P-116

OPHN1 syndrome among three siblings with X-linked developmental disorders; the first case in South Korea

Myeong Geun Jeong, M.D., Soyoung Lee, M.D. Ph. D.

Department of Rehabilitation Medicine, Keimyung University Dongsan Hospital, Keimyung University School of Medicine, Daegu, Republic of Korea

Introduction

The OPHN1 gene, located in Xq12, encodes an oligophrenin-1 protein crucial for fetal nervous tissue development and migration. OPHN1 syndrome, an X-linked intellectual disabilities (XLIDs), presents with mental retardation, cerebellar hypoplasia and distinctive facial features. While primarily affecting males, females who carry a mutation in the OPHN1 gene may display mild developmental delays, mild learning disabilities and mild cognitive impairments. This report presents three cases of OPHN1-associated XLID within a single family.

Case Report

A 23-month-old boy, visited the rehabilitation department due to a general developmental delay. He was first child and was born at full term via normal vaginal delivery. He had a total score of 82.5% on the Gross Motor Function Measure (GMFM), indicating a developmental level of 10-11 months. According to the Denver Developmental Screening Test II (DDST-II), he demonstrated skills equivalent to 16 months in the personal-social domain, 15 months in the language domain, and 11 months in both the gross and fine motor domains. At 7 years of age, his Pediatric Balance Scale (PBS) score was 44. Preschool Receptive-Expressive Language Scale (PRES) assessment showed receptive language development at 47 months, expressive language at 41 months, and integrated language at 44 months. The results of the Korean Developmental Test of Visual Perception-2 showed very poor general visual perception and visual-motor integration in the 1st percentile, and inferior motor-reduced visual perception in the 5th percentile. Brain MRI revealed a prominent cystic lesion in the retrocerebellar convexity suggesting mega-cisterna magna findings (Figure 1).

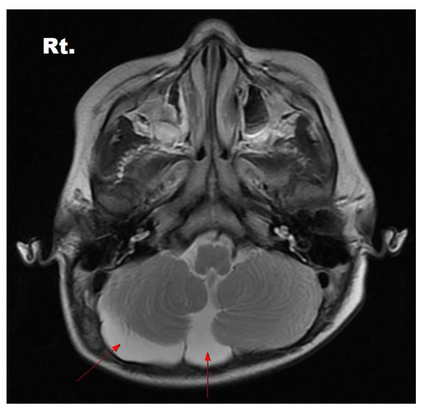

Figure 1.
The brain MRI T2-weighted image performed in the first male child on 16 months. The red arrows refer a cystic lesion in the retrocerebellar convexity.

His younger brother, a correctional age (CA) of 17-month-old, also visited the rehabilitation department due to developmental delays. He was born at 38 weeks via normal vaginal delivery. At the age of 17.5 months, the GMFM assessment revealed 6-7 months developmental level. According to the DDST-II, he demonstrated skills equivalent to 9 months in the personal-social and language domains, and 10 months in fine motor domain. He had a retrocerebellar cystic mass and diffuse frontal cortical atrophy since birth and was born at an intrauterine gestational age of 38 weeks (Figure 2). At 5 years of age, PBS score was 34, and deficiencies in task performance and tool use were noted on the Hand Function Test. According to the results of the Sequenced Language Scale for Infants, receptive language development was at 26 months and expressive language at 23 months. His total IQ was 45 points using the Social Maturity Scale (SMS), indicating moderate intellectual disability.

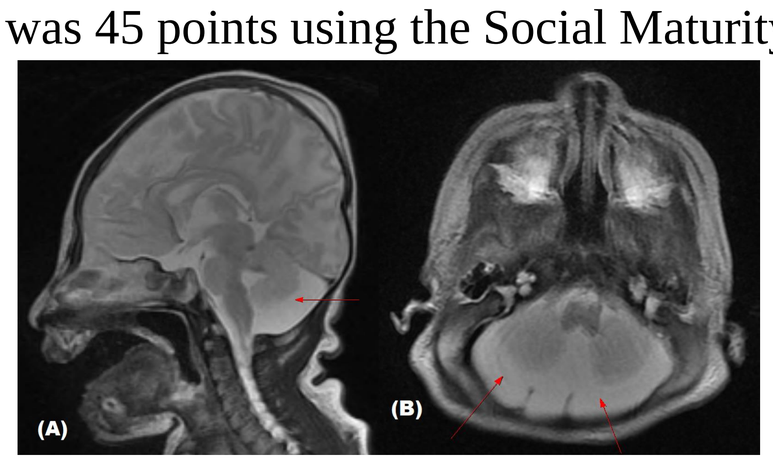

Figure 2.
The brain MRI T2-weighted image performed in the second male child on the 3rd day after birth. The red arrows refer a retrocerebellar cystic mass.
(A) T2-weighted sagittal view (B) T2-weighted axial view

The youngest sister was born at 39 weeks by normal vaginal delivery. At her 12-month assessment, her gross motor development was assessed at 10.5-11 months on the DDST-II, while her language, fine motor and personal-social development were within the normal range. At 4 years of age, PRES showed expressive language development at 41 months, falling in the 4th percentile, and integrated language at 44 months, indicating a mild developmental delay in language.

The genetic testing was performed to diagnose the factor of delayed development that shows differences in developmental delay based on sex. Chromosomal microarray and PCR testing confirmed a hemizygous 360 kbp deletion containing part of OPHN1 and deletion of exons 1 and 2 in both male siblings. Additional CMA and PCR family testing revealed the heterozygous deletion in the unaffected mother and younger sister.

Discussion

This is the first case of OPHN-related XLID reported in a family in Korea. This case shows that the OPHN1 gene mutation occurred in a family consisting of a boy with severe symptoms and a girl with mild symptoms. In addition, developmental milestones that may have been within the normal range during infancy and early childhood may show differences as they enter school age. In this case, the younger sister showed such differences, so it seems necessary to assess development periodically until development is complete, even if it was initially within the normal range. Finally, for patients with genetic variants, an accurate diagnosis that takes into account the patient's genetic background and symptoms is necessary to set and manage goals for precision rehabilitation therapy and promote functional improvement.