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Original research article

Dilatation of Virchow–Robin spaces in children hospitalized at pediatric neurology department

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A B S T R A C T

Background and purpose: Dilated Virchow–Robin spaces (dVRs) have been revealed by magnetic resonance imaging (MRI) in patients with various neurological disorders. However, their etiology and clinical importance have not been discovered yet. The aim of the study was to estimate dVRs occurrence in hospitalized children and determine dVRs localization and their association with different nervous system diseases.

Material and methods: Contrast-enhanced brain MRI examinations with the use of 1.5 T GE device were performed in children with different diseases of nervous system, who were hospitalized at Pediatric Neurology Department, Chair of Children and Adolescent Neurology, Jagiellonian University in the years 2010–2011. The mean age of examined children was 11.58 years, and the studied group included 27 boys and 26 girls.

Results: Within two years, MRI examinations of the brain were performed in 1348 children and dVRs were found in 53 of them (3.93%). Among children with dVRs, 15 were diagnosed with headache (28.3%) and 18 with epilepsy (33.96%). Other diagnoses were less frequent and occurred in 37.7%. Generalized dVRs and those localized in the subcortical nuclei were most frequently found.

Conclusions: Higher incidence of dVRs was found in children with headache and epilepsy. No association was found between localization of dVRs and symptomatology of different nervous system diseases except for large dVRs probably due to the pressure on the surrounding tissues.

1. Introduction

Virchow–Robin spaces (VRs) are projections of pia mater encircling wall of the cerebral arteries and penetrating from subarachnoid space into cerebral parenchyma [1–3]. Virchow–Robin spaces are normal anatomical structures of central nervous system, usually smaller than 2 mm but sometimes can be dilated (dVRs) [1]. Visualization of VRs depends on magnetic resonance (MR) technical specifications (sequence, magnetic field intensity) [1,4]. High-resolution MR revealed VRs in 100% of examined healthy subjects of whom only 1.6% had dVRs. On the other hand, standard MR revealed VRs in 80% of pediatric patients but dVRs were not found. The authors concluded that dVRs were variants of VRs in healthy patients but need clinical consideration in the case of nervous system

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disease [4]. There are only few histological reports of dVRs [5]. It is still unknown whether dVRs are congenital or acquired [6]. Their occurrence and dilatation increase with age. Correlation between dilatation of VRs and their anatomical background is being looked for [7].

Three localizations of dVRs have been described: type I along lenticulostriate arteries in the basal ganglia, type II along perforating arteries between gray and white matter and type III in the diencephalon [1]. Additionally, paraventricular localization has been observed [8]. Localization and signal intensity enable dVRs identification and differentiation from other pathological findings like lacunar infarctions, cystic periventricular leukomalacia, multiple sclerosis, cryptococcosis, mucopolysaccharidosis, cystic brain tumors, neurocysticercosis, arachnoid cysts and neuroepithelial cysts or adrenoleukodystrophy. The size of VRs dilatation is variable and sometimes produces mass effect [1,9]. Association of dVRs with perforating cerebral arteries is being explored with special attention [10]. Significant dVRs in the right temporo-occipital region and semioval center have been reported in older women with memory deficits and cognitive dysfunction [11]. Correlation of dVRs with stenosis of internal carotid artery is being looked for. Results of recent studies have revealed association between these two variables [12].

Ten years ago, reports concerning dVRs were casuistic and clinically divergent [10]. Even nowadays, it is still not unequivocal whether dVRs result from disease progression or are developmental variant [13]. Determination of radiological importance and clinical association is needed in patients with dVRs. Fast introduction of adequate treatment is the goal of the performed studies. DVRs localized in the obstructive areas of the brain (basal ganglia, midbrain) may lead to hydrocephalus which needs surgical intervention [2,9].

The aim of our study was to estimate dVRs occurrence in children hospitalized at pediatric neurology clinic and determine dVRs localization and their clinical importance.

