Neuroimaging indications for children with macrocephaly

Makrosefalisi Olan Hastalarda Nörogörüntülemenin Tanısal Değeri

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ABSTRACT

Objective: The goal of this study was to determine the relative frequencies of benign external hydrocephalus (BEH), hydrocephalus and other conditions in a large series of imaging studies performed for macrocephaly and identify additional risk factors for patients with macrocephaly that would most likely benefit from neuroimaging evaluation.

Material and Methods: Medical records at our center were searched for the term macrocephaly retrospectively. The search extended from 1th January 2014 to 1th June 2019. Patients older than 36 months of age were excluded. Information about age, gender, symptoms and clinical signs (seizures, neurologic abnormalities on exam such as hypotonia), neuroimaging findings, developmental delay, family history of macrocephaly and head circumference (HC) were collected for each patient.

Results: A total of 103 patients were included in the analysis. The mean age at the time of imaging was 9 months (±5.5 months). Twenty-one (20.3%) of the subjects were female and 82 (79.6%) were male. Twenty-nine of the imaging studies were magnetic resonance imaging, 26 were computed tomography and 65 were head ultrasounds. Patients with abnormal neuroimaging results had significantly higher rates of developmental delay or abnormal neurologic exam than patients with normal neuroimaging results or BEH ($p=0.003$ and $p<0.0001$). There was no significant difference between the neuroimaging results of patients with and without positive family history of macrocephaly.

Conclusion: This study suggests that neuroimaging for macrocephaly has almost negligible diagnostic yield unless having developmental delay or abnormal neurological examination.

Key Words: Benign external hydrocephalus, Macrocephaly, Neuroimaging

ÖZ

Amaç: Bu çalışmada makrosefali için yapılan görüntülemelerde benign eksternal hidrosefali (BEH), hidrosefali ve diğer ilişkili durumların göreceli sıklıklarını belirlemek ve nörogörüntüleme değerlendirmesinden fayda sağlayacak olan makrosefali hastaları için ek risk faktörlerini tespit etmek amaçlanmıştır.

Gereç ve Yöntemler: Merkezimizdeki 1 Ocak 2014 ile 1 Haziran 2019 tarihleri arasındaki tıbbi kayıtlar geriye dönük olarak makrosefali tanı kodu ile tarandı. 36 aylıktan büyük hastalar çıkarılarak yapılan taramada her hasta için yaş, cinsiyet, semptomlar ve klinik bulgular (nöbetler, hipotoni gibi muayenede nörolojik anormallikler), nörogörüntüleme bulguları, gelişimsel gecikme, ailede makrosefali öyküsü ve baş çevresi bilgileri elde edildi.

Bulgular: Toplamda 103 hasta taramaya dahil oldu. Ortalama görüntüleme yaşı 9 aydı. (±5.5 ay). Yirmi bir hasta kız (%20.38), seksen iki hasta ise erkekti (%79.61). Yapılan nörogörüntelemelerden yirmi bir tanesi manyetik rezonans görüntülemesi, yirmi altısı bilgisayarlı tomografi ve altmış beş tanesi transfontanel ultrasonografiydi. Anormal nörogörüntüleme bulguları gelişimsel geriliği veya anormal nörolojik bulgusu olanlarda diğer gruplara (BEH ve normal görüntüleme) göre anlamlı olarak daha yüksek saptandı ($p=0.003$ ve $p<0.0001$).

Sonuç: Bu çalışmayla makrosefalisi olan hastalarda gelişme geriliği veya anormal nörolojik muayene bulgusu saptanmamışsa yapılan nörogörüntülemelerin tanısal katkısı olmadığı ortaya konulmuştur.

Anahtar Sözcükler: Benign eksternal hidrosefali, Makrosefali, Nörogörüntüleme

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INTRODUCTION

Macrocephaly is a very common neuropediatric condition for referral of infants to pediatric neurology office practices and defined as head circumference (HC) greater than two standard deviations above the mean, or greater than 97th percentile (1). Most infants and children with macrocephaly can be due to benign causes. The most common cause of infant with macrocephaly have either familial macrocephaly or benign external hydrocephalus (BEH). Conditions that causes macrocephaly are rarely require treatment (2). The main sign calling for urgent intervention is the degree of acceleration in head growth, a tense anterior fontanel, dilated scalp veins, irritability, gross motor delay, hypotonia, seizures (3).

Despite head ultrasound (HUS) findings suggesting benign macrocephaly of infancy and normal neurologic examination results, patients are referred for further evaluation and additional neuroimaging by computed tomography or magnetic resonance imaging (4). Consequently, the number of infants subjected to imaging for macrocephaly is high and the diagnostic yield is low.

