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Original Article

Is Idiopathic Cuneate Gyrus Herniation an Isolated Variant or a Coexisting Finding in Pediatric Cases? An Magnetic Resonance Imaging Based Study

Pediatrik Hastalarda İdiyopatik Kuneat Girus Herniasyonu Tesadüfi mi Yoksa Eşlik Eden Bir Bulgu mu? Manyetik Rezonans Görüntüleme Temelli Çalışma

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ABSTRACT

Objective: We aimed to investigate whether idiopathic cuneate gyrus herniation (ICH) is an anomaly or a normal variant, its prevalence, whether there is a coexisting finding or pathology, as well as to characterize it with magnetic resonance imaging (MRI) findings.

Method: We evaluated 0-17-year-olds' brain MR images from January 2021-August 2023 at our clinic. Standard brain protocols utilize 1.5 Tesla MRI scanners. ICH and congenital brain abnormalities were evaluated in optimal brain MRIs. Malformations were classified as posterior fossa anomalies (PFA), commissural and cortical developmental anomalies (CCDA), and midline malformations.

Results: Our study comprised 691 pediatric brain MRIs with a mean age of 5.93±3.4 years, with 48.77% male and 51.23% female. The mean age of 32 ICH (+) patients was 6.19±4.02 years, with 40.63% male and 59.37% female. The prevalence of ICH was 32/691 (4.6%). In 63 (9.11%) congenital brain malformation patients, ICH presence differed (p=0.005). Congenital brain malformation patients with ICH showed a significantly higher PFA rate (n=8) than without ICH. The frequency of CCDA (n=23) and the association of PFA and CCDA (n=12) were significantly higher in ICH patients with congenital brain malformation. The frequency of congenital brain malformation was higher in 32 ICH (+) patients, with a rate of 50% (p<0.001).

Conclusion: We found that ICH is more frequent than reported and may be associated with congenital brain malformations. ICH must be differentiated from pathology to avoid unnecessary procedures. Congenital brain abnormalities may accompany ICH and should be carefully screened.

Keywords: Brain herniation, cuneate gyrus, idiopathic, malformation

ÖZ

Amaç: İdiyopatik kuneat girus herniasyonunun (IKH) anomali veya normal bir varyant mı olduğunu, prevalansını, eşlik eden ek bulgu ya da patoloji varlığını araştırmayı ve manyetik rezonans görüntüleme (MRG) bulguları ile tanımlamayı amaçladık.

Yöntem: Kliniğimizde Ocak 2021-Ağustos 2023 arasında çekilmiş 0-17 yaş aralığında pediatrik beyin MR görüntüleri retrospektif tarandı. Tetkikler 1.5 Tesla MRG tarayıcı ile standart beyin protokolü uygulanarak gerçekleştirilmiştir. Optimal görüntü kalitesine sahip olguların beyin MRG'leri IKH ve konjenital beyin malformasyonu varlığı yönünden değerlendirildi. Malformasyon saptanan olgular posterior fossa anomalisi (PFA), komissural ve kortikal gelişim anomalileri (KKGA), orta hat malformasyonları olarak gruplandırıldı.

Bulgular: Çalışma kapsamına alınan 691 olguda ortalama yaş 5,93±3,4 idi. %48,77'i erkek, %51,23'ü kadındı. IKH (+) 32 olgunun yaş ortalaması 6,19±4,02 olup %40,63'ü erkek, %59,37'i kadındı. IKH prevelansı 32/691 (%4,6) idi. Altmış üç (%9,11) olguda konjenital beyin malformasyonu saptanmış olup IKH (+) ve IKH (-) grupta anlamlı farklılık gösterdi (p=0,005). Konjenital beyin malformasyonlu IKH (+) olgularda PFA olan bireylerin (n=8) frekansı IKH (-) gruptan anlamlı yüksekti. Konjenital beyin malformasyonlu bireylerde IKH (-) olanlarda KKGA (n=23) ve PFA ile KKGA birlikteliği (n=12) olanların frekansı anlamlı yüksekti. IKH (+) olan 32 olguda konjenital beyin malformasyonu görülme oranı %50 ile oldukça yüksekti (p<0,001).

