World Journal of Biology Pharmacy and Health Sciences
eISSN: 2582-5542
Cross Ref DOI: 10.30574/wjbphs
Journal homepage: https://wjbphs.com/

(CASE REPORT)

Diabetes mellitus type 1(DM-1) in a child with usher syndrome

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World Journal of Biology Pharmacy and Health Sciences, 2023, 16(01), 229–232

Publication history: Received on 30 July 2023; revised on 04 September 2023; accepted on 07 September 2023

Article DOI: https://doi.org/10.30574/wjbphs.2023.16.1.0377

Abstract

Usher Syndrome is a rare genetic (autosomal recessive) disorder that characterized by partial or total hearing loss caused by defective inner ear and vision loss caused by retinitis pigmentosa which worsens by time. We report on a 9 year-old child who was diagnosed by genetic testing via whole exome sequencing (WES) with Usher Syndrome. At the age of two years and three months, the patient developed type 1 Diabetes Mellitus (DM-1).

The aim of this article is to provide a comprehensive review of Usher Syndrome. The postulated association of Usher Syndrome and diabetes mellitus type 1 pathogenesis is also highlighted.

Keywords: Diabetes Mellitus type 1; Usher Syndrome; Whole exome sequencing (WES) association; Pathophysiolgy; Hearing; Vision; Genetic

1. Introduction

Usher Syndrome is named after the Scottish ophthalmologist Charles Usher, who examined the pathology and transmission of a group of 69 patients with retinitis pigmentosa in 1914. However, it was first described in 1858 by Albercht Von Grafe who reported a case of a deaf child with retinitis pigmentosa (1-7). It is the most common childhood condition that affects both hearing and vision. The retinas of the eyes are slowly damaged over time. It is the most frequent genetic disorder inherited as an autosomal recessive disorder. The estimated incidence is one in 6000 people world-wide, with rates as high as one in 12500 in Germany. In Norway the incidence is estimated to be approximately one in 28000. Type 1 is the most common among the Ashkenizi jewish population, while type 3 is rarely found outside Ashkenizi jewsh and Finish population. It occurs roughly as one in 23000 people in United State of America (8-13) The symptoms of the syndrome (depend on the type), generally three types are describe;

- Type 1, includes deafness at birth and severe balance problems. Vision problems often begin before the child is 10 years old. Vision gets worse as they grow.
- Type 2, includes moderate to severe hearing loss but no balance problem. Vision problems often are found during adulthood.
- Type 3, includes normal to near normal hearing and balance. Hearing and vision problems often occur during the teen years. The child may develop balance problem as they get old. (1,3,5,7 9,11,13). Most children diagnosed with Usher Syndrome have type 1 or type 2.

Usher Syndrome is a severe disease with significant vision and hearing impairment. It is genetically hetrogeneous with variable genes and mutations. Advancing in massive sequening technologies will certainly change the approaches for molecular diagnosis(14-21).

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In this article, we report a 9 year- old child who was diagnosed, based on genetic testing, with Usher Syndrome who developed type 1 Diabetes Melitus (DM- 1).

2. Case Summary

A nine years and six months old male child was born with congenital profound deafness. He was the product of full term, 39 weeks of gestation, normal pregnancy and who was delivered by emergency caeserian section as a result of birth asphyxia. No history of neonatal sepsis nor jaundice. The parents were consanguneious. No maternal history of hypertension, diabetes, hyperlipidaemia or drug intake. No hamily history of deafness, visual disorders or diabetes mellitus type 1. The patient had developmental delay, walked at three years and six months of age, with balance disturbance due to vestibular disorder and low I.Q.He required choclear implantation. At two years of age, the patient developed type 1 diabetes mellitus and was maintained on insulin. On physical examination, there was no obvious dysmorphism with normal growth. Visual acutty and retinal examination appear normal, with no retinitis pigmentosa.

Laboratory investigations revealed normal complete blood count, thyroid function tests, lipid, liver and renal profiles. Haemoglobin A1 c was 9. Whole Exome Sequencing (WES) analysis revealed a homozygous frame shift pathogenic varient in MYO 7A gene which is associated with autosomal recessive nonsyndromic deafness-2(DFNB 2) and Usher Syndrome type 2B.

3. Discussion

Usher Syndrome type 1 was suggested clinically. The child presented at a younger age with profound deafness and have severe balance and developmental delay. Visual changes as times go. The diagnosis was confirmed by Whole Exome Sequencing (WES) analysis genetic testing which revealed homozygous frame shift pathogenic varient in MYO 7A gene which is associated with autosomal recessive nonsyndromic deafness-2 (DFNB 2) i.e OMIM 600060 (and Usher Syndrome type 1 B (USH 1 B) i.e OMIM 276900. (1-9, 14-21)

Usher Syndrome is known to be associated with congenital hyperinsulinism. This was due to mutation A B C C 8 gene.(22,23) A homozygous A B C C 8 deletion is expected to result in a completly non functional beta-cell K (ATP) channel as in with SUR 1 knock out. (24-27)To date, review of the English literature, failed to show any report of diabetes either type 1 or type 2. Further studies arr needed. Possible association between Usher Synsrome and type 1 diabetes mellitus (DM). Type 1 diabetes mellitus, also known as juvenile diabetes, is an autoimmune disease which might lead to destruction of beta cells and hence insulin deficiency.

4. Conclusion

In conclusion, whole exome sequencing (WES) analysis could be used as o powerful tool in diagnosis of Usher Syndrome. Further, gene characterization and mutation in the child and family are needed for better understanding the pathophysiology.

Compliance with ethical standards

Acknowledgments

The authors would like to thank Dr. Abdulrahman NA Al Jurayyan, Resident in radiology, and Mr. Ibrahim NA AlJurayyan, Medical student, for their help and assistance in preparing this manuscript.

Disclosure of conflict of interest

The authors have no conflicts of interest to declare.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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