mean but plots disproportionately above that for stature[1]. Macrocephaly may be due to megalencephaly, hydrocephalus, cranial hyperostosis, or other conditions. Macrocephaly is relatively frequent at birth and is a common cause for genetic consultation. For practical purposes, +2 SD is reasonable as a threshold for considering further investigation and counseling, but many normal infants will also be included if HC alone is used as the diagnostic criterion.

Benign macrocephaly of infancy is a common problem in pediatric neurology practice[2]. Therefore, measurement of HC is an important diagnostic tool for discovering intracranial expansive conditions in infants. A limited number of studies regarding macrocephaly at birth have been performed in Korea.

Jeong et al.[3] used ultrasonography to investigate the characteristics and significance of macrocephaly at birth in Korean infants and Jeong et al's study is the first study to investigate macrocephaly based on the 2007 Korean National Growth Charts. This study showed that macrocephaly was twice as prevalent in boys as in girls and that height at birth correlated with OFC. The majority of patients had no remarkable abnormality on ultrasonography. Some patients were diagnosed with germinal matrix hemorrhage (GMH) and an enlarged subarachnoid space. GMH without intraventricular hemorrhage (IVH) usually disappears within a year[4]. Full-term infants with subarachnoid space enlargement have normal development, a normal neurologic examination, and usually do not require surgical intervention. This study identified an enlarged subarachnoid space in 6.7% of the patients.

The majority of patients with isolated macrocephaly have few neurological symptoms or physical abnormalities and show normal development or intelligence or both[5]. Neverthless, macrocephaly is a common reason for a medical genetics referral as there are many genetic conditions associated with it. According to the Online Mendelian Inheritance in Man (OMIM) Database, 225 syndromes are associated with macrocephaly.

The degree of severity of the macrocephaly is an important predictor of prognosis. The finding of mild macrocephaly (<+2.5 SD), even in the presence of subtle signs, such as enlarged subarachnoid spaces or frontal bossing, carries a good prognosis[6].

Nonsyndromic macrocephaly is not associated with any other prominent physical

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trait or major malformation. Minor craniofacial changes can be present but those are due to the secondary effects of the enlarged cranial vault. These changes include a prominent or high forehead and a dolichocephalic head shape[7]. Increased width of the cranial base can at times produce mild hypertelorism and down slanting palpebral fissures.

Syndromic macrocephaly is diagnosed when significant abnormalities are associated with generalized brain enlargement. Megalencephaly causing macrocephaly is considered a disorder of neuronal and glial proliferation. Syndromic macrocephaly may be associated with minor or major brain anomalies. Although macrocephaly rarely results from chromosomal anomalies, it has recently been described in patients with chromosomal microdeletion syndromes[7]. Patients with syndromic macrocephaly, who may frequently suffer from mental retardation, must be differentiated from patients with nonsyndromic macrocephaly, which has a good prognosis. Therefore, studies suggest considering karyotyping and microarray-based comparative genomic hybridization in macrocephalic patients without a definitive diagnosis[7].

In syndromic macrocephaly, significant abnormalities are associated with the generalized brain enlargement. Syndromic macrocephaly should be distinguished from other genetic syndromes in which macrocephaly is a clinically predominant finding. The nongenetic macrocephalies are due to secondary effects of environmental events such as those related to neonatal IVH or infection. Benign extracerebral fluid collections are a relatively common cause of nongenetic macrocephalies. However, routine measurements of HC are of value mainly for early detection of hydrocephalic conditions and, to a certain degree, intracranial cysts during the first 10 months of life. Increased HC as a initial symptom seems important only for infants with hydrocephalus and patients with cysts[8]. For intracranial tumors and other expansive conditions, increased HC is very rarely the initial symptom that causes suspicion and leads to diagnosis. Instead, other symptoms, such as vomiting, irritability, drowsiness, or headache, are more common as the initial symptoms.

In Norway, measurements of HC are performed at regular intervals during the first year of life. Serial OFC measurements and clinical follow-up are necessary to accurately determine the course of macrocephaly. Routine measurements of HC during the first year of life mainly detect infants with hydrocephalus or cysts; other expansive conditions yield other symptoms[8].

In a neonate suspected of having macrocephaly, consideration should be given to detailed ultrasonography, magnetic resonance imaging (MRI), family history, and genetic counseling, including karyotyping and more detailed genetic testing. Radiologic findings of macrocephaly at birth are often benign. However, a benign ultrasonography finding does not guarantee that there will be benign long-term neurological and neurophysiological outcomes. Ultrasonography is the initial procedure recommended since it accurately evaluates ventricular size, extraaxial fluid, and congenital malformations[6].

Primary megalencephaly (PMG) is defined as an HC above the 98th percentile that most likely is due to brain enlargement and is not secondary to disease. PMG at birth is a risk factor for low intelligence level[8]. The macrocephaly observed in autism becomes manifest around 1–3 years of age and is typically not present at birth[9]. Most children with phosphate tensin homolog (PTEN) mutations are macrocephalic[10]. The conditions associated with macrocephaly in combination with generalized somatic overgrowth include the syndromes of Sotos, Weaver, Beckwith-Wiedemann and others[7]. Relative macrocephaly may be present in Fragile X syndrome[7]. Of all the leukodystrophies, Alexander disease and Canavan disease are most clearly associated with macrocephaly. Macrocephaly is present in the neonate in glutaric aciduria, type 1, an inborn error of metabolism associated with neuronal or glial dysfunction[11].

Physical examination and history alone may identify a syndromic disorder. If there is no neurological dysfunction, a brain imaging study may not be needed, and the possibility of PMG should be considered. When developmental concerns exist, a brain MRI is usually performed. In the absence of an informative MRI phenotype, tests such as chromosome study, array-comparative genomic hybridisation and fragile X molecular screening are often performed[7]. Metabolic screening with urine organic acids analysis and blood acylcarnitine profile may also be considered. Lysosomal enzyme screening is indicated if the clinical picture suggests a storage disorder. An MRI phenotype showing a predominant leukodystrophy warrants specific diagnostic testing such as enzyme or gene analysis.

In conclusion, serial measurements of OFC are important in the evaluation of conditions with macrocephaly. Because identification of macrocephaly can lead to correct syndrome identification, the careful assessment of the OFC remains a crucial part of pediatric neurologic evaluation.

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