Sonuç: Çalışmamızda IKH'nin literatürde belirtilenden daha yüksek bir prevelansa sahip olduğunu ve konjenital beyin malformasyonlarında eşlikçi olabildiğini gösterdik. IKH'nin tanınması patolojilerden ayırt etmede ve gereksiz işlemleri önlemede önemlidir. Olgular IKH'ye eşlik edebilecek konjenital beyin malformasyonları yönünden de dikkatlice taranmalıdır.

Anahtar kelimeler: Beyin herniasyonu, kuneat girus, idiyopatik, malformasyon

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INTRODUCTION

Brain herniation is a serious neuropathology that refers to the displacement of brain tissue from one location to another. Acute and chronic pathologies such as trauma, brain tumors, intracranial hemorrhages, cerebral edema, hydrocephalus, and infections are among the causes of acquired brain herniations[1,2]. Idiopathic brain herniation (IBH) is the abnormal displacement of brain tissue towards adjacent anatomical structures, without a known cause. It is rarely described in the literature[3] and has been reported to develop in the cuneate gyrus, precuneal gyrus, parahippocampal gyrus, lateral temporal lobe, and inferior temporal gyrus[3-6].

The cuneus is located medial to the occipital lobe, between the calcarine sulcus and the lingual gyrus, and just anterior to the precuneus on the medial aspect of the parietal lobe. It is formed by the differentiation of the dorsal part of the neural tube and is shaped by specific developmental patterns, gene expression, and morphogenetic movements during the early developmental stages of the brain[7,8]. Located in both cerebral hemispheres, the cuneus has important roles in cognitive and visual processes: it is located in the primary and secondary visual cortex and plays a critical role in the processing of visual information. It is especially activated in response to visual stimuli and is closely connected to the primary visual cortex[8].

"Idiopathic cuneate gyrus herniation (ICH)" indicates that the herniation occurs without a known cause. There is no reliable information on the actual prevalence or incidence of ICH, and as of the time of this report, only thirteen cases have been reported in the literature[3,9,10]. The etiology is unclear, but in idiopathic cases, there may be abnormalities at the time of brain development. Some of the cases described in the literature appear wholly coincidental, whereas some have clinical symptoms, such as headaches. In the literature, in a case with parahippocampal idiopathic brain herniation, this benign condition was mistakenly biopsied for a mass[10]. For these reasons, it should be noted that ICH may in fact be a normal finding: there may be accompanying anomalies or cranial pathologies, and it is important to differentiate these from the masses in order to prevent unnecessary interventions. The etiopathogenesis of congenital brain malformations is diverse and complex, with some of these being genetically based and some others sporadic and in addition, the components of malformations grouped under one heading are usually more than one.

Based on clinical experience, we hypothesized that ICH and congenital brain malformations may coexist. Therefore, in this study, we aimed to investigate whether ICH is an anomaly or a normal variant, what is its prevalence in childhood, whether there is an accompanying finding or pathology in the cases, and to define it with magnetic resonance imaging (MRI) findings.

MATERIALS and METHODS

Study Design and Population

Our study was planned as a single-center retrospective analysis. Pediatric brain MR images obtained in our clinic between January 2021 and August 2023 were retrospectively evaluated. A pediatric radiologist and a radiologist with more than five years of experience in pediatric neuroradiology, performed the MRI evaluations by consensus. The medical records of all patients were analyzed using the hospital automation system. The MRI evaluations were made using the INFINITT picture archiving and communication system [PACS 3.0.11.4 (BN11)] (INFINITT Healthcare Co., Seoul, Korea) software.

Patients aged 0 to 17 years with optimal brain MRI images were included in the study. Those showing pathologies that may cause acquired herniation (trauma, ischemia, infection, neoplasia history, diagnosed or follow-up neurological disease) were excluded, as well as those patients with poor image quality and technical artifacts in brain MRI images. The study was conducted in accordance with the Helsinki Declaration's standards and was approved by University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar City Hospital's Ethics Committee (decision number: 2023/514/258/26, date: 27.09.2023).

