

Gomez-Lopez-Hernandez Syndrome: A Rare Neurocutaneous Syndrome

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A six-year-old boy presented with generalized tonic-clonic seizures and myoclonic jerks; the patient was treated with anti-epileptic medication and his seizures ceased into remission. During the physical examination, the patient had bilateral parietal alopecia with insensitivity to painful stimuli at the site of alopecia. MRI brain showed rhombencephalosynapsis with dysgenesis of the corpus callosum. The patient was diagnosed with Gomez-Lopez-Hernandez Syndrome which was previously overlooked.

We report the first case in the Kingdom of Bahrain, to the best of our knowledge. This presentation elaborates further on this rare neurocutaneous disorder which was missed for several years.

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Gomez-Lopez-Hernandez Syndrome (GLHS), also called cerebellotrigeminal dermal dysplasia, is a rare neurocutaneous syndrome characterized by a triad of findings: partial alopecia of the scalp, trigeminal anesthesia and rhombencephalosynapsis¹.

Rhombencephalosynapsis is defined by the absence of the cerebellar vermis, fusion of the cerebellar hemispheres across the midsagittal plane, dentate nuclei appearing as an almost single structure consisting of contributions by the left and right hemispheres and fusion of the superior cerebellar peduncles. Additional features of GLHS include craniofacial dysmorphic features such as brachycephaly, midface hypoplasia and hypertelorism due to underdeveloped malar and maxillary bones; the patients are at risk to develop corneal opacities secondary to trigeminal anesthesia. Cognitive functions are usually impaired².

The aim of this presentation is to report a case of GLHS, which were initially overlooked leading to late diagnosis.

THE CASE

A six-year-old boy, product of lower segment cesarean section due to the failure of progress in the second stage of labor, presented with generalized tonic-clonic seizures and myoclonic jerks. The mother had gestational diabetes mellitus and was on insulin injections and managed for preeclampsia. The birthweight was 3,140 grams; head circumference was 35 cm and the Apgar score of 5, 7 and 8 at 1, 5 and 10 minutes, respectively. The patient remained in the neonatal intensive

care unit (NICU) for ten days for further evaluation of his relatively large head, brachycephaly and frontal bossing.

Antenatal ultrasound study showed dilated lateral ventricles of the brain. Subsequent skull ultrasound confirmed mild dilatation of the lateral and third ventricles. He did not require neurosurgical interventions. At 10 months of age, CT brain did not reveal hydrocephalus or craniosynostosis. The patient continued to develop appropriately for his age. He had normal motor activity both gross and fine, good socialization; however, he had delayed speech. At the age of one year, the patient had short non-febrile generalized tonic-clonic seizures occurring in clusters, but antiepileptic medications were not started. At the age of four years, he had a recurrence of generalized tonic-clonic seizures, and myoclonic jerks for which he was started on Sodium Valproate, which controlled the seizures and later ceased into remission.

Episodic head nodding was noted. On examination, the patient's head circumference measured 52 cm (85 percentile) and weighed 16 kilos (15 percentile). There was a clear disproportion between weight and head size percentiles. The patient had subtle dysmorphic features, such as frontal bossing and hypertelorism, see figure 1. The patient was fixing and following well with full extraocular movements, pupils were equal and reactive to light, no corneal opacities, no facial weakness; gag reflex was normal and tongue protrusion in the midline. No motor deficits or ataxia were noted. However, bilateral focal alopecia extending over the parietal regions was noted and loss of sensation over the corresponding areas which was overlooked previously, see figure 2.

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Figure 1: Frontal Bossing of the Forehead and Hypertelorism



Figure 2 (A)



Figure 2 (B)

Figure 2 (A and B): Bilateral Parietal Alopecia on Left and Right Side

Electroencephalography (EEG) was normal; MRI brain revealed rhombencephalosynapsis with fusion of the cerebellar hemispheres and absent vermis in addition to dysgenesis of corpus callosum but no clear cortical dysplasia, see figures 3, 4 and 5.

