Research Paper

Genetic Assessment of Mucopolysaccharidosis Type IV and the First Pathological Mutation of c.313A>G in the Iranian Population

Seyed Mehdi Shafaat[1], Mehrdad Hashemi[2], Ahmad Majd[1], Maryam Abiri[3], *Sirous Zeinali[4,5]

1. Department of Biology, Islamic Azad University, North Tehran Branch, Tehran, Iran.
2. Department of Molecular Genetics, Islamic Azad University, Tehran Medical Branch, Tehran, Iran.
3. Department of Genetics and Molecular Biology, Iran University of Medical Sciences, Tehran, Iran.
4. Department of Molecular Medical, Biotechnology Research Center, Pasteur Institute of Iran, Tehran, Iran.

Use your device to scan and read the article online

Citation Shafaat S, Hashemi M, Majd A, Abiri M, Zeinali S. [Genetic Assessment of Two Iranian Patients With Mucopolysaccharidosis Type IV (Morquio syndrome) Using Next Generation Sequencing Technique and Observing the Pathological Mutation of c.313A>G for the First Time in the Iranian Population (Persian)]. Quarterly of "The Horizon of Medical Sciences". 2020; 26(2):182-191. https://doi.org/10.32598/hms.26.2.3275.1

https://doi.org/10.32598/hms.26.2.3275.1

Received: 20 Oct 2019
Accepted: 27 Nov 2019
Available Online: 01 Apr 2020

Key words:
Mucopolysaccharidosis, MPS, Morquio a Syndrome, NGS

ABSTRACT

Aims Morquio syndrome is a mucopolysaccharidosis (type 4) that has autosomal recessive inheritance. Moreover, it is caused by defects in the two genes; GALNS (Murcio A) and GLB1 (Murcio B). The prevalence rate of this condition is estimated to be about 1 per 200000 live births globally. Besides, Middle Eastern cases shape the greatest ratio, due to higher rates of consanguineous marriages. The most frequent clinical manifestations of the disease include skeletal abnormalities, hearing and vision problems, decreased physical growth, and cardiac malformations.

Methods & Materials This study investigated the pathogenic mutations in two Iranian individuals. Both cases were the result of consanguineous marriages with mucopolysaccharidosis type 4 (A or B types, each). Following of genomic DNA extraction, Whole Exome Sequencing was conducted for the study patients. Then, for the validation of observed pathogenic mutations, sanger sequencing was performed for the patients.

Findings Two explored patients demonstrated homozygote mutations. Mutation analysis of the GLB1 gene revealed c.443G>A mutation in one patient and GALNS gene c.313A>G in the other.

Conclusion Two pathogenic mutations in GLB1 and GALNS gene were found in 2 Iranian patients in this study. The NGS was a desirable and reliable technique for detecting these two mutations. The c.313A> G mutation in the GALNS gene was novel and had not been reported in the world.

Extended Abstract

1. Introduction

This case report article presented two patients with the same genetic disease. In both cases, the genetic mutation causing the disease was detected. Besides, for the first time in the world, a new mutation was observed.

Wang et al. (2010) studied 24 Chinese patients with Morquio A Syndrome (MPS IVA). They observed 27 pathogenic mutations in the GALNS gene of these patients; of which, 16 mutations were reported prior to their study. Approximately 63% of the mutations they observed in these

* *Corresponding Author:*
Sirous Zeinali, PhD.
Address: Molecular Medical Department, Biotechnology Research Center, Pasteur Institute of Iran, Tehran, Iran.
Tel: +98 (912) 1372040
E-mail: zeinali@kawsar.ir

patients were not detected elswewehre, globally. Their prediction was that some of these mutations may be specific to this population. The G340D mutation was the most common type in this population [1]. Caciotti A et al. genetically analyzed 21 MPS patients, and 4 of whom presented Morquio B syndrome. As a result of determining the GLB1 gene sequence in these 4 patients, c.443G>A mutation was observed in one of the patients for the first time [2]. The current study aimed to find the mutations that caused Morquio syndrome in two Iranian children.

2. Materials and Methods

The present study investigated two patients with Morquio syndrome. Moreover, both patinets were from consanguineous marriage and referred to Dr. Zinley's medical genetics laboratory through their specialist physician. The required blood samples were obtained from the study patients and their parents. The materials used in this project included DNA extraction kit, PCR kit, the kit required to determine the product sequence of PCRs, NGS device and its accessories, sampler, microtube, and sampler tip.

3. Results

In both patients, the disease-causing mutation was observed in the form of homozygote. One of the patients developed c.443G>A mutation in exon 4 of the GLB1 gene. Besides, the other patient generated c.313A>G mutation in exon 3 of the GALNS gene (Table 1).

4. Discussion

One of the mutations had already been reported in other studies; however, the other mutation was first reported in this study. To obtain expand the achieved results and mutations data in relation to this genetic disease, it is necessary to investigated larger sample sizes. Accordingly, the number of unreported genetic mutations could be observed in the Iranian population. A study limitation was the lack of funding for conducting the genetic research.

5. Conclusion

According to the literature on various types of mucopolysaccharidosis, we hope that the present study results be of great help in diagnosing prenatal disease of type 4 mucopolysaccharidosis. A new unreported mutation has been observed in this study for the first time; thus, it is suggested that a larger statistical population of Iranian patients with mucopolysaccharidosis be genetically studied. Such explorations could provide a more comprehensive report of pathogenic mutations in these patients.

Ethical Considerations

Compliance with ethical guidelines

The present study has been approved by the Ethics Committee of Kowsar Human Genetics Research Center under the attached form No. 98/6299.

Table 1. Types of MPS Disease With the Names of the Enzyme, Related Gene, Type of Inheritance, and Type of Increased GAG

Disease Type	Enzymatic Defects (genes)	Inheritance	Increased GAG
MPS I Horner's syndrome	α-L-iduronidase (IDUA)	Autosomal recessive	HS & DS
MPS II Hunter syndrome	Iduronate Sulfatase (IDS)	Dependent on the recessive sex	HS & DS
MPS III (A-D) San Filippo syndrome	A: Heparan sulfamidase (SGSH) B: N-acetylglucosaminidase (NAGLU) C: Heparan-α-glucosaminide N-acetyltransferase (HGSNAT) D: N-acetylglucosamine 6-sulfatase (GNS)	Autosomal recessive	HS
MPS IV (A and B) Morquio syndrome	A: galatosamine-6-sulfatase (GALNS) B: β-galactosidase (GLB1)	Autosomal recessive	A: CS and KS B: KS
MPS VI Maroteaux-Lamy syndrome	Arylsulfatase B (ARSB)	Autosomal recessive	DS
MPS VII Sly syndrome	B-glucuronidase (GUSB)	Autosomal recessive	HS, DS, and CS
MPS IX Natowicz syndrome	Hyaluronidase (HYAL1)	Autosomal recessive	HA

Funding

This study has been extracted from the PhD. thesis of Seyed Mehdi Shafaat in the field of Biology, Molecular Genetics, Islamic Azad University, Tehran North Branch.

Authors' contributions

All authors contributed in designing, running, and writing all parts of the research.

Conflicts of interest

According to the authors, there is no conflicts of interest in this article.

Acknowledgements

We would like to thank all the colleagues of Kowsar Human Genetics Research Center who contributed to this research project.