MRI Technique and Analysis

MR imaging was performed with a 1.5 Tesla (T) MRI scanner (Philips Ingenia, The Netherlands). Axial spin echo T1W (TR/TE= 470-570/12-30 ms), axial and sagittal T2W (TR/TE= 4500-6000/90-110 ms), axial and coronal FLAIR (TR/TE= 6000-9000/100-120 ms), and diffusion weighted imaging (DWI) (b=0, 500, 1000) sequences were used to obtain structural images of the whole brain for anatomical reference. All sequences were obtained with 5 mm slices. To assess the presence of ICH, any displacement of the bilateral cuneate gyri in the occipital lobe towards the superior cerebellar cisterns medially, was visually observed (Figures 1, 2). The findings detected on T1A and T2A axial images were confirmed on sagittal images, unilateral or bilateral presence was also evaluated (Figure 3). All MRI images were also evaluated

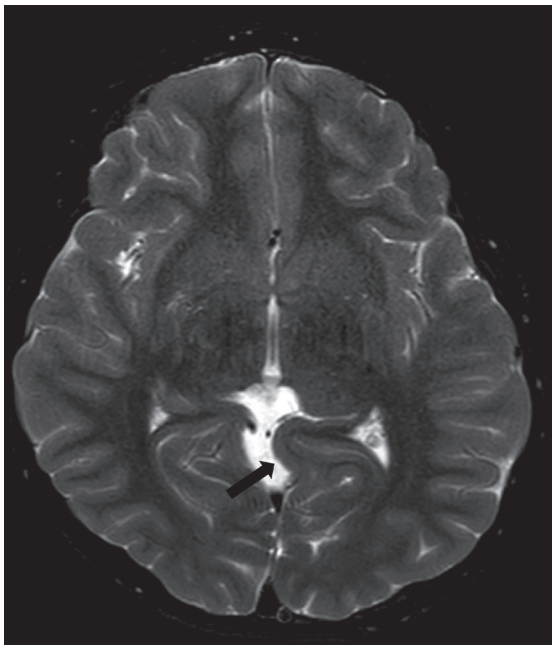

Figure 1. Axial T2-weighted brain MR image shows unilateral cuneate gyrus herniation on the left (black arrow)

MR: Magnetic resonance

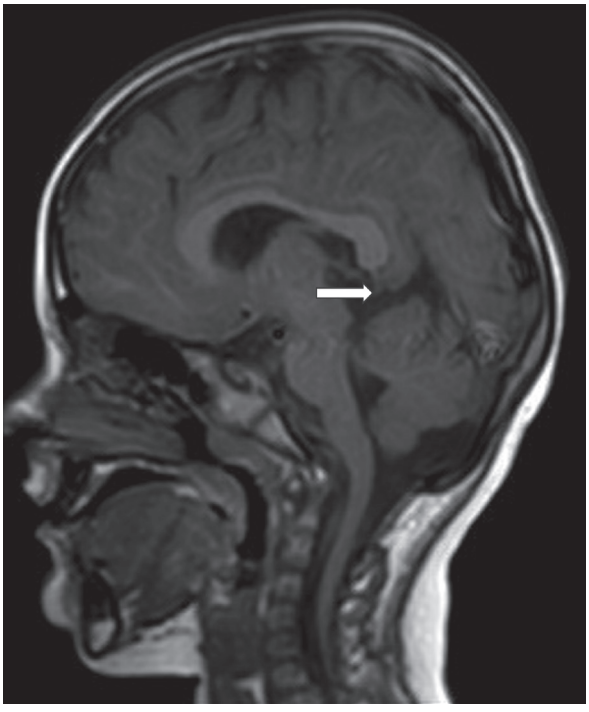

Figure 2. In the sagittal T1-weighted MR image of the same patient as Figure 1, the herniated cuneuate gyrus extends towards the superior cerebellar cistern (white arrow)

MR: Magnetic resonance

for neurologic pathologies, other common variations, and congenital brain anomalies.

A morphologic-based approach was used to classify congenital malformations in MRI scans[11]. Accordingly, malformations were divided into posterior fossa malformations, commissural and cortical developmental anomalies (CCDA), as well as midline malformations. Posterior fossa malformations included Chiari malformations and hindbrain malformations (Dandy Walker spectrum and various other malformations). Cortical and commissural developmental anomalies were further divided into commissural anomalies (callosal dysgenesis spectrum) and cortical developmental malformations. Cortical developmental malformations were further subdivided into those secondary to glial/neuronal proliferation or apoptosis, malformations secondary to neuronal migration abnormalities, and postmigrational developmental disorders.

