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Supratentorial Intracranial Anomalies in Myelomeningocele Patients

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ABSTRACT

AIM: To assess associated cerebral supratentorial anomalies in patients who underwent myelomeningocele repair in hopes of developing a better morphological apprehension of the forebrain's anomalies in this category of patients.

MATERIAL and METHODS: This retrospective observational study assessed 426 pediatric patients who underwent myelomeningocele repair between January 2013 and December 2020. Cranial MRIs with T1- and T2-weighted sequences were obtained as part of the postoperative assessment to determine the presence of associated supratentorial anomalies in pediatric patients following myelomeningocele repair.

RESULTS: The most common supratentorial anomalies identified in patients who underwent myelomeningocele repair are associated with the configuration of the corpus callosum (CC). Moreover, the complete agenesis of the CC was noticed in 9 (2.1%) subjects, whereas partial agenesis was identified in 148 (34.7%) subjects. Hypoplasia of the CC was observed in three (0.7%) patients. Gray matter heterotopia were the second most commonly observed supratentorial anomalies in 110 (25.8%) patients. Furthermore, the absence of the septum pellucidum was observed in two (0.47%) of the total patients. The widening of the interhemispheric fissure and abnormal maturation of the white matter were observed in 10 (2.34%) patients and 11 (2.58%) patients, respectively. Polymicrogyria, a consequence of abnormal cortical organization, was identified in 22.53% of the patients (96 patients) included in our series.

CONCLUSION: This study confirms that, except for hydrocephalus and Chiari malformation, other associated cerebral supratentorial anomalies may be observed in patients with myelomeningocele. However, only limited research has confirmed the interconnection between the cerebral supratentorial anomalies and cognitive function. Therefore, this study emphasizes the necessity for further supplementary studies, in conjunction with accurate postnatal followups, in order to assess the real significance and repercussions of these anomalies on neurological development and also to establish how these structural changes in brain anatomy translate clinically.

KEYWORDS: Spinal dysraphism, Myelomeningocele, Cerebral anomalies, Supratentorial anomalies, MRI

ABBREVIATIONS: MRI: Magnetic resonance imaging, **CC:** Corpus callosum, **CSF:** Cerebrospinal fluid

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INTRODUCTION

Myelomeningocele, one of the open forms of spinal dysraphism, has been shown to have a high prevalence rate, especially in low- and middle-income countries, despite the vast public health nutrition and education programs conducted to raise awareness over the importance of folic acid fortification and supplementation. It is well known that significant complications in spina bifida patients are often due to spinal cord lesions causing motor and sensory deficits, spinal cord tethering, hydrocephalus, or type II Chiari malformation.

The co-occurrence of myelomeningocele with Chiari malformation and hydrocephalus has been confirmed in medical practice, with the enlargement of the cerebral ventricles being an important comorbidity factor in this pathology. Historically, around 80% of patients born with myelomeningocele tend to require the placement of a ventriculoperitoneal shunt to control hydrocephalus (3). However, advancements made in the fetal surgery sphere have significantly reduced the need for shunt placement.

The aim of this study is to assess, apart from hydrocephalus, other associated cerebral anomalies in patients that underwent myelomeningocele repair in hopes of developing a better morphological apprehension of the forebrain's anomalies in this category of patients.

MATERIAL and METHODS

This retrospective cross-sectional study complies with the guidelines of the Declaration of Helsinki and was conducted with the approval of the Institutional Ethics Committee (IRB no 2020/0618). This study included 426 pediatric patients (213 females and 213 males) that underwent surgery for myelomeningocele between January 2013 and December 2020.

Cranial magnetic resonance imaging (MRI) data with T1- and T2-weighted sequences in all three anatomical planes were obtained as part of the postoperative assessment in order to determine the presence of associated structural supratentorial anomalies in pediatric patients following myelomeningocele repair, aside from hydrocephalus and Chiari malformation.