The goal of this study was to determine the relative frequencies of BEH, hydrocephalus and other conditions in a large series of imaging studies performed for macrocephaly and identify additional risk factors for patients with macrocephaly that would most likely benefit from neuroimaging evaluation.

METHODS

Medical records at our center were used to identify patients with macrocephaly by ICD-10 codes (Q75.3) retrospectively. The search extended from 1th January 2014 to 1th June 2019. Patients older than 36 months of age were excluded. This age was selected because after the age of three, the growth rate of the HC plateaus. Information about age, gender, symptoms and clinical signs (seizures, neurologic abnormalities on examination such as hypotonia), neuroimaging, family history of macrocephaly and HC were collected for each patient. A positive family history for macrocephaly was based on parental report and was recorded if documentation was present in the medical records by the clinician, and if not documented it was considered as unknown. Developmental assessment was defined from the documentation by the child neurologist's note (in objective or assessment sections).

Patients whose HC above the 97th percentiles were included. Children with histories of head trauma, intracranial hemorrhage, CNS infection and developmental delay without macrocephaly were excluded. Neuroimaging modalities were brain MRI, head CT and head ultrasound (HUS) to evaluate macrocephaly. The confirmatory imaging modality of macrocephaly was included for patients who had multiple neuroimaging studies.

Brain imaging results were grouped as normal, benign external hydrocephalus (BEH), abnormal with high clinical yield for macrocephaly, and abnormal with low clinical yield for macrocephaly. If a patient undergone further investigation or surgical intervention due to the imaging result, it was classified as an abnormal finding with high clinical yield. An abnormal finding with low clinical yield was considered if the imaging was abnormal however did not necessitated surgical intervention or further investigation related to macrocephaly such as periventricular leukomalacia (2).

Ethical approval was obtained from Ankara City Hospital (E-19-096/7.11.2019)

Statistical analysis

SPSS statistical analysis software package version 11.5 (SPSS Inc., Chicago, IL) was used in the statistical analysis. Demographic variables were assessed using descriptive statistics. Associations between categorical variables were assessed using Fisher's exact test and the chi-square test. The significant threshold was set at $p < 0.05$.

RESULTS

150 patients with macrocephaly were identified by investigating our database. Thirty-seven patients were excluded because the neuroimaging indication did not include macrocephaly. Ten patients were not actually macrocephalic. Of the remaining 103 patients had 120 neuroimaging studies. The mean age at the time of imaging was 9 months (±5.5 months). Twenty-one (20.38%) of the subjects were female and 82 (79.61%) were male. Twenty-nine of the imaging studies were brain MRI, 26 were CT head and 65 were HUS. Sixteen patients received CT (5 patients) or MRI (11 patients) as a confirmatory test. According to those imaging studies, 29 (28.15%) patients had normal findings, 46 (44.66%) had BEH, 28 (27.18%) patients had abnormal results. Twelve patients of the abnormal imaging results group had findings that were highly clinical yield including four with marked hydrocephalus requiring neurosurgical intervention, four with chronic subdural fluid collection for no accidental trauma and four patients with a Chiari 1 malformation and hydrocephalus.

Of the 12 patients with highly clinical yield group had abnormal neurological examination and/or developmental delay. Abnormal neurological findings on examination included sunset gaze, distended veins, bulging fontanel, irritability, hypertonia in bilateral lower limbs, and axial hypotonia. Patients with abnormal imaging findings with low clinical yield are showed in Figure 1.

Patients with abnormal neuroimaging results had significantly higher rates of developmental delay or abnormal neurologic exam than patients with normal neuroimaging results or BEH ($p=0.003$ and $p<0.0001$, Table I).