Statistical Analysis

The relationship between congenital anomalies and ICH was statistically evaluated. The SPSS version 22.0 was used for statistical analysis, and complementary statistical methods were used to evaluate the data (mean, standard deviation, median, frequency, percentage,

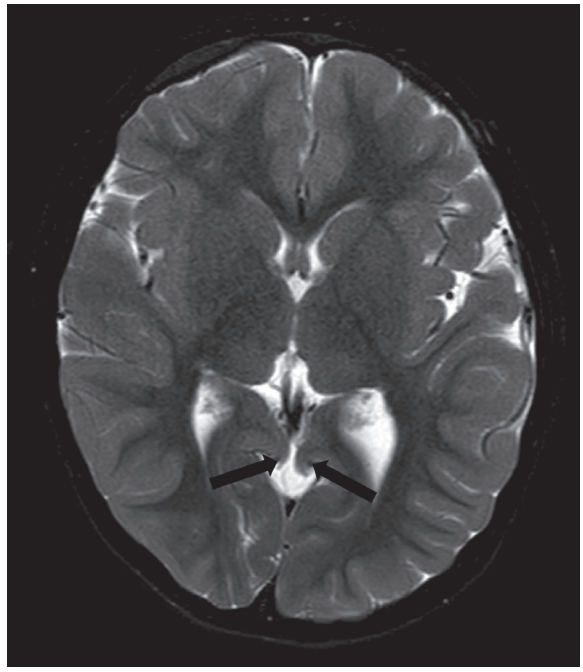

Figure 3. In another case, axial T2-weighted MR image shows bilateral cuneate gyrus herniation (black arrows)

MR: Magnetic resonance

minimum, and maximum). Fisher's exact test was used to evaluate the relationship between congenital brain malformations and the presence of ICH; Fisher-Freeman-Halton exact test was used to evaluate the relationship between subgroups of congenital brain malformations and the presence of ICH. A p-value <0.05 was considered statistically significant.

RESULTS

In the study, 738 brain MRI examinations were analyzed according to the inclusion and exclusion criteria. In line with these, twelve cases were excluded due to a diagnosed neurologic disease (cerebral palsy, periventricular leukomalacia, multiple sclerosis), eight cases due to brain mass, six cases due to meningitis, nine cases due to acute or sequelae trauma findings, and twelve cases due to poor image quality. Some 691 brain MRI scans included in the study were evaluated for the presence of ICH, variations, and anomalies (Figure 4). The mean age of these patients was 5.93±3.4 years. There were 337 (48.77%) males and 354 (51.23%) females. The number of ICH (+) cases was 32 (4.6%) and 659 cases were ICH (-).

The mean age of ICH (+) cases was 6.19±4.02 years. The gender distribution of ICH (+) cases was 13 (40.63%) males and 19 (59.37%) females. Among ICH (+) cases, right ICH was seen in 10, left ICH in 5, and bilateral ICH in 17 cases. The prevalence of ICH was 32/691 (4.6%) in our population, and in all ICH (+) cases, the herniated cuneate gyrus was located toward the superior cerebellar cistern. MRI signal characteristics of the herniated parenchyma were normal in all ICH (+) cases.

In those that were ICH (-), the mean age and gender distribution were 5.72±3.21 years and 341 (52.75%) males and 318 (48.25%) females, respectively.

Congenital brain malformations were detected in 63 (9.11%) of the 691 screened cases. Among these patients, 16 (25.4%) were ICH (+) and 47 (74.6%) were ICH (-). The incidence of congenital malformations was statistically significantly higher in ICH (+) patients than in ICH (-) patients (50% vs. 7.1%) (p<0.001) (Table 1).

The distribution of the presence of ICH among the subgroups of patients with congenital brain malformations is shown in Table 2. Accordingly, in 16 ICH (+) patients, eight had posterior fossa anomalies (PFA), five had anomalies of commissural and cortical development, two had midline malformations and one had a combination of midline malformation, and posterior fossa anomaly. None of the eight patients with posterior fossa malformations had Chiari malformation. Of these patients, two had pontocerebellar hypoplasia, one had cerebellar hypoplasia, one had a cerebellar hypoplasia + arachnoid cyst, one had cerebellar dysplasia, two had mega cisterna magna, and one had vermis hypoplasia. No compression sign or secondary