An abnormal callosal configuration was classified as complete agenesis, partial agenesis, and hypoplasia. Moreover, hypoplasia was used to describe a thinner CC, but with a normal anterior–posterior extent. Subependymal, focal subcortical, and diffuse subcortical gray matter heterotopia were presented in our study. On the other hand, polymicrogyria was defined as an abnormal folding pattern and increased thickness of the cerebral cortex with a distorted cortical white matter junction. The other types of lissencephaly consisted of agyria, defined as cortical areas wherein the sulci are more than three centimeters apart, and pachygyria, defined as wide gyri with sulci between 1.5 and 3 centimeters apart.

RESULTS

Table I shows the supratentorial anomalies observed in our patients.

Table I: Magnetic Resonance Imaging Findings in Patients that Underwent Myelomeningocele Repair

Supratentorial anomalies	Number of Patients %
Total agenesis of Corpus Callosum	2.1
Partial agenesis of Corpus callosum	34.7
Hypoplasia of Corpus Callosum	0.7
Heterotopic grey matter	25.82
Polymicrogyria	22.53
Pachygyria	10.56
Agyria	5.86
Wide interhemispheric fissure	2.34
Missing septum pellucidum	0.47
Immature white matter	2.58

The most common cerebral supratentorial anomaly identified in patients who underwent myelomeningocele repair involved the configuration of the CC; complete agenesis (Figure 1) was observed in nine subjects (2.1%), while partial agenesis (Figure 2) was observed in 148 subjects (34.7%). Three of our patients (0.7%) had hypoplasia of the CC. The second most common anomaly in our study was gray matter heterotopia (Figure 3), as observed in 25.82% of the patients (110 patients). The absence of the septum pellucidum was observed in two subjects (0.47%). Wide interhemispheric fissures and the abnormal maturation of the white matter were observed in 2.34% (10 subjects) and 2.58% (11 subjects) of the cases, respectively. Polymicrogyria was observed in 22.53% of the patients (96 patients) included in our series (Figure 4).

Furthermore, the consequences of abnormal cortical organization and abnormal neuronal migration (e.g., polymicrogyria, pachygyria (Figure 5), agyria) were determined in almost 40% of the patients (166 patients).

DISCUSSION

Different theories of pathogenesis have been proposed in an attempt to confirm the co-occurrence of abnormalities regarding the supratentorial neuroectoderm and the surrounding mesoderm. The cerebrospinal fluid (CSF) leak from a myelomeningocele lesion is known to result in reduced ventricular distension (22,23). Considering the fact that neural development is influenced by ventricular expansion, the absenteeism of a CSF driving stimulus averts not only the posterior fossa but also the supratentorial neural structures from completely developing. The paucity of foundation for the developing telencephalic hemispheres leads to some anomalies, such as heterotopia, ectopia, disruption of the cerebral gyri, and dysgenesis of the CC (6,25,27,29,36).

Mashayekhi et al. investigated deficient cortical development using an animal model and suggested that CSF obstruction

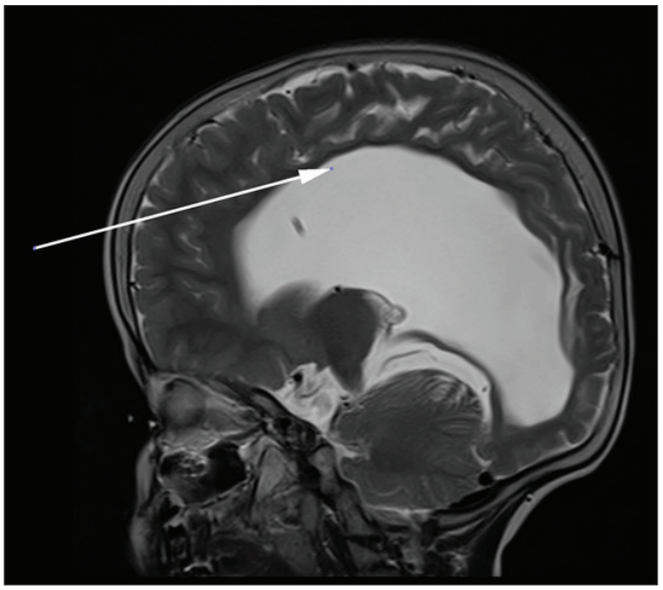

Figure 1: Hydrocephalus and total agenesis of corpus callosum (white arrow) are seen on the sagittal plane of T2-weighted imaging.

