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CASE REPORT

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Isolated rhomboencephalosynapsis – a rare cerebellar anomaly

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Summary

Background: Rhomboencephalosynapsis (RES, RS) is a unique entity usually recognized in infancy based on neuroimaging. Cerebellar fusion and absence of cerebellar vermis is often associated with supratentorial findings. Since now there are about 50 cases described worldwide, with approximately 36 patients diagnosed by MRI. The authors present the first in Poland case of this uncommon malformation and review the literature.

Case Report: The authors describe a 28-month-old-girl with microcephaly and proper psychomotor development. The family history was unrelevant. Based on MRI the congenital malformation of posterior fossa-rhombencephalosynapsis was confirmed

Conclusions: Presented patient is a typical example of MRI usefulness especially in patients with RES. RES symptoms are mild and that is why the diagnosis is usually made only in adulthood.

Key words: rhomboencephalosynapsis • cerebellar malformation • children

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Background

Rhomboencephalosynapsis (RES) is a rare congenital malformation of the posterior fossa characterized by hypogenesis or agenesis of the vermis, dorsal fusion of the cerebellar hemispheres, fusion of dentate nuclei and superior cerebellar peduncles [1,2]. This malformation was described by Obersteiner in 1914 on the basis of a postmortem examination; the name of the condition was given by Gross and Hoff in 1959. RES is also the main component of Gomez-Lopez-Hernandez syndrome (GLHS), cerebello-trigeminal-dermal dysplasia, VACTERL (vertebral anomalies, anal atresia, cardiovascular defects, esophageal atresia and/or tracheo--esophageal fistula, renal and limb/radial anomalies), and VACTERL-H (VACTERL association with hydrocephalus). Sener et al estimated the frequency of RES at 0.13% in a series of 3000 pediatric patients with performed MRI [3–5].

Case Reports

A 28-month-old girl admitted for developmental delay and microcephaly. She was the first child of a non-consanguineous couple of Polish origin, born at term by vaginal delivery. Her birth weight was 3250 g and the Apgar score was 10 points. There was a family history of spontaneous abortions. The child did not experience apnea or seizures.

Examination at admission revealed a non-specific facial dysmorphia (low-set ears, hypertelorism). Neurological examination showed microcephaly (HC=47 cm, <3 percentile), bilateral strabismus convergens, hypotonia with preserved tendon reflexes, unstable and broad-based gait. Psychological assessment confirmed proper psychomotor development and revealed an IQ of 89 (according to Psyche-Cattell scale). Electroencephalography (EEG), ultrasonography of abdomen, electrocardiography, echocardiography, and neurophysiological examinations were normal (ENG, EMG). Seizures were not observed before or during hospitalization. Ophthalmologic evaluation showed clear corneas and normal fundi. MRI of the head (Figures 1–3) disclosed a rare congenital anomaly – of posterior fossa elements – rhomboencephalosynapsis. For morphological assessment of brain structures, only T2-weighted images

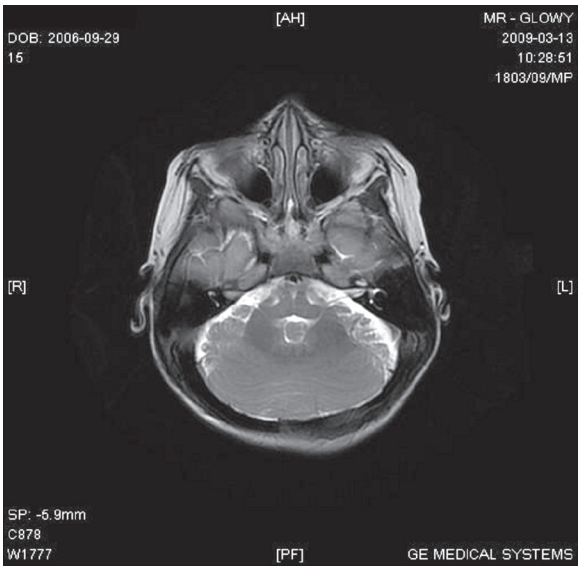

Figure 1. Axial T2-weighted images.

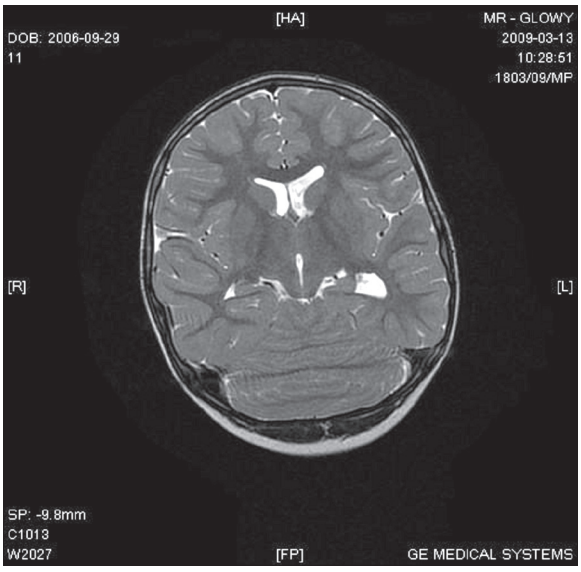

Figure 2. Coronal T2-weighted images. On these consecutive slices, both in axial and coronal plane of T2-weighted images, congenital malformation of posterior fossa elements – rhombencephalosynapsis – fusion of cerebellar hemispheres – fused transverse cerebellar folia and partial hypogenesis of vermis are visible.