2. Materials and methods

Children included in the study were hospitalized at the Pediatric Neurology Department, Chair of Children and Adolescent Neurology, Jagiellonian University, within two years (2010–2011). The Department provides 24-h specialist health care for 3.2 million population of Małopolska district and children at the age range from 1 month to 17 years are hospitalized. A total of 1348 examinations of brain MR were performed in the analyzed time period. In 53 cases, dVRs were revealed. There were 26 girls and 27 boys at the age range from 1 to 17 years (mean age 11.58 years). There were 4 children in the age group of 1–2 years, 23 in the age group of 7–12 years and 26 in the age group of 13–17 years. Clinical diagnoses of 53 children with dVRs are listed in Table 1.

Table 1 – Clinical diagnosis of 53 children with dilated Virchow–Robin spaces.

Clinical diagnosis	Number of children
Epilepsy	18
Migraine	9
Headaches	6
Neurodevelopmental disorders	3
Visual disorders	3
Learning difficulties	3
Gait disorders	2
Conversions	1
Ataxia	1
Dystonia	1
Spinal cord syndrome	1
CMT1A neuropathy	1
Transient ischemic attack	1
Neurofibromatosis type I	1
Cystic brain tumor	1
Inflammation of brain stem in the course of chickenpox	1

CMT – Charcot-Marie-Tooth.

Magnetic resonance examinations were performed in the Magnetic Resonance Laboratory in the same hospital, in similar conditions. The amount of injected contrast was normalized for body weight. Performance of MR examination was based on clinical indications.

Ophthalmic examination was performed in every child and was normal in 47 of them and in 6 revealed pathological changes. Slight edema of optic nerve discs was observed in 2 children, myopia in 2, and astigmatism and decreased visual acuity in single cases.

Electroencephalography (EEG) with standard activation procedures was performed in 34 children. Localized changes were found in 15 of them, generalized paroxysmal changes in 11, generalized slow activity in two and EEG recording was normal in six children. Transcranial Doppler examination was performed in eight children and was normal in seven of them. Asymmetry of cerebral blood flow in the anterior cerebral arteries was found in one of them (lower velocity of cerebral blood flow in the left anterior cerebral artery was found). Psychological evaluation revealed important findings in three children. Serious emotional disturbances were detected in two children and cognitive development disharmony in one child. Electromyography, evoked potentials and enzymatic tests were performed in single cases.

3. Results

Dilated Virchow–Robin spaces were described in 53 out of 1348 brain MR of children included into the study. This relatively high percentage (3.93%) prompts further investigation. Dilated Virchow–Robin spaces were incidental findings in every case and did not cause introduction of specific treatment e.g. surgical one. The thorough analysis revealed generalized and localized dVRs.

Generalized dVRs were found in 20 children – six of them were in the age group of 7–12 years and nine in the age group of 13–17 years. Localized dVRs were found in 33 patients and unilateral localization was described in 13 of them. Paraventricular localization was found in four patients (bilateral in two and unilateral in other two). Localized dVRs were found in all of the youngest patients aged 1–2 years and in 17 patients aged 7–12 years and in 17 patients aged 13–17 years. Characteristics of localized dVRs are presented in Tables 2 and 3. Additionally, association between dVRs localization and clinical diagnosis is

Table 2 – Bilateral localized dilated Virchow–Robin spaces.

Brain region	Number of children[a]
Subcortical nuclei	11
Semioval center	2
Corona radiata	1
Frontal lobes	4
Parietal lobes	4
Temporal lobes	2
Occipital lobes	1
Paraventricular	2 (parietal region, occipital region)
Posterior forceps	2
Ventricular triangles	1
Hippocampi	1

[a] In six patients bilateral localized changes were found in more than one region

Table 3 – Unilateral localized dilated Virchow–Robin spaces.

Brain region	Number of children[a]
Subcortical nuclei	3 (right hemisphere 2, left hemisphere 1)
Semioval center	1 (right hemisphere)
Paraventricular	2 (right parietal region, left occipital region)
Right frontal lobe, insula, right parietal lobe	1
Right temporal lobe	1
Left frontal lobe	1
Truncus of corpus callosum	2
Posterior forceps	2 (right hemisphere)
Hippocampi	1 (right hemisphere)

[a] In one patient unilateral localized changes were found in more than one region

presented in Table 4. Figs. 1–4 show brain MR images of patients with the biggest localized dVRs. Moreover, results of brain MR of 53 children with dVRs were analyzed in the aspect of other pathological changes, which are presented in Table 5.

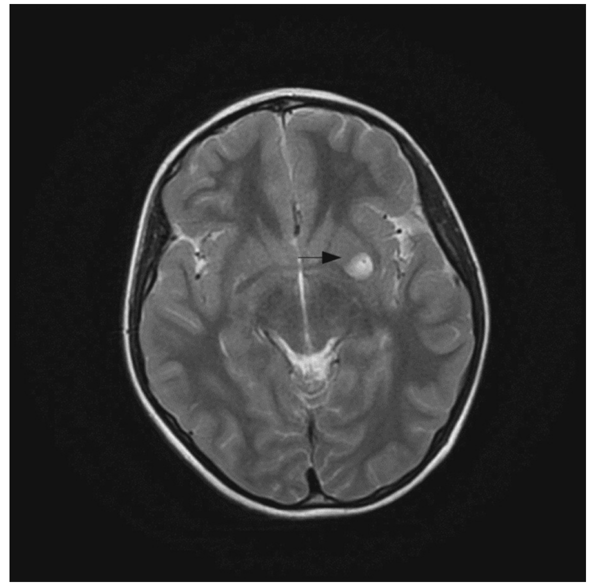

Fig. 1 – Brain MRI of 7-year-old boy with right-sided dystonic movements. Large dilated Virchow–Robin spaces (13 mm × 10 mm × 8 mm) localized in the left putamen (axial T2-weighted image).

4. Discussion

Incidence of dVRs among all children who had brain MR was 3.93% and was higher than that reported in the literature (2.96%) [14], probably due to the fact that this study concerned only children who were hospitalized at pediatric neurology department. Dilated Virchow–Robin spaces found in our patients were predominantly of small size. Contradictory to our results, Heier et al. [15] revealed high incidence of large dVRs (38.48%) among patients with dVRs.

Nowadays, association of MR results with post-mortem histological changes is explored. Virchow–Robin spaces form

Table 4 – Association between dilated Virchow–Robin spaces location and clinical diagnosis.

Brain region	Number of children with clinical diagnosis
Generalized	10 – epilepsy, 5 – migraine, 2 – headache, 1 – gait disorders, 1 – visual disorders, 1 – inflammation of brain stem in the course of chickenpox
Subcortical nuclei	5 – epilepsy, 2 – headache, 2 – neurodevelopmental disorders, 1 – migraine, 1 – learning difficulties, 1 – dystonia, 1 – visual disturbances, 1 – ataxia, 1 – gait disorders
Semioval center	1 – epilepsy, 1 – migraine, 1 – learning difficulties
Corona radiata	1 – cystic brain tumor
Frontal lobes	2 – migraine, 1 – epilepsy, 1 – neurodevelopmental disorders, 1 – gait disorders
Parietal lobes	2 – neurodevelopmental disorders, 1 – neurofibromatosis type 1, 1 – epilepsy, 1 – headache
Temporal lobes	1 – neurofibromatosis type 1, 1 – epilepsy, 1 – learning difficulties
Occipital lobes	1 – neurofibromatosis type 1
Paraventricular	1 – transient ischemic attack, 1 – epilepsy, 1 – spinal cord syndrome, 1 – visual disturbances
Corpus callosum	1 – headache, 1 – neurodevelopmental disorders
Posterior forceps	2 – migraine, 1 – CMT1A neuropathy, 1 – neurodevelopmental disorders
Ventricular triangles	1 – epilepsy
Hippocampi	1 – conversions, 1 – learning difficulties
Insula	1 – neurodevelopmental disorders

CMT – Charcot-Marie-Tooth.

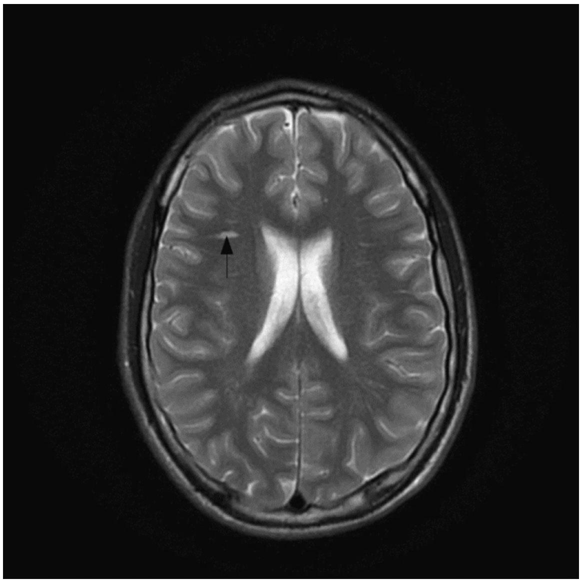

Fig. 2 – Brain MRI of 15-year-old boy with migraine with sensory and dysphasic aura (right-sided sensory symptoms, left-sided headache). Dilated Virchow–Robin spaces localized in the semioval center of right frontal lobe 3 mm × 10 mm (axial T2-weighted image).

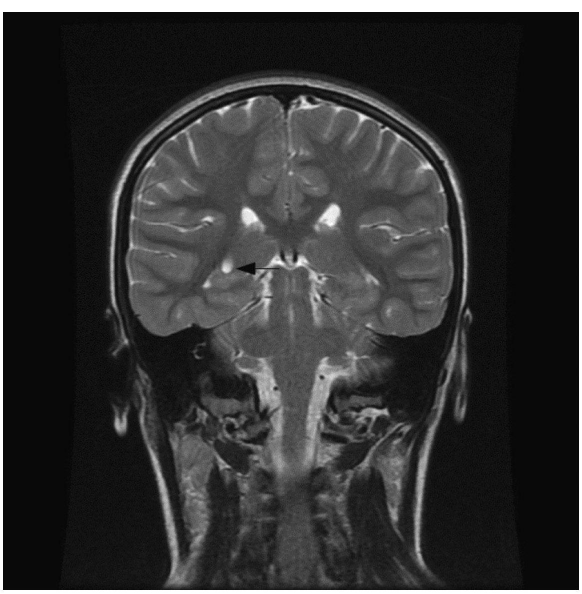

Fig. 3 – Brain MRI of 10-year-old girl with learning difficulties, right-sided headache at temporal region. Dilated Virchow–Robin spaces (7 mm × 5 mm) localized in the topography of right hippocampus (coronal T2-weighted image).

canal network in both hemispheres and connect their convexes, basal cisterns and ventricular system. They play an important role in maintenance of brain elasticity and compensation of intracranial pressure [8].

Convey et al. [16] described enlarged VRs in patients with macrocephaly and malformation of capillary vessels. Dilated Virchow–Robin spaces were associated with obstructive dilatation of lateral ventricles and dilatation of venous sinuses in these patients with cerebellar tonsillar herniation. No child from our study group had macrocephaly.

Zhu et al. [17] evaluated 1818 MR examinations of adult patients and revealed association between size of VRs dilatation and patients' age, value of blood pressure and MR markers of small vessel disease (volume of hyperintense white matter foci and occurrence of lacunar infarcts). Results of this study indicate that dVRs should be considered as additional MR marker of small cerebral arteries disease. In adult patients,

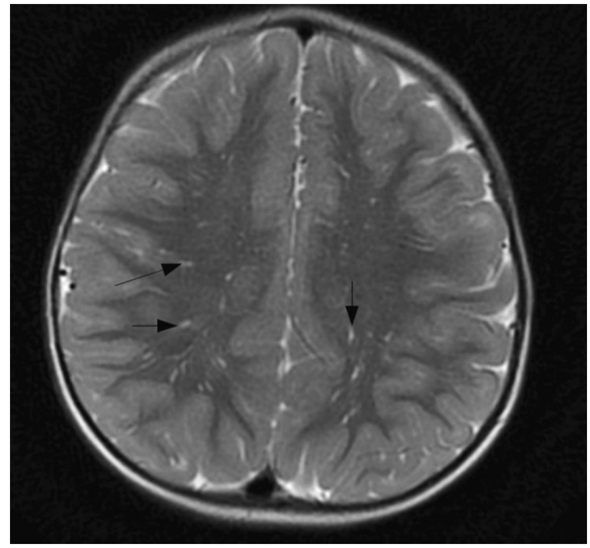

Fig. 4 – Brain MRI of 2-year-old boy with neurofibromatosis type 1. Dilated Virchow–Robin spaces in white matter of temporal, occipital and parietal lobes, bilaterally (5.6 mm) (axial T2-weighted image).