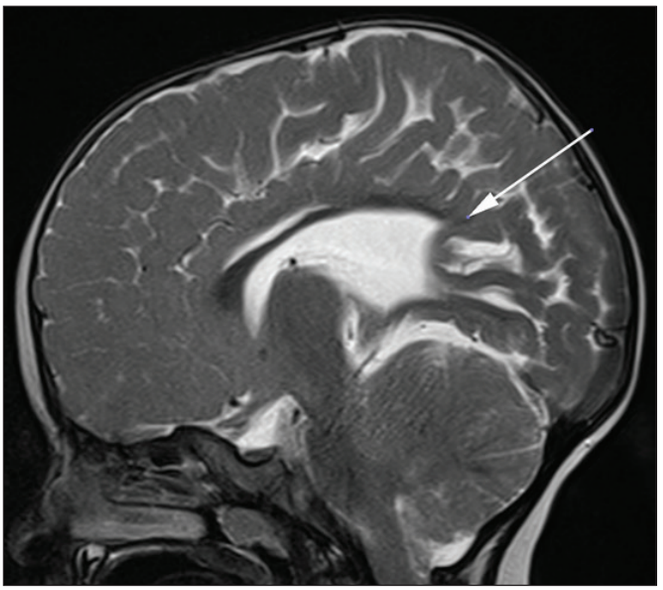

Figure 2: Partial agenesis of corpus callosum. Corpus posterior and splenium part of corpus callosum is absent (white arrow) and gyri is seen in a "sunray appearance" on the sagittal plane of T2-weighted imaging

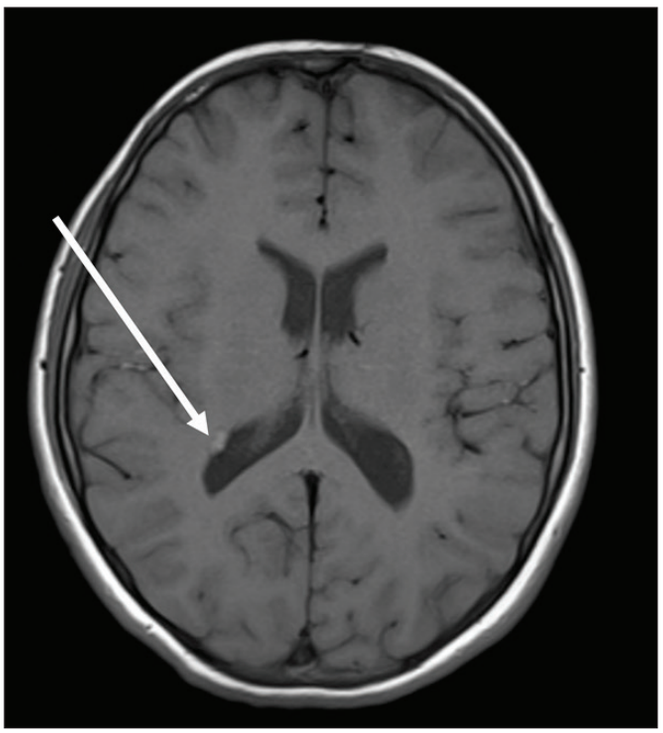

Figure 3: Heterotopia. Subependymal nodule with indistinct margins in the wall of the right lateral ventricle (white arrow) is visible on the axial plane of T1-weighted imaging.