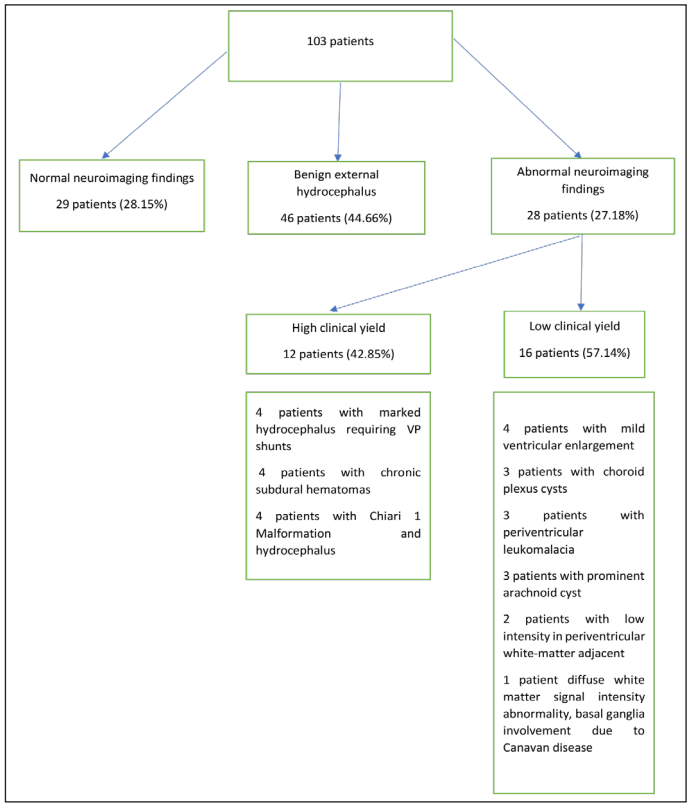

Figure 1: Neuroimaging results

Patients with high clinical yield findings had also significantly higher rates of developmental delay or abnormal neurological examination findings than other patients (Developmental delay: 8/12 patients vs. 21/91 patients, p=0.004, abnormal neurologic exam: 8/12 patients vs. 31/91 patients, p=0.003).

Twenty-nine patients of the 103 patients had developmental delays in addition to macrocephaly. Of those 14 had abnormal results, 6 had BEH and 9 had normal MRI results. Thirty-nine patients had abnormal neurological examination findings, eighteen of these had abnormal imaging results and eight had BEH (Table I).

Of 43 children's family history data were available. Twenty-nine patients had a positive family history of macrocephaly and 14 patients had a negative family history of macrocephaly. There was no significant difference between the neuroimaging results of patients with and without positive family history of macrocephaly.

DISCUSSION

Our study described potential risk factors for the indication of neuroimaging in macrocephaly. Abnormal neurological examination and developmental delay were found to be a risk factor for abnormal imaging in a child with macrocephaly. Similar results were reported by previous studies. Haws et al. (4) showed that 30% of patients with abnormal neurological examination findings had abnormal neuroimaging findings. Developmental delay was accepted as a potential risk factor in Sampson et al.'s study. They found 25 of 168 patients (14.88%) having delays and 5 had abnormal imaging and seven had BEH (2). In our study, patients with abnormal neuroimaging results had significantly higher rates of developmental delay or abnormal neurologic exam than patients with normal neuroimaging results or BEH (p=0.003 and p<0.0001). Because of these findings, developmental delay and abnormal neurological examination in a child with macrocephaly were accepted as the indication for neuroimaging. In those patients, there was no significant difference between the neuroimaging results of patients with and without positive family history of macrocephaly. These findings suggest familial macrocephaly does not eliminate the need for imaging if other features exist such as abnormal neurological examination or developmental delay.

In this study, the patients were evaluated with HUS, HCT, and brain MRI. Some of them were examined with more than one imaging modality. Only, sixteen patients had confirmatory brain MRI or head CT modalities after HUS. Thus, HUS is considered as an appropriate screening tool to manage patients with an open fontanelle and macrocephaly and no neurological findings as in previous studies (2, 5).

BEH is the most common etiology of macrocephaly in infants and is more common in the male population (6,7). It has typical neuroimaging findings of enlargement of the subarachnoid spaces especially over the frontal lobes and normal or enlarged lateral and third ventricles (7). In various studies, the male preponderance ranges from 52% to 80% (8-13). In our study, the gender distribution is likely with 79.3% boys. A population based study reported that BEH has an incidence of about 0.4 per 1000 live births (3). In a previous study 34% of children with macrocephaly had BEH (2). Similarly, we found as a rate of 44.66% BEH in our study. Although BEH is referred to as a benign condition, patients with BEH may exhibit mild developmental delay and attention problems later in life (14,

Table I: Neuroimaging results.

	Normal neuroimaging	BEH	Abnormal neuroimaging	Total	p
Developmental delay	9	6	14	29	0.003
Abnormal neurological examination	13	8	18	39	<0.0001
Positive family history of macrocephaly	12	10	7	29	0.8

BEH: *Benign external hydrocephalus.*

15). Haws et al. (4) found that 48.6% of patients with BEH had developmental delays at follow-up clinical visits. In our study the rate of abnormal neurological examination and developmental delay was significantly lower in patients with BEH. Only 6 of 46 patients with BEH had developmental delays.

One limitation of this study is its retrospective nature and charts were reviewed for clinician's records of child examinations. There was no standardized scale utilized when identifying developmental delay. Another limitation of this study is the possibility of the asymptomatic patients with macrocephaly could have been omitted.

CONCLUSION

This study suggests that neuroimaging for macrocephaly has almost negligible diagnostic yield unless having developmental delay or abnormal neurological examination.

Compliance with Ethical Standards:

Conflict of Interest: On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

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