A report of a rare syndrome: Alazami Syndrome

Irmak Erdoğan [1], Nihal Olgaç Dündar [2], Rabia Meral[3], Pınar Gençpınar [2], Bumin Nuri Dündar [4]

[1] SBU Tepecik Training and Research Hospital, Pediatric Neurology Clinic, Izmir [2] İzmir Katip Celebi University Faculty of Medicine, Department of Pediatric Neurology
[3] SBU Tepecik Training and Research Hospital, Pediatric Endocrinology Clinic, Izmir [4] Izmir Katip Celebi University Faculty of Medicine, Department of Pediatric Endocrinology

ICNC 2022
17th INTERNATIONAL CHILD NEUROLOGY CONGRESS
ANTALYA, TURKEY | OCTOBER 3-7, 2022

ABSTRACT

La Ribonucleoprotein 7 (LARP7) encodes a protein which is found in the 7SK snRNP (small nuclear ribonucleoprotein). This snRNP complex inhibits a cyclin-dependent kinase, positive transcription elongation factor b, which is required for paused RNA polymerase II at a promoter to begin transcription elongation. Alazami Syndrome is caused by homozygous or compound heterozygous mutation in the LARP7 gene on chromosome 4q25 (1). Alazami Syndrome is an autosomal recessive disorder characterized by severe growth restriction at birth, short stature, severe intellectual disability and recognizable dysmorphic facial features (triangular face, broad nose, wide mouth, full lips, widely spaced teeth, deeply set eyes) (1,2). With the increased utilization of WES, the diagnosis of Alazami syndrome is expected to increase in the general population across all ethnic groups.

CASE

Two sisters aged 9 and 5 years are being followed up in a multidisciplinary manner due to global developmental delay, growth retardation and intellectual disability. Both of the sisters with a third degree consanguinity were born at term with low birth weight. Both of them are microcephalic and have low weight-height percentiles. On physical examination of a 9 year-old girl, weight: 15 kg (-4.07 SD), height: 112 cm (-3.16 SD), and for the 5 year-old sister, weight: 13.5 kg (-2.32 SD), height: 94 cm (-3.31 SD). The first sibling had a generalized tonic-clonic seizure when she was 3 years old and her seizures were controlled with levetiracetam. EEG and cranial MRI was normal. Drooling, ulnar hypoplasia and ulnar deviation in both hands and abducens palsy detected in the second sibling. Both have severe speech delay, triangular shape face, broad nose, deeply set eyes and widely spaced teeth. Karyotype, microarray and inherited panel were found to be normal for both of the sisters. WES was performed and they both have homozygous c.946C>T variants in the LARP7 gene.

Photo 1: Few prominent facial features can be noted form these images, such as the wide and depressed nasal bridge, triangular face, low set ears, widely spaced teeth

CONCLUSION

Alazami Syndrome is an autosomal recessive disorder with homozygous and compound heterozygous variants described. Genetic counseling is important for the affected families. Management should be multidisciplinary with a lifelong follow up. With the increased utilization of WES, the diagnosis of Alazami syndrome is expected to increase in the general population across all ethnic groups

KEYWORDS

Primordial dwarfism, developmental delay, facial dysmorphism, genetic syndrome, speech delay

REFERENCES

1) Alazami AM, Al-Owain M, Alzahrani F, Shuaib T, Al-Shamrani H, Al-Falki YH, Al-Qahtani SM, Alsheddi T, Colak D, Alkuraya FS. Loss of function mutation in LARP7, chaperone of 7SK ncRNA, causes a syndrome of facial dysmorphism, intellectual disability, and primordial dwarfism. Hum Mutat. 2012 Oct;33(10):1429-34.
2) Hollink IH, Alfadhel M, Al-Wakeel AS, Ababneh F, Pfundt R, de Man SA, Jamra RA, Rolfs A, Bertoli-Avella AM, van de Laar IM. Broadening the phenotypic spectrum of pathogenic LARP7 variants: two cases with intellectual disability, variable growth retardation and distinct facial features. J Hum Genet. 2016 Mar;61(3):229-33.