ISSN 2307-8960 (online)

World Journal of *Clinical Cases*

World J Clin Cases 2021 October 16; 9(29): 8627-8952

Published by Baishideng Publishing Group Inc

World Journal of Clinical Cases

Contents

Thrice Monthly Volume 9 Number 29 October 16, 2021

REVIEW

MINIREVIEWS

ORIGINAL ARTICLE

Clinical and Translational Research

Retrospective Study

World Journal of Clinical Cases

Thrice Monthly Volume 9 Number 29 October 16, 2021

Contents

World Journal of Clinical Cases

Thrice Monthly Volume 9 Number 29 October 16, 2021

Contents

World Journal of Clinical Cases

Thrice Monthly Volume 9 Number 29 October 16, 2021

Contents

ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Jiiang-Huei Jeng, DDS, PhD, Professor, School of Dentistry and Department of Dentistry, National Taiwan University Medical College and National Taiwan University Hospital, School of Dentistry, College of Dental Medicine, Kaohsiung Medical University, Taipei 100, Taiwan. jhjeng@ntu.edu.tw

AIMS AND SCOPE

The primary aim of *World Journal of Clinical Cases* (*WJCC*, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

INDEXING/ABSTRACTING

The *WJCC* is now indexed in Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, PubMed, and PubMed Central. The 2021 Edition of Journal Citation Reports® cites the 2020 impact factor (IF) for *WJCC* as 1.337; IF without journal self cites: 1.301; 5-year IF: 1.742; Journal Citation Indicator: 0.33; Ranking: 119 among 169 journals in medicine, general and internal; and Quartile category: Q3. The *WJCC*'s CiteScore for 2020 is 0.8 and Scopus CiteScore rank 2020: General Medicine is 493/793.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Jia-Hui Li*; **Production Department Director:** *Xiang Li*; **Editorial Office Director:** *Jin-Lei Wang*.

NAME OF JOURNAL
World Journal of Clinical Cases

ISSN
ISSN 2307-8960 (online)

LAUNCH DATE
April 16, 2013

FREQUENCY
Thrice Monthly

EDITORS-IN-CHIEF
Dennis A Bloomfield, Sandro Vento, Bao-Gan Peng

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/2307-8960/editorialboard.htm

PUBLICATION DATE
October 16, 2021

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

World Journal of Clinical Cases

Submit a Manuscript: https://www.f6publishing.com

World J Clin Cases 2021 October 16; 9(29): 8797-8803

DOI: 10.12998/wjcc.v9.i29.8797

ISSN 2307-8960 (online)

CASE REPORT

Whole-genome amplification/preimplantation genetic testing for propionic acidemia of successful pregnancy in an obligate carrier Mexican couple: A case report

Adina Neumann, Miguel Angel Alcantara-Ortigoza, Ariadna González-del Angel, Nestor Alejandro Zarate Díaz, Javier Sam Santana, Leonardo M Porchia, Esther López-Bayghen

ORCID number: Adina Neumann 0000-0002-2563-8540; Miguel Angel Alcantara-Ortigoza 0000-0003-0592-8214; Ariadna González-del Angel 0000-0002-7096-0969; Nestor Alejandro Zarate Díaz 0000-0002-1904-4738; Javier Sam Santana 0000-0003-4038-3125; Leonardo M Porchia 0000-0002-4082-7606; Esther López-Bayghen 0000-0002-2849-7587.

Author contributions: The project was conceived by Neumann A and López-Bayghen E; Data acquisition was performed by Neumann A, González-del Angel A, Alcantara-Ortigoza MA, Santana JS and Zarate Díaz NA, where González-del Angel A and Alcantara-Ortigoza MA assessed genetic data, sequencing, and alignments, Neumann A collected genomic data, Santana JS and Zarate Díaz NA were handling the case as the embryologist and clinician, respectively, collecting information regarding the parental history and IVF data; data analysis and interpretation were performed by Neumann A, González-del Angel A, and Alcantara-Ortigoza MA; Neumann A, Zarate Díaz NA, Porchia LM, and López-Bayghen E drafted the article and critically revised it; all authors have approved the final version of the

Adina Neumann, Laboratorio de Investigación y Diagnóstico Molecular, Ingenes, Mexico City 05320, Mexico

Miguel Angel Alcantara-Ortigoza, Ariadna González-del Angel, Laboratorio de Biología Molecular, Subdirección de Investigación Médica, Instituto Nacional de Pediatría, Mexico City 04530, Mexico