Table 5 – Other changes in brain magnetic resonance of 53 children with dilated Virchow–Robin spaces.

Type of changes	Number of children
Inflammation of craniofacial structures	11
Asymmetry of different structures of cerebral hemispheres	11
None	8
Pineal cyst	8
Arachnoid cyst	7
Demyelinating and dysmyelinating foci	6
Cavum septum pellucidum and cavum Vergae cyst	2
Fornix dysgenesis	1
Fluid space in the area of right foramen of Monro	1
Pachygyria and polymicrogyria in the right hemisphere	1
Corpus callosum hypoplasia	1
Asymmetry of falx cerebri	1
Paraventricular neuroglial cyst on the right side	1

occurrence of silent cerebral infarct should be differentiated from dVRs in some cases [18]. Higher incidence of dVRs has been also reported in patients with idiopathic normotensive hydrocephalus [19].

In the majority of children, dVRs have been associated with mental retardation, epilepsy, headaches and macrocephaly [13,14]. Headaches were present in 12, developmental disturbances in 17 and psychiatric disorders in 18 out of 37 patients with dVRs reported by Rollins et al. [14]. Similarly, the most frequent clinical diagnoses in our examined group of children with dVRs were headaches and epilepsy. Both generalized and localized in the subcortical nuclei dVRs were the most common ones. Correlation of localized dVRs in the semioval center with autism [20] as well as with migraine [3] and macrocephaly [21] has been found in the literature. Also occurrence of epilepsy in children has been linked with presence of dVRs in this localization [22]. In our group, dVRs in this localization were described only in three patients, one each with headaches, epilepsy and learning difficulties. Dilated Virchow–Robin spaces occur rarely in small children. Brockmann et al. [23] described two 3-year-old boys with dVRs and coordination disturbances, additionally in one of them slight hemihypertrophy of the face occurred in the following two years. Our group consisted mainly of older (≥7 years old) children, only four patients were at the age range from 1 to 2 years, one child with neurofibromatosis type 1, one with ataxia and two with neurodevelopmental disorders. Fayeye et al. [9] described the case of a 6-year-old boy with large dVRs (giant or tumefactive dVRs), localized in the midbrain which caused obstructive hydrocephalus and needed surgical treatment.

Only four patients from our group had significant dVRs (>5 mm); none of them, however, required surgical treatment. One of these patients had symptoms which could correspond to the affected area (dVRs in the left putamen and right-sided dystonic movements).

Currently, influence of dVRs on cerebrospinal tracts is being estimated [24]. Pathological space-occupying lesions (like brain tumors) may affect these tracts which can be visualized with the use of diffusion tensor imaging and tractography. It seems that in some cases dVRs may be nonspecific, e.g. in a child with neuroinfection caused by *Streptococcus pneumoniae* and with associated cerebral pseudomicroabscesses [25]. On the other hand, in patients with myotonic dystrophy dVRs may precede other symptoms of this disease [26]. Clinico-radiological correlation has also been found in children with adrenoleukodystrophy. Presence of higher number of more significant dVRs was associated with early phase of the disease or even its more benign course [27]. Literature review and our own observations prompt further investigations of dVRs clinical significance.

5. Conclusions

1. Among children hospitalized with different nervous system disorders, dVRs were described more frequently in those with headaches and epilepsy.
2. Localization of dVRs was rather accidental than associated with specific neurological symptoms. However, in the case of large dVRs one should keep in mind possible impairment of surrounding structure due to the mass effect.

Conflict of interest

None declared.

Acknowledgement and financial support

None declared.

Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

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