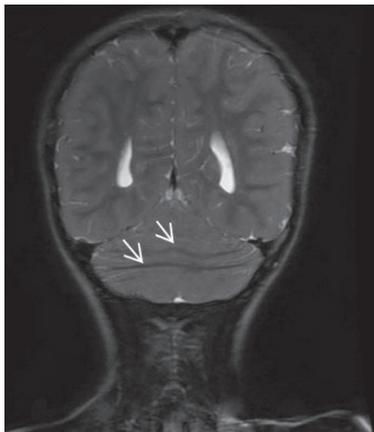


Figure 3: Rhombencephalosynapsis with Continuation of Cerebellar Sulci Across the Midline with Absence of Vermis



Figure 4: Fusion of the Cerebellar Hemispheres with Absence of Cerebellar Vermis



Figure 5: Thinning and Partial Dysgenesis of Corpus Callosum

Chromosomal microarray test was unremarkable. Based on the clinical and radiological findings, the patient was diagnosed with Gomez-Lopez-Hernandez Syndrome or cerebellotrigeminal dermal dysplasia.

DISCUSSION

Gomez-Lopez-Hernandez syndrome is a rare disorder first described in 1979 by Gomez and in 1982 by Lopez-Hernandez^{3,4}. The etiology of GLHS remains unknown, but a genetic cause seems likely². Reported cases are sporadic and all but one had been born to non-consanguineous parents⁵. The number of males and females affected is equal and there is no gender difference regarding severity². No chromosomal abnormalities have been reported in GLHS. Experimental animal study on nax mouse revealed that a novel recessive mutation of the lysosomal monoesterase Acp2 gene induces distorted cerebellar cortex, ataxia and delayed hair appearance, which might represent an animal model for GLHS⁶.

Other genes may be considered as potential for GLHS. The homeobox genes Tlx-1 and Tlx-3 are both early

expressed in placode-derived cranial neurons including the trigeminal placodes, and the hindbrain in chicken⁷. However, the involvement of these genes in GLHS remains to be demonstrated. Rhombencephalosynapsis constitutes a consistent key feature of GLHS.

Rhombencephalosynapsis typically occurs as an isolated cerebellar anomaly, but may be associated with other brain malformations including hydrocephalus, aplasia of septum pellucidum, dysgenesis of the corpus callosum, hippocampal abnormalities and fusion of the fornices⁸.

Rhombencephalosynapsis occurs not only in GLHS, but also in conjunction with VACTERL features and holopresencephaly^{10,11}. In GLHS, alopecia is focal, bilateral, congenital, and predominantly located in the parieto-occipital region. However, alopecia can be markedly asymmetric or even unilateral. Less frequent localizations are the temporal, frontoparietal or temporoparietal regions. In some cases, alopecia may be easily concealed by the surrounding scalp hair and must be carefully looked for⁹.

Trigeminal anesthesia most commonly affects the ophthalmic branch, causing abnormal forehead sensation and corneal reflexes⁹. Ataxia and muscular hypotonia are the most common neurological manifestations of rhombencephalosynapsis and GLHS. The symptoms vary considerably in severity but are mostly mild, and only a few patients are partly restricted in daily life activities⁸. Head nodding stereotypies consist of side-to-side “no” movements and up-and-down “yes” movements. The resulting disruption may severely interfere with social skills, particularly in children with normal cognitive functions². Cognitive impairment has been found in most previously reported patients^{10,12}. Craniofacial phenotype in GLHS typically includes midface hypoplasia, turricephaly and/or brachycephaly, low-set and posteriorly rotated ears, hypertelorism, and strabismus; these dysmorphic signs are present in most, but not all cases. Most patients with GLHS are not associated with other diseases².

Seizures have been reported in several patients with GLHS. In a study by Gomy et al, seizures were found in 4 of 12 patients with GLHS⁵. Absence seizures and partial seizures are usually controlled by antiepileptic medication. Our patient had generalized tonic-clonic seizures and myoclonic jerks which ceased into remission. Because not all patients develop seizures, the rhombencephalosynapsis itself is not the underlying cause, but the degrees of cerebral involvement may contribute to seizure phenotypes¹².

It is possible that GLHS or rhombencephalosynapsis is being under-recognized by pediatric neurologists. Patients with scalp alopecia should be examined for other features of GLHS and MRI should be performed for identification of rhombencephalosynapsis.

CONCLUSION

Gomez-Lopez-Hernandez syndrome is a rare neurocutaneous disorder. It is most likely a genetic condition, although the exact genetic defect remains elusive. The disorder affects the cerebellar development and the trigeminal placode during embryogenesis. Our case represents one of the unique hindbrain malformations and highlights the need for further study.

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