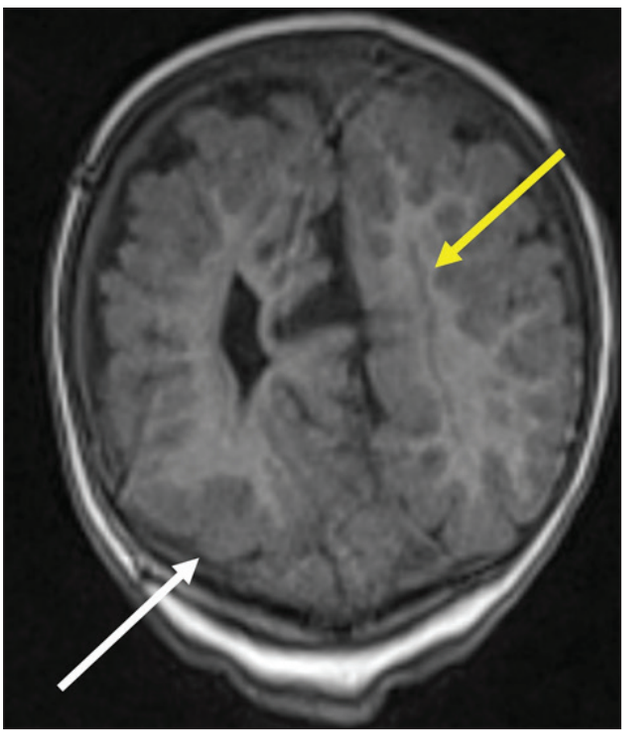

Figure 4: On the axial plane of T1-weighted imaging, cortex thickening representing polymicrogyria (white arrow) in the right occipital lobe with grey matter heterotopia (yellow arrow) is observed.

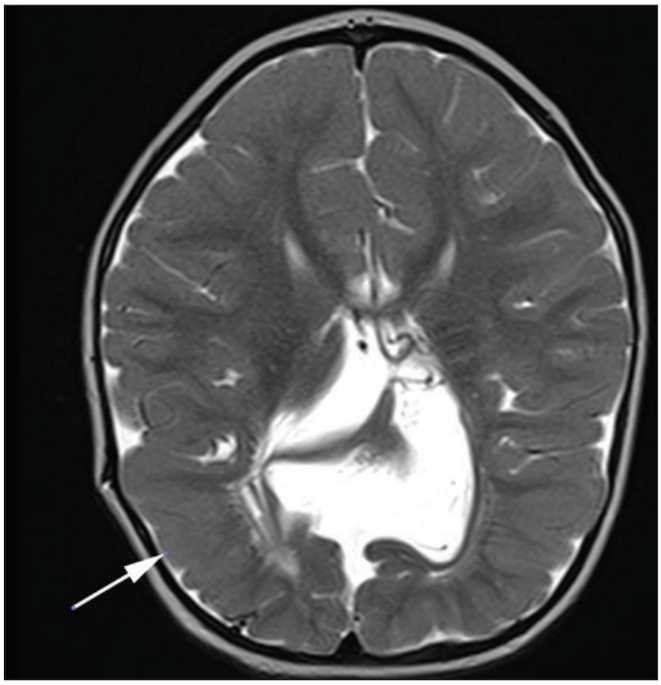

Figure 5: Pachygyria. The broad gyri of the parietal lobe (white arrow) are seen on the axial plane of T2-weighted imaging.

will primarily influence the activity of the cells in the germinal epithelium of the developing cortex (21). Several studies on the pathogenesis of cortical malformations in fetuses with meningomyelocele have concluded that neuroepithelial or ependymal denudation and abnormal neural migration can happen before the onset of ventricle enlargement and Arnold-Chiari II malformation (7,32).

In the present study, the most common supratentorial anomaly that was observed involved the configuration of the CC (160 patients); complete agenesis of the CC was observed in 9 (2.1%) subjects, whereas partial agenesis was observed in 148 (34.7%) subjects. In 3 (0.7%) patients hypoplasia of the CC was observed. These findings are consistent with those reported by Müller et al.'s study, revealing a rate of 2.7% for total agenesis and 27% for partial agenesis in 37 patients evaluated for different cerebral abnormalities associated with myelomeningocele (28).

The epidemiological data on the incidence of CC agenesis in co-occurrence with spinal dysraphism is limited (1). Depending on the main parts of the CC that are undeveloped, partial agenesis may be associated with either a congenital genetic disease or destructive lesion caused by secondary hydrocephalus (2,20,24).

CC and gyral anomalies have been described in patients with spinal dysraphism, but they are not considered to be specific to neural tube defects (16,17). Prenatal myelomeningocele repair shows no influence on the proportion of abnormal CC or heterotopias (38). The physiological development of the CC is based on an uneventful closure of the neural tube and adequate development of the massa commissuralis and cerebral hemispheres (15-18,36).

Fletcher et al. reported that in myelomeningocele lesions that are visualized above the level of the 12 thoracic vertebrae (T12), more severe abnormalities in brain development were observed (9). Similarly, Trigo et al. reported that the prospect of cerebral abnormalities was higher in subjects with a nonsacral lesion and larger lateral ventricles (37).

