Research Article (Araştırma Makalesi)

Magnetic Resonance Imaging Findings and Accompanying Malformations in Pediatric Patients with Gray Matter Heterotopia

Gri Cevher Heterotopisi Bulunan Pediatrik Hastaların Manyetik Rezonans Görüntüleme Bulguları ve Eşlik Eden Malformasyonların Değerlendirilmesi

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Özet

Amaç: Çalışmanın amacı, pediatrik hastalarda saptanan gri cevher heterotopilerini manyetik rezonans görüntüleme bulgularına göre sınıflandırmak ve eşlik eden serebral malformasyonları tanımlamaktır.

Gereç ve Yöntemler: Ocak 2012-Haziran 2020 tarihleri arasında beyin manyetik rezonans görüntülemelerinde heterotopi tespit ettiğimiz tüm çocuk hastaların görüntüleri retrospektif olarak değerlendirildi. Heterotopinin tipi, yeri ve eşlik eden serebral anomaliler incelendi.

Bulgular: Çalışmaya gri cevher heterotopisi bulunan ortalama yaşı 7.80±4.53 yıl (2-16 yıl) olan 22'si erkek, 20'si kız toplam 42 hasta dahil edildi. Hastaların 33'ünde (%78.6) subependimal, 7'sinde (%16.7) subkortikal ve 2'sinde (%4.7) bant heterotopi saptandı. Yirmi dört hastanın epilepsisi vardı.

Sonuç: Çalışmamıza göre pediatrik hastalarda en sık subependimal heterotopi görüldü. Subependimal heterotopiler en sık lateral ventriküllerin trigon kısmında yerleşmişti. Subkortikal heterotopilerin tümü frontalde ve unifokal yerleşimli idi. Bant heterotopiler bilateral serebral hemisferde subkortikal bölgede simetrik yerleşimli idi. Başlıca eşlik eden serebral anomaliler Chiari 2 malformasyonu ve korpus kallosum agenezisi idi. Pediatrik hastalarda hasta yönetimi açısından heterotopinin tipinin ve ilişkili serebral anomalilerin tanımlanması önemlidir.

Anahtar kelimeler: Gri cevher heterotopisi, Malformasyon, Manyetik rezonans görüntüleme, Pediatri, Subependimal

Abstract

Objective: The aim of the study is to classify gray matter heterotopias detected in pediatric patients according to magnetic resonance imaging findings and to define the accompanying cerebral malformations.

Material and Methods: Images of all pediatric patients who were detected to have heterotopia in brain magnetic resonance imaging between January 2012 and June 2020 were retrospectively evaluated. The type, location of heterotopia, and accompanying cerebral anomalies were analyzed.

Results: A total of 42 patients, 22 male, and 20 female, with a mean age of 7.80±4.53 years (2-16 years) with gray matter heterotopia were included in the study. Of the patients 33 (78.6%) had subependymal, 7 (16.7%) had subcortical, and 2 (4.7%) had band heterotopia. Twenty-four patients had epilepsy.

Conclusion: According to our study, subependymal heterotopia was most common in pediatric patients. The subependymal heterotopias were most commonly located in the trigon region of the lateral ventricles. All of the subcortical heterotopies were located in the frontal and unifocal. Band heterotopias were located symmetrically in the subcortical region of the bilateral cerebral hemispheres. The main accompanying anomalies were Chiari II malformation, and corpus callosum agenesis. Defining the type of heterotopia and associated anomalies in pediatric patients is important for patient management.

Keywords: Gray Matter Heterotopia, Magnetic resonance imaging, Malformation, Pediatrics, Subependymal

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INTRODUCTION

Gray matter heterotopia is a cortical formation disorder that results from the cessation of the normal migration of neurons from the wall of the lateral ventricles to the cortex. In the brain, normal neurons are located in abnormal localizations (1-3). It is mostly detected in children or young adults with epilepsy who have neurodevelopmental anomalies. Sometimes, it can be seen coincidentally without causing any clinical findings (4,5). Heterotopia is the most common congenital anomaly in epilepsy with early-onset and genetic predisposition (6-8).

Magnetic resonance imaging (MRI) is a superior imaging method compared to computed tomography (CT) in the diagnosis of heterotopia with its high soft-tissue resolution. According to MRI findings, heterotopia is divided into three subependymal, subcortical, and band heterotopia (9-10). Subependymal heterotopia consists of gray matter clusters located in the subependymal region of the ventricular wall. These heterotopic neuron clusters often bulge into the ventricular lumen. Subcortical heterotopia is nodular or curvilinear gray matter foci within the subcortical and deep white matter. Band heterotopia, on the other hand, is bands of gray matter with smooth edges, unrelated to the cortex, running parallel to the ventricles in the white matter (11-13). The aim of this study is to classify the heterotopias we detected in pediatric patients according to MRI findings and to define accompanying cerebral malformations.