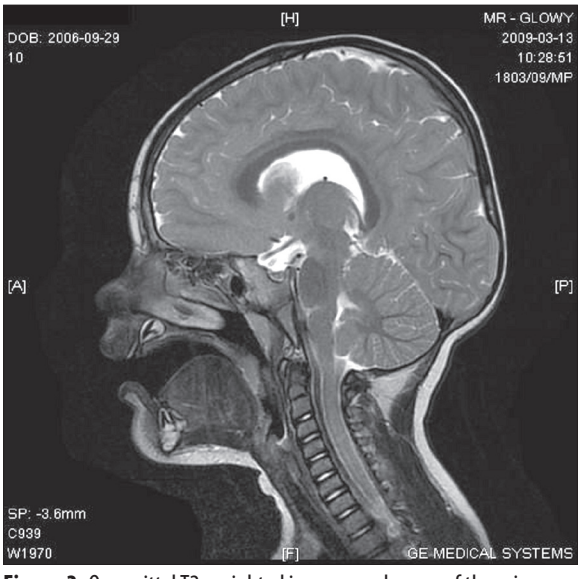

Figure 3. On sagittal T2-weighted image, an absence of the primary fissure of the cerebellum is seen.

were selected. Her MRI scan showed fusion of cerebellar hemispheres, fused transverse cerebellar folia and partial hypogenesis of vermis. Cerebellum itself was normal-sized, slightly reduced in transverse diameter, not really hypoplastic. Additionally, there was no primary fissure of cerebellum (normally visible on sagittal planes). Corpus callosum and septum pellucidum were preserved, the lateral ventricles were not dilated and the gyration appeared normal. The Inferior olivary nuclei were present in the MRI of the medulla oblongata. Based on the performed work-up, metabolic abnormalities and chromosomal rearrangements were excluded.

Discussion

RES results from abnormal cerebellar development between 28 and 41 days of gestation [1,2,6]. According to the hypothesis formed by Utsunomiya et al, the fusion of the cerebellar hemisphere is not caused by maldevelopment of the vermis but probably by primary failure of vermian differentiation [6]. Modern concepts of neuroembryology take into account the genetic gradients along the three axes of the neural tube during development. Rhomboencephalosynapsis might be regarded as a defect in the dorsoventral gradient of the vertical axis and in the mediolateral gradient of the horizontal axis. Underexpression of dorsalizing genes, except for RE, is involved in septo-optic dysplasia. Based on embryogenic research track cerebellar primordium is unpaired and genetic experimental study in mice showed disturbed expression of the homeobox-containing genes *Otx* and *Gx* [2,6]. According to Sarnat et al., more important genes with dorsalizing effect in the vertical axis belong to BMD and PAX families [7].

RES can manifest either as an isolated malformation of the posterior fossa structures or in association with other abnormalities (RES "plus") including other CNS and/or systemic anomalies [1,2,5,8]. Abnormalities reported in association with RES are variable: hydrocephalus, ventriculomegaly, absent/rudimentary/dysgenic corpus callosum, absence of the septum pellucidum, fused thalami, tectum and fornicles, hypoplasia of the temporal lobes, olivary nuclei, anterior commissure and optic chiasma, agenesis of the posterior lobe of the pituitary, large clefts supratentorially, hippocampal hypoplasia, multiple synosthoses of cranial sutures [4,5,8]. Pasquier at al reported a morphological analysis of 40 fetuses (between 14 and 35 weeks of gestation).

Systemic disturbances associated with RES include cardiovascular, respiratory, urinary system and skeletal abnormalities (spinal segmentation, mild scoliosis, genu valgum, polydactyly, hexadactyly, phalangeal hypoplasia,

duplication of the thumbs). In the presented case, rhomboencephalosynapsis is an isolated pathology [1,2,5].

The clinical spectra of RES depend mostly on supratentorial midline anomalies. Typical clinical manifestations include: truncal and/or limb ataxia, muscular hypotonia, spasticity, abnormal eye movements, strabismus, dysarthria, head stereotypies (head rolling), and developmental delay [1,2,5]. The severity of neurological dysfunction ranges from mild to severe. The patient described in this report demonstrated relatively mild motor abnormalities and cognitive impairment [9,10]. Other studies report similar data; the symptoms usually do not restrict daily activities [10]. Attention problems and disorders of cognitive function are known to be frequent disturbances coexisting with cerebellar malformations [9]. Based on the literature data, cognitive functions in RES are mostly impaired. Berquin et al showed smaller vermian volume in boys with attention deficit disorder. Probably, an impaired cerebellar-thalamo-prefrontal circuit may be responsible for the observed deficits [1,2,9]. Self-mutilation and obsessive--compulsive disorder were also reported in patients with RES. According to Toelle et al. and Chemli et al., there are RES patients with normal intellectual development, cognitive and language functions [1,5]. Among ophthalmologic abnormalities in RES Philips et al described prenuclear ocular motor dysfunction: A-pattern strabismus and superior oblique overaction [11]. Other eye or visual pathway abnormalities included microphthalmia, optic nerve atrophy or hypoplasia, septo-optic dysplasia, absence of the optic chiasm.

The cause of RES is still unknown. The chromosomal analyses in previous cases were normal except for a patient described by Truwit et al, who was found to carry interstitial deletion of chromosome 2q and an unbalanced subtelomeric translocation t(2p;10q) [3]. Demaerel et al. suggested an association between RES and maternal ethosuximide or phenylcyclidine treatment [2].

Our case is a typical example of MRI usefulness, especially in patients with unspecified developmental delay. Normal cognitive functions do not exclude the diagnosis either. We would like to make the clinicians aware that if the symptoms are mild, the diagnosis is usually made in adulthood. Non-syndromic RES may be even asymptomatic and that is why the diagnosis can be easily missed. This is of particular importance in prenatal diagnosis [12].

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