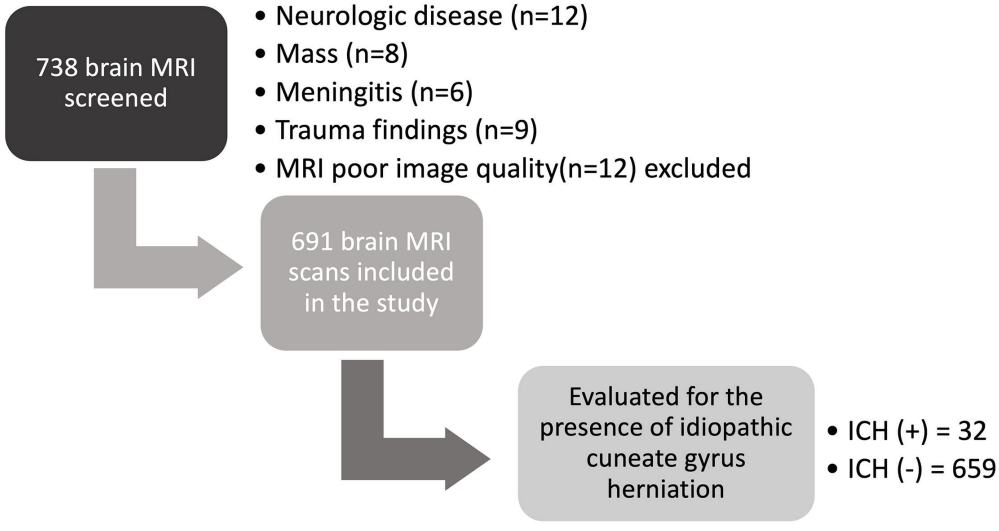

Figure 4. The determination of our study population according to the inclusion and exclusion criteria and the summary of our study findings are presented in the diagram

MRI: Magnetic resonance imaging, ICH: Idiopathic cuneate gyrus herniation

herniation was detected due to the existing pathologies. Of the 47 ICH (-) patients, 11 had PFA, 23 had CCDA, 12 had an association of PFA with CCDA, and one had a midline malformation. There was a statistically significant difference in terms of anomalies between ICH (+) and ICH (-) patients with congenital brain malformations (p=0.005). This variance is due to the difference in the rates of PFA and posterior fossa+ CCDA in ICH (+) and ICH (-) patients. In patients with congenital brain malformations, the frequency of patients with PFA (n=8) in the ICH (+) group was significantly higher than in the ICH (-) group (p=0.005). In addition, the frequency of commissural anomalies (n=23) and posterior fossa+ CCDA (n=12), is significantly higher in the ICH (-) group with congenital brain malformations (p=0.005). Among all cases evaluated in our study, there were only two Dandy-Walker malformations, and these were ICH (-). In these cases, there was no evidence of obstructive hydrocephalus or a large volume or tumoural herniation requiring a cystoperitoneal shunt.

DISCUSSION

In this study, we investigated for the first time the prevalence of ICH by MRI in childhood and the presence of coexisting congenital malformations; thus, our findings are unique and introductory. We found that ICH has a higher prevalence than reported in the literature, and we demonstrated the coexistence of ICH in congenital brain malformations.

Table 1. Distribution in terms of presence of ICH in patients with congenital brain malformations

CBM		ICH (+)	ICH (-)	Total
CBM (+)	Count, %	16 (25.4%)	47 (74.6%)	63 (100.0%)
	% within ICH	50	7.1	9.1
	% of total	2.3	6.8	9.1
CBM (-)	Count, %	16 (2.5%)	612 (97.5%)	628 (100%)
	% within ICH	50	92.9	90.9
	% of total	2.3	88.6	90.9
Total	Count, %	32 (4.6%)	659 (95.4%)	691 (100.0%)

CBM: Congenital brain malformation, ICH: Idiopathic cuneate gyrus herniation

Table 2. Distribution among subgroups of patients with congenital brain malformations in terms of the presence of ICH

CBM		ICH (+)	ICH (-)	Total CBM
Posterior fossa anomalies	Count	8_a (42.1%)	11_b (57.9%)	19 (100%)
	% in ICH	50.0	23.4	30.2
	% total	12.7	17.5	30.2
Comissural-cortical developmental anomalies	Count	5_a (17.9%)	23_a (82.1%)	28 (100%)
	% in ICH	31.3	48.9	44.4
	% total	7.9	36.5	44.4
Posterior fossa anomalies + comissural-cortical developmental anomalies	Count	0_a (0.0%)	12_b (100.0%)	12 (100.0%)
	% in ICH	0	25.5	19
	% total		19	19
Midline malformation	Count	2_a (66.7%)	1_a (33.3%)	3
	% in ICH	12.5	2.1	4.8
	% total	3.2	1.6	4.8
Midline malformation + posterior fossa anomalies	Count	1_a (100.0%)	0_a (0.0%)	1 (100.0%)
	% in ICH	6.3	0.0	1.6
	% total	1.6	0.0	1.6
Total CBM	Count, %	16 (25.4%)	47 (74.6%)	63 (100.0%)

Each subscript letter donates a subset of each categories whose column proportions do not differ significantly from each other at the 0,05 level
CBM: Congenital brain malformation, ICH: Idiopathic cuneate gyrus herniation

ICH is an abnormal displacement of brain tissue from the cuneus region to the adjacent anatomical structure, without a known cause. In order to detect the presence of ICH, this condition should be recognised, and the relevant anatomical region should be carefully evaluated on a brain MRI. When ICH, which is an unusual condition, is detected, pathologic conditions such as mass and edema should be differentiated initially. As the etiology of ICH has not been fully elucidated, abnormalities during embryologic development may be considered[10]. To our knowledge, thirteen ICH (+) cases have been reported in the literature, eleven of which were reported by Maldjian and Adam[9] in a comprehensive computed tomography (CT) prevalence study. As a case report, only one adult case was reported by Duarte et al.[10] and a pediatric case reported by Koc et al.[3] is also available. Another case of idiopathic brain herniation reported in the literature was misinterpreted as a mass on an MRI and a biopsy showed normal brain tissue[12]. In this report, a 41-year-old man was admitted to the hospital with right-sided atypical trigeminal neuralgia, and radiological imaging revealed an abnormal left ambient cistern, which was interpreted as a mesial temporal lobe or extramedullary ambient cistern mass lesion. Surgical exploration for biopsy revealed an abnormal anatomy of the posterior fossa and parahippocampal herniation into the perimesencephalic cistern, which was confirmed to be normal brain tissue by biopsy and defined as idiopathic brain herniation. This case shows us the importance of radiological and clinical recognition of ICH, which is a benign condition among idiopathic brain herniations. Unlike ICH, acquired brain herniations require treatment of the causative pathologic condition, and the approach depends on the cause of the herniation, its severity, and the patient's general health status and symptoms. Treatment may include emergency or elective surgery or other medical interventions.

There is only one prevalence study for ICH in the literature, performed by Maldjian and Adams[9]. In this CT-based study, the prevalence of ICH was reported as 0.73%[9]. In our MRI-based study, we found a prevalence of 4.6%. The CT prevalence study was performed in patients presenting to the emergency department and since the age of the study population was not specified, we believe it includes the entire adult as well as the paediatric population. The higher soft tissue resolution of MR compared to CT does have an impact on the numerical difference between our study and the CT study, but this alone did not explain the discrepancy. We also believe that the fact that our study was performed in a paediatric population, including not only emergency but also outpatient-urgent patient groups, and was performed in a tertiary care center, is also noteworthy. We suspect that the detection rate will increase along with the awareness of "idiopathic brain hernias", which we believe is not fully known by both clinicians and radiologists. In addition, the fact that the rate is higher in the paediatric population compared to the general population suggests the possibility that ICH may become involutional over time, or that those with accompanying severe malformations may not reach advanced ages. However, prospective long-term studies including larger case series are required to substantiate this assumption.

In the multicenter population-based EUROCAT study of the epidemiology of congenital brain malformations in Europe, 4,927 cases with congenital cerebral anomalies were identified, with a prevalence (adjusted for under-reporting) of 9.8 [95% confidence interval (CI): 8.5 to 11.2] per 10,000 births. Forty-eight percent of all cases were reported as an isolated cerebral anomaly. It was emphasized that the incidence varied considerably between regions and according to the regularity of record-keeping. The study also reported that the prevalence increased by 2.4% per year (95% CI: 1.3% to 3.5%), excluding genetic or chromosomal conditions, with increases occurring only for congenital formations of the corpus callosum (3.0% per year) and 'other reduction deformities of the brain' (2.8% per year)[13]. In our study, the rate of congenital brain malformations was relatively high, at 9.11%, however the majority of our patients with congenital brain malformations had callosal anomalies with 28.57% (n=18) and posterior fossa malformations with 52.38% (n=33). In our ICH (+) patients, malformations were seen in 50% of the cases, and 50% of these were posterior fossa malformations. The high rate of accompanying congenital brain malformations in our ICH (+) patients suggested that ICH may not be an isolated variant, but rather a finding that is associated with congenital brain malformations that may be caused by an abnormality during embryonic developmental stages. ICH (+) cases should be carefully evaluated for these possible malformations. In the literature, it has been reported that this anomaly may be due to a defect in the meningeal embryogenesis stage. During early development, the meningeal layer separating the telencephalon and diencephalon regresses as differentiation progresses, and the thalamic tissue becomes contiguous with the base of the cerebrum. As embryonic development progresses, the median part of the tentorium becomes invaginated, and only the lateral parts remain. As theorized in the Chiari type II malformation, the local influence of the factors

regulating this development on the tentorial dura may cause a dural defect, leading to small focal herniation of the parenchyma[10,14-16]. In this context, prospective MRI-based studies including thin-section contrast-enhanced sequences in large case groups, may be useful to evaluate the dural defect.

In acquired brain herniations, headaches, nausea, vomiting, altered consciousness, and neurologic deficits often occur clinically, due to increased cerebral pressure. Specific symptoms may be observed depending on the localization. In IBH cases in the literature, headache was described as a clinical finding in some cases, and trigeminal neuralgia was reported as an additional finding in another case. Aside from these, no significant additional pathology, variation, or anomaly was described in the cases. However, the posterior part of the cuneate gyrus has projections from the fovea, and the anterior portion has projections from the peripheral visual field. Sequelae may occur due to the abnormally positioned area, or the patient may adapt his or her vision by using the other visual field, and progress with normal vision throughout his or her life[9,10]. Visual evoked fields or functional MRI may be helpful to demonstrate this, however no such study is available in the literature. In our study, headache was defined in five of the ICH (+) cases. No congenital brain malformation was found in any of these cases, and there was no specific clinical symptom in the other cases in our study.

We endeavoured to evaluate the relationship between ICH and congenital malformations, which are hypothesised to start in the intrauterine period. We know that paediatric brain tumours are caused by disorders in developmentally regulated signalling pathways, but tumours are evaluated under a separate heading from malformations. Among paediatric brain tumours, congenital brain tumours are the most likely to cause primary herniation, however congenital brain tumours are extremely rare. Other brain tumours that are more common in paediatric age may cause secondary herniation, such as cerebellar tonsil, uncal, and subfalcin herniations. Secondary herniation sites that can be caused by both congenital and acquired tumours are anatomically distant from ICH, however we are unable to determine whether a congenital tumour in the occipital lobe can cause ICH. This can be considered as a limitation, and it should be the subject of another study.

Study Limitations

Our study had some other limitations. Firstly, it has a retrospective design, and we could not establish a standardized imaging protocol. Although our sample was large, the number of samples in our variation and anomaly subgroups was small. Another limitation is that it was conducted in a pediatric population: for a prevalence study, a more comprehensive survey, including the adult population, may be useful. Finally, our retrospective study design did not allow us to perform an additional evaluation of cuneal region function in our patients. We identified headache as a clinical finding in the retrospective file searches of our patients, however we could not obtain information about visual symptomatology.

CONCLUSION

In conclusion, our childhood-based study showed that the prevalence of ICH is higher than reported in the literature. Congenital malformations accompanying ICH in our cases may be coincidental or may be one of the signs of an effect in the early stages of embryonic development. Therefore, knowledge of ICH is necessary to differentiate it from pathology and to prevent unnecessary procedures. In addition, knowing that ICH may be accompanied by congenital malformations is important in terms of careful screening of brain tissue for congenital malformations in ICH cases.

Ethics

Ethics Committee Approval: The study was conducted in accordance with the Helsinki Declaration's standards and was approved by University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar City Hospital's Ethics Committee (decision number: 2023/514/258/26, date: 27.09.2023).

Informed Consent: Retrospective study.

Author Contributions

Concept: E.C., Design: H.G.D., E.C., Data Collection and Processing: H.G.D., E.C., Analysis and Interpretation: H.G.D., E.C., Literature Search: H.G.D., E.C., Writing: H.G.D.

Conflict of Interest: The authors have no conflict of interest to declare.

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