MATERIALS AND METHODS

Study population

In the study, images of all pediatric patients with heterotopia detected in brain MRI examinations between January 2012 and June 2020 were evaluated retrospectively. The study was in accordance with the 1964 Helsinki declaration and its later amendments. The study was approved by the Firat University non-interventional research ethics committee (Date: 30/06/2020, Number of sessions: 2020/10-13). Patients with such artifacts as to prevent the images from being evaluated, patients with unclear radiological heterotopia diagnosis and incomplete MRI sequences were excluded from the study.

Image acquisition

A 1.5 and 3T Tesla scanner (Philips Medical Systems, Ingenia, Netherlands) was used to acquire magnetic resonance images. Sagittal T1 and T2-weighted images, sagittal FLAIR (fluid-attenuated inversion recovery) or sagittal DIR (Double inversion recovery) and their reformatted images, SWI (Susceptibility-weighted imaging), DWI (Diffusion-weighted imaging) and ADC (Apparent diffusion coefficient) sequences were obtained for brain MRI protocol.

Imaging Analysis

Demographic characteristics and symptoms of the patients were recorded. After detecting heterotopia foci that are isointense with gray matter in all sequences located in abnormal localization on imaging, the type and location of heterotopia and accompanying cerebral anomalies were evaluated. The type of heterotopia was divided into three categories subependymal, subcortical, and band heterotopia (1,9).

Statistical Analysis

IBM SPSS 22 (Statistical Package for the Social Sciences for windows) package program was used for statistical analysis of the study. After the demographic and radiological data of the patients included in the study were recorded, descriptive analysis methods were applied. Descriptive statistics were expressed as mean±standard deviation for continuous variables and as frequency and percentage for categorical variables.

RESULTS

A total of 42 patients, 22 (52.4%) boys, and 20 (47.6%) girls, with heterotopia detected in brain MRI, were included in the study. The mean age of the patients was 7.80±4.53 years (2-16 years). Thirty-three (78.6%) of the patients included in the study had subependymal, 7 (16.7%) subcortical, and 2 (4.7%) band heterotopia. Symptoms were epilepsy in 24 (57.1%) patients, developmental delay in 17 (40.4%) patients, and headache in 4 (9.5%) patients.

Seventeen of the patients with subependymal heterotopia were girls and 16 were boys, with a mean age of 7.57±4.43 years (2-15 years). The symptoms of 17 (51.5%) patients were epilepsy, 15 (45.4%) patients developmental delay, 4 (12.1%) patients headaches. These heterotopies were unilateral or bilateral and focal or multifocal in the subependymal parts of the lateral ventricles (**Figure 1** and **2**).

Nineteen (57.5%) were bilateral and 14 (42.5%) were unilaterally located. Of the unilaterally located ones, 10 were focal and 4 were multifocal. Unilateral ones were most commonly located on the left side with 11 patients. The most common localization was the trigone and body of the lateral ventricles. This was followed by the frontal, occipital and temporal parts of the lateral ventricles, respectively. The most common accompanying cerebral anomaly was Chiari II malformation (CM-II) in 11 (33.3%) patients. Four (12.1%) patients had corpus callosum agenesis. All patients with CM-II and agenesis of the corpus callosum had ventriculomegaly. All patients with CM-II had undergone surgery for meningomyelocele, and of these patients, 5 (45.4%) had absence of the septum pellucidum and 4 (36.3%) had dysgenesis of the corpus callosum. The radiological findings of children with subependymal heterotopia accompanied by cerebral anomaly are presented in **Table 1**.

The patients with subcortical heterotopia were 5 boys and 2 girls, with a mean age of 7.85±5.52 years (3-16 years). While the symptom of 5 (71.4%) patients was epilepsy, 2 (28.6%) had developmental delay. In all patients,

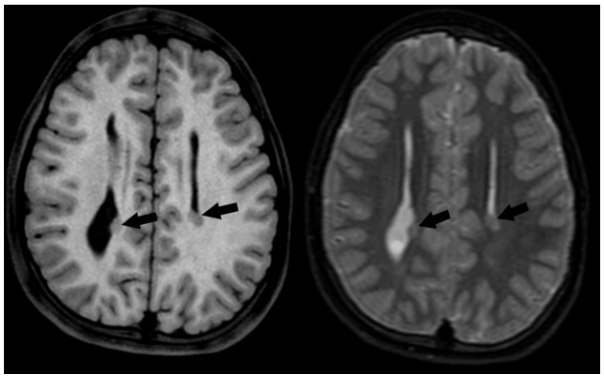

Figure 1. A 12-year-old boy patient with developmental delay. T1-weighted and T2-weighted axial brain MR images showed subependymal heterotopia that is isointense with gray matter in the trunk of the bilateral lateral ventricles and bulging towards the ventricles (arrows).

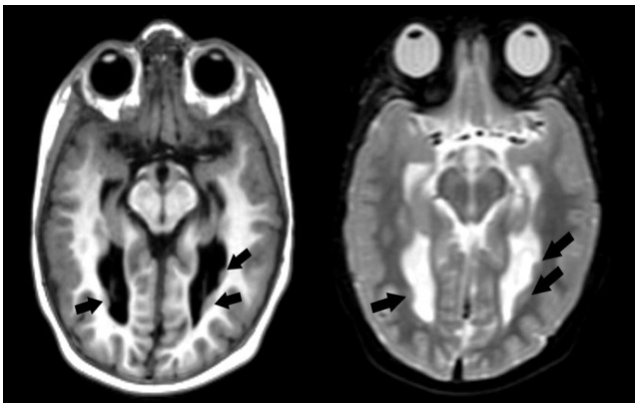

Figure 2. A 3-year-old girl with developmental delay. T1-weighted and T2-weighted axial brain MRI showed subependymal heterotopia that is isointense with gray matter in the occipital part of the bilateral lateral ventricles and bulging towards the ventricles (arrows).

Table 1. Findings of patients with subependymal heterotopia with cerebral anomalies.

Age/Gender	Symptom	Periventricular location	Related cerebral anomalies	
5/M	DD	B-trigon	CM-II	
7/F	Epilepsy	B-temporal	CM-II	
2/F	DD	B-trigon	CM-II	
14/M	Epilepsy	B-trigon	CM-II	
12/M	DD	B-trigon, occipital	CM-II	
2/F	DD	Left occipital	CM-II	
15/F	Epilepsy	B- trigon	CM-II	ASP
14/M	Epilepsy	B-trigon	CM-II	ASP, CCD
5/F	DD	B-trigon	CM-II	ASP, CCD
12/F	Epilepsy, DD	B-trigon, occipital	CM-II	ASP, CCD
3/F	DD	B-trigon, occipital	CM-II	ASP, CCD
4/F	Epilepsy	B-trigon	CCA	
12/M	DD	B-corpus	CCA	
6/F	Epilepsy	Left frontal	CCA	
4/F	Epilepsy, DD	B-trigon	CCA	
2/M	DD	Right corpus	Ventriculomegaly	

M: Male, F: Female, DD: Developmental Delay, B: Bilateral, CM-II: Chiari II malformation, ASP: Absence of septum pellucidum, CCD: Corpus callosum dysgenesis, CCA: Corpus callosum agenesis

gray matter heterotopies were unilateral and unifocal, and 4 (57.1%) were located in the right frontal, and 3 (42.8%) were located in the left frontal (**Figure 3**). One (14.3%) of the patients had corpus callosum agenesis and 1 (14.3%) had ventriculomegaly, and this patient had undergone surgery for occipital encephalocele.

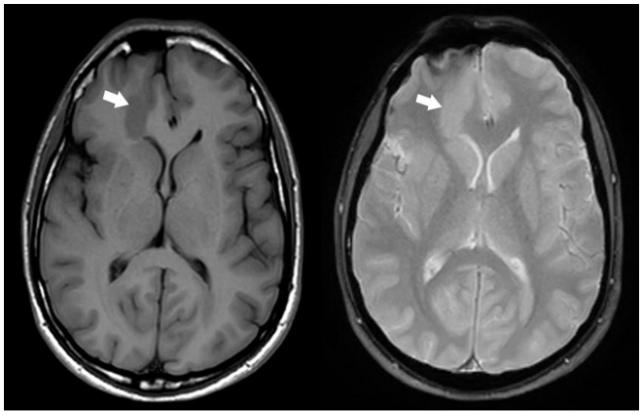

Figure 3. A 16-year-old boy patient with epileptic seizures. T1-weighted and T2-weighted axial brain MRI showed isointense subcortical heterotopia with gray matter in the right frontal subcortical white matter (arrows).

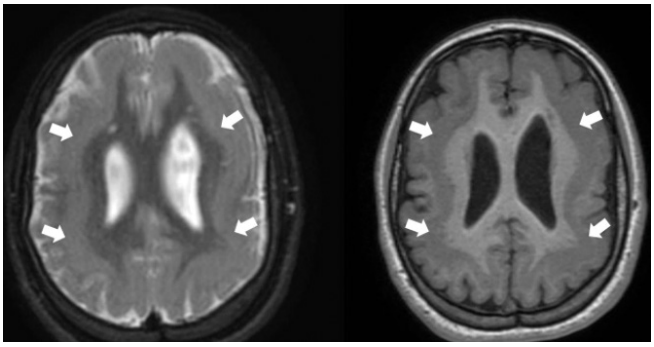

Figure 4. A 11-year-old boy with epileptic seizures; T2-weighted and T1-weighted axial brain MRI showed symmetrical and isointense band heterotopia with gray matter in bilateral subcortical white matter (arrows).

The mean age of 2 patients, 1 girl, and 1 boy, with band heterotopia, was 11.5±0.70 years (11-12 years). Both patients had epilepsy and heterotopia was located subcortically as a symmetrical band in the bilateral cerebral hemispheres (**Figure 4**). Pachygria was present in 1 (50%) of the patients. The radiological findings of children with subependymal and band heterotopia are presented in **Table 2**.

DISCUSSION

Gray matter heterotopia is a neuronal migration disorder characterized by the localization of normal gray matter neurons and glial cells within the white matter. It constitutes 15% of cortical developmental malformations and is seen in 2% of all epilepsy patients (14).

7-8 weeks of pregnancy during the embryological development of the brain, neuroblasts in the ventricular neuroepithelium proliferate and between the 8th and 26th weeks of pregnancy, they migrate from the germinal matrix layer to the cortex. This migration is especially maximum between the 8th and 16th weeks. Gray matter heterotopia develops as a result of the interruption of this neuronal migration occurring in the intrauterine period due to genetic, infection, and trauma (15,16).

Gray matter heterotopias are classified as subependymal, subcortical, and band heterotopia according to MRI (9,10). In our study, patients belonging to three groups were also present. Subependymal heterotopies are the most common group (17,18). Donkol et al. in their study with patients with gray matter heterotopia found the most patients with subependymal heterotopia and the least amount of band heterotopia (19). In a

Table 2: Findings of patients with subcortical and band heterotopia.

Age/Gender	Symptom	Heterotopia type	Heterotopia location	Related cerebral anomalies
16/M	Epilepsy	Subcortical	Right frontal	-
10/M	DD	Subcortical	Right frontal	Ventriculomegaly
3/F	Epilepsy	Subcortical	Left frontal	-
6/M	DD	Subcortical	Right frontal	Corpus callosum agenesis
3/F	Epilepsy	Subcortical	Left frontal	-
14/M	Epilepsy	Subcortical	Right frontal	-
3/M	Epilepsy	Subcortical	Left frontal	-
12/F	Epilepsy	Band	Bilateral subcortical	-
11/M	Epilepsy	Band	Bilateral subcortical	Pachygyria

M: Male, F: Female, DD: Developmental Delay

study conducted in 36 pediatric patients with gray matter heterotopia, there were no patients with subcortical heterotopia but most patients were with subependymal heterotopia, and the most common localization of subependymal heterotopias was found to be the frontal of the lateral ventricles (20). Di Nora et al. evaluated the clinical and imaging findings of 22 children with gray matter heterotopia. They indicated that the most common is periventricular nodular heterotopia (11). In our study, we found mostly subependymal, then subcortical, and least band heterotopia pediatric patients. The most common location of subependymal heterotopias was the trigone part of the lateral ventricles.

The clinical findings are determined by the type and location of heterotopia and accompanying malformations. Although mostly similar symptoms are seen, the severity of the symptoms varies according to the type of heterotopia. The most common clinical finding is epileptic seizures (1,16,21,22). In addition, developmental delay and neurological defects may be seen in some patients (1,22). Sometimes it can be detected completely coincidentally without causing any symptoms (4,5). Epilepsy was the most common and developmental delay was observed less frequently in our patients. According to some studies, the incidence of epilepsy in patients with heterotopia is higher in women than in men (1,12,17). In our study, epilepsy was observed in an equal number of male and female patients.

MRI distinguishes between gray and white matter with its high soft-tissue resolution, and thus gray matter clusters located in white matter can be easily detected with MRI (1,14,16). In addition, MRI provides the evaluation of other cerebral anomalies accompanying heterotopia. According to some studies, gray matter heterotopia is seen together with cerebral anomalies such as agenesis of the corpus callosum, CM-II, meningomyelocele, encephalocele, and ventriculomegaly (1,16,19). In our study, cerebral anomalies such as CM-II, corpus callosum agenesis, ventriculomegaly, occipital encephalocele, and pachygyria were accompanied.

The limitations of our study are the small number of patients, it is a retrospective study, and the lack of clinical data of the patients.

According to our study, subependymal heterotopia was most common in pediatric patients. The most common cerebral anomaly accompanying subependymal heterotopias was CM-II. The most common location of subependymal heterotopias was the trigone part of the lateral ventricles. All of the subcortical heterotopies were located in the frontal and unifocal. Defining the type of heterotopia and associated anomalies in pediatric patients is important for patient management.

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Ethical Approval: The study was in accordance with the 1964 Helsinki declaration and its later amendments. The study was approved by the Firat University non-interventional research ethics committee (Date: 30/06/2020, Number of sessions: 2020/10-13).

Author Contribution: All authors contributed equally to the article.

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