Miguel Angel Alcantara-Ortigoza, Ariadna González-del Angel, DNA-GEN S.C. Centro de Alta Especialidad en Genética Humana, Mexico City 14070, Mexico

Nestor Alejandro Zarate Díaz, Javier Sam Santana, Investigación Clínica, Ingenes, Puebla 72820, Mexico

Leonardo M Porchia, Esther López-Bayghen, Departamento de Toxicología, Centro de Investigación y de Estudios Avanzados del Instituto Politécnico Nacional, Mexico City 07360, Mexico

Corresponding author: Esther López-Bayghen, PhD, Professor, Departamento de Toxicología, Centro de Investigación y de Estudios Avanzados del Instituto Politécnico Nacional, Avenida Instituto Politécnico Nacional 2508, San Pedro Zacatenco, Mexico City 07360, Mexico. ebayghen@cinvestav.mx

Abstract

BACKGROUND

Identifying a potential single monogenetic disorder in healthy couples is costly due to the Assisted Reproduction facilities' current methodology for screening, which focuses on the detecting multiple genetic disorders at once. Here, we report the successful application of a low-cost and fast preimplantation genetic testing for monogenic/single gene defects (PGT-M) approach for detecting propionic acidemia (PA) in embryos obtained from a confirmed heterozygous propionyl-CoA carboxylase alpha subunit (*PCCA*) couple.

CASE SUMMARY

A fertile 32-years old Mexican couple with denied consanguinity sought antenatal genetic counseling. They were suspected obligate PA carriers due to a previous deceased PA male newborn with an unknown *PCCA*/propionyl-CoA carboxylase

manuscript.

Informed consent statement: Both patients provided written informed consent to participate in this study, in accordance with the Declaration of Helsinki. Written informed consent was obtained from the patient(s) for their anonymized information to be published in this article.

Conflict-of-interest statement: The authors have no relevant financial or non-financial interests to disclose.

CARE Checklist (2016) statement: The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

Manuscript source: Unsolicited manuscript

Specialty type: Reproductive biology

Country/Territory of origin: Mexico

Peer-review report's scientific quality classification

Grade A (Excellent): A
Grade B (Very good): 0
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

Received: December 16, 2020
Peer-review started: December 16, 2020
First decision: July 16, 2021
Revised: July 28, 2020

beta subunit (*PCCB*) genotype. Next-Generation Sequencing revealed a heterozygous genotype for a pathogenic *PCCA* variant (c.2041-1G>T, ClinVar:RCV-000802701.1; dbSNP:rs1367867218) in both parents. The couple requested *in vitro* fertilization (IVF) and PGT-M for PA. From IVF, 12 oocytes were collected and fertilized, of which two resulted in high-quality embryos. Trophectoderm biopsies and Whole Genome Amplification by a fragmentation/amplification-based method were performed and revealed that the two embryos were euploid. End-point polymerase chain reaction and further Sanger sequencing of the exon-intron borders revealed a wild-type *PCCA* male embryo and a heterozygous c.2041-1G>T female embryo. Both embryos were transferred, resulting in a clinical pregnancy and the delivery of a healthy male newborn (38 wk, weight: 4080 g, length: 49 cm, APGAR 9/9). The absence of PA was confirmed by expanded newborn screening.

CONCLUSION

We show that using PGT-M with Whole Genome Amplification templates, coupled with IVF, can reduce the transmission of a pathogenic variant of the *PCCA* gene.

Key Words: Propionic acidemia; Autosomal recessive; Propionyl-CoA carboxylase alpha subunit (*PCCA*) gene; Preimplantation genetic testing; Next-generation sequencing; Embryo transfer

Core Tip: Propionic acidemia is an uncommon monogenetic disorder resulting in inherited severe complications and death. A heterozygous genotype for a pathogenic variant of the propionyl-Coenzyme A carboxylase alpha subunit gene (*PCCA*) was located in a fertile Mexican couple. Here we show that a couple can reduce the transmission of a pathogenic variant of a gene using *in vitro* fertilization, genetic counseling, and sequencing of a whole genome amplification template. Furthermore, after embryo transfer, we report the delivery of a healthy male newborn without propionic acidemia.

Citation: Neumann A, Alcantara-Ortigoza MA, González-del Angel A, Zarate Díaz NA, Santana JS, Porchia LM, López-Bayghen E. Whole-genome amplification/preimplantation genetic testing for propionic acidemia of successful pregnancy in an obligate carrier Mexican couple: A case report. *World J Clin Cases* 2021; 9(29): 8797-8803
URL: https://www.wjgnet.com/2307-8960/full/v9/i29/8797.htm
DOI: https://dx.doi.org/10.12998/wjcc.v9.i29.8797

INTRODUCTION

For fertile, healthy couples, the diagnosis of genetic disorders occurs postnatally when the disease's characteristics are present. However, for genetic disorders in which the fetus suffers from a detrimental illness, the probability of conceiving and delivering a healthy newborn decrease dramatically. Therefore, many at-risk couples attend Assisted Reproduction facilities for Preimplantation Genetic Testing for Monogenic/single gene defects (PGT-M). However, the cost associated with PGT-M, which includes the assessment of over 200 genetic disorders, can be expensive and, for some patients, preventative. Therefore, there is a need for alternative methods when the cost is an issue or the disorder is not covered under standard PGT-M. Propionic acidemia (PA, MIM#606054) is an autosomal recessive, life-threatening metabolic disorder caused by a deficiency in the mitochondrial enzyme propionyl-CoA carboxylase (PCC). PCC carboxylates propionyl-CoA to methylmalonyl-CoA and reduced/abolished PCC activity results in elevated blood concentrations of levocarnitine ester of propionyl-CoA[1]. PCC is composed of alpha and beta subunits encoded by the *PCCA* (13q32.3, MIM*232000) and *PCCB* (3q22.3, MIM*232050) genes,

Accepted: September 7, 2021
Article in press: September 7, 2021
Published online: October 16, 2021

P-Reviewer: Kim HS
S-Editor: Zhang H
L-Editor: A
P-Editor: Li JH

respectively[1]. Shortly after birth, approximately 65% of all PA patients present with symptoms, such as vomiting, lethargy, refuse feeding, hypotonia, and other clinical data[2]. If not treated, PA may progress to a severe illness with neurologic, cardiologic, hematologic, hepatic, and pancreatic complications or death[1,2]. Since 80% of all PA cases worldwide are caused by a single-nucleotide or other small pathogenic changes, which results in loss of PCC activity[1,2], suspected carriers of *PCCA* or *PCCB* pathogenic genetic variants would benefit from PGT-M. Here, we report the successful application of a low-cost and fast PGT-M approach for PA in embryos obtained from a confirmed heterozygous *PCCA* couple, which resulted in a clinical pregnancy and delivery of a healthy newborn male.

CASE PRESENTATION

Chief complaints

A 32-years old healthy Mexican couple with denied consanguinity sought antenatal genetic counseling, after giving birth to PA male.

History of present illness

They were suspected of being obligate PA carriers due to a previous full-term delivered male (3200 g), who passed one month after birth and presented with PA's classical clinical profile. Diagnosis of PA in the deceased newborn was biochemically suspected through an acylcarnitine profile during newborn screening (elevated serum propionyl carnitine) and further confirmed by elevated urine organic acids concentrations (methyl citrate, 3-hydroxypropionate, 2-hydroxyisovaleric, 3-hydroxybutyric, 3-hydroxy propionic).

History of past illness

No significant past medical history associated with PA.

Personal and family history

Both parents originated from different states in Mexico. Moreover, they indicated no knowledge of any family history of PA.

Physical examination

Neither parent presented with any symptoms or risk factors for being a PA carrier.

Laboratory examinations

Due to a lack of any previous complication of either parent with respect to reproductive health or otherwise, no laboratory examinations were performed.

Imaging examinations

No imaging studies were performed.

PATHOLOGICAL EXAMINATION

Since the pathogenic PA genotype could not be confirmed for the deceased newborn, both parents were subjected to next-generation sequencing (NGS) for the *PCCA* and *PCCB* genes. Quality of the parental genomic DNA, obtained from peripheral blood samples, was evaluated using the Qubit™ Flex Fluorometer (Life Technologies, Singapore). Targets were captured by hybridization to create libraries through Nextera Rapid Capture Exome (Illumina Inc., San Diego, CA, United States) and then sequenced on an Illumina HiSeq2000 2 × 150 platform (San Diego, CA, United States). The bioinformatics pipeline included an overall quality evaluation of the raw output reads with FastQC v0.11.8, trimming of adapters and filtering of low-quality reads using Trimmomatic v0.35, alignment of the filtered reads against the GRCh38 human reference sequence using the Bowtie2 software v2.3.4.1, and calling and annotation of single nucleