Genetics of Mondini Malformation

Rozita Jalilian[1] and Nima Rezaei[1,2]

[1] *Research Center for Immunodeficiencies, Children's Medical Center, Pediatrics Center of Excellence, Tehran University of Medical Sciences, Tehran, Iran*

[2] *Molecular Immunology Research Center; and Department of Immunology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran*

The Mondini malformation is a rare congenital inner ear malformation, characterized by cochlear abnormality with dilatation of the vestibule, aqueduct ampullar ends of the semicircular canals, and incomplete partition of the cochlea (1). These deformities may result in a perilymph fistula between subarachnoid space and the middle ear, which may result in cerebrospinal fluid (CSF) leakage, leading to rhinorrhea or otorrhea. CSF fistula can predispose affected individuals to recurrent meningitis. This abnormality happens due to arrest of cochlea development in seventh week of gestation and it is commonly associated with hearing impairment (2). The hearing loss is mainly sensorineural, but conductive hearing impairment due to CSF leakage or other disorders may accompany. Recurrent meningitis is the clue of diagnosis (3).

There is a recent article, entitled "Recurrent bacterial meningitis in a child with hearing impairment, Mondini dysplasia: a case report", published in the Acta Medica Iranica. We read this paper with great interest. The authors presented a case of recurrent meningitis who was referred for evaluating possible immunodeficiencies as the cause of recurrent meningitis. It should be noted that although primary immunodeficiency should be considered in the list of differential diagnosis in cases with recurrent serious infections, other underlying causes, particularly anatomical defects should be excluded (4).

The presented patient had history of impaired hearing and recurrent bacterial meningitis, while computed tomography scan suggested Mondini malformation (5). Meantime no further investigations to genetically confirm the diagnosis was not made. Meantime no discussion was made on gene loci and indeed it is not clear how some other congenital syndromes, which could have been associated with this malformation, were excluded.

It should be mentioned that some gene loci have been identified in association of this Mondini malformation.

Mutations of the *SLC26A4* gene have been found in individuals with enlargement of vestibular aqueduct or Mondini dysplasia. While several mutations have already been identified, IVS7-2A>G seems to be one of the most common one (6). *SLC26A4* mutations cause both Pendred syndrome and DFNB4, which are two autosomal recessive disorders, commonly present with sensorineural hearing loss due to vestibular aqueduct enlargement or incomplete partition of cochlea (Mondini dysplasia) (7). *TBX1* gene haploinsufficiency and point mutations can cause Di George syndrome, which could also be associated with Mondini dysplasia. Moreover some other congenital syndromes have been associated with this disorder, including Klippel-Feil syndrome and chromosomal trisomies (2). Considering such associations, providing genetic analysis and genetic counseling would be useful to exclude other syndromes, when Mondini dysplasia is suspected.

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Corresponding Author: Nima Rezaei
Children's Medical Center Hospital, Dr. Qarib St, Keshavarz Blvd, Tehran 14194, Iran
Tel: +98 21 6692 9234, Fax: +98 21 6692 9235, E-mail: rezaei_nima@tums.ac.ir

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