Consistent with some other series reported in the literature (14,17,19), dysmorphology of the CC was the most frequent anomaly observed in our study. Elgamal et al. reported a 48.5% rate of CC anomalies in 83 patients diagnosed with spinal open neural tube defects (8); Soylemez et al. in a study that included 47 patients that underwent postnatal repair for spina bifida reported a 27.65% rate of dysgenesis of the CC (35). Moreover, the dysmorphology of the CC had a rate of 37.5% (160 patients) in our patients.

The second most common anomaly found in our patients was represented by gray matter heterotopia and was noticed in 110 patients (25.8%) that underwent myelomeningocele repair. In our study, gray matter heterotopia was identified at a lower rate compared with the results reported by Cameron—a 38% rate of heterotopias in patients with myelomeningocele and Chiari malformation (4). Some studies have reported that cortical heterotopias appear to be associated with seizures and developmental disabilities, while subependymal type seems to only have a minor clinical impact (5,39).

In our study, polymicrogyria was identified in 22.53% of the patients (96 patients) that underwent myelomeningocele repair. However, compared with our study, Peach observed a higher rate of polymicrogyria in his study subjects (55%) (30). Polymicrogyria is known to occur when an injury to the developing brain happens in the late migration phase or after the neuronal migration has stopped (13,21,34). Furthermore, the extent of involvement and its area are considered factors that influence the clinical aspects of the study subjects with polymicrogyria (20).

Other consequences of the abnormal migration of neurons are represented by agyria and pachygyria, which present with a heterogeneous spectrum of clinical manifestations, resulting in relatively severe cognitive and motor disabilities in association with epileptic seizures (11). In our study, the consequences of abnormal migration (i.e., polymicrogyria, pachygyria, and agyria) were determined in almost 40% of the patients.

Enlargement of the intracerebral ventricles, Chiari malformation, and different anomalies of the CC, cortical thickness and gyrification, gray matter volume, and total brain volume have a major impact on the patients' cognitive outcomes. However, the distinction between their individual impacts on cognition is a complex process. The prenatal repair of myelomeningocele compared with postnatal repair has shown no significant impact on corpus callosal abnormalities, gyral abnormalities, and heterotopia (12,31).

A retrospective study by Schneider et al. aimed to correlate cerebral anomalies identified in spinal dysraphism patients with cognitive function. Brain malformations and cognitive detriments were less commonly identified in the closed form of spinal dysraphism (33).

Hydrocephalus, stenogyria, CC, and midbrain anomalies were associated with diminished cognitive function. Neurodevelopmental and neurobehavioral deficits have been described in patients with spinal dysraphism; the co-occurrence of an abnormal CC with a ventricular dilation over 15 millimeters has been shown to be associated with an increased risk of suboptimal neurodevelopment (10,26,38,40). However, further research is needed to better understand the precise clinical impact and long-term functional outcomes of associated supratentorial anomalies in myelomeningocele patients.

CONCLUSION

This study confirms that, except for hydrocephalus and Chiari malformation, other associated cerebral supratentorial anomalies can be observed in patients with myelomeningocele. However, further research on the interconnection between cerebral supratentorial anomalies and cognitive function is needed. This study emphasizes the necessity for further supplementary studies, in conjunction with accurate postnatal followups, in order to assess the real significance and repercussions of these anomalies on neurological development and also to establish how these structural changes in brain anatomy translate clinically.

Declarations

Funding: All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

Availability of data and materials: The datasets used during the current study are available from the corresponding author upon request.

Disclosure: The authors have no conflicts of interest to declare.

AUTHORSHIP CONTRIBUTION

Study conception and design: LAY, IA, BO, RC, OA, DU

Data collection: LAY, IA, BO, RC, OA, DU

Analysis and interpretation of results: LAY, IA, BO

Draft manuscript preparation: LAY, IA, BO, RC, OA, DU

Critical revision of the article: LAY, IA, BO, RC, OA, DU

All authors (LAY, IA, BO, RC, OA, DU) reviewed the results and approved the final version of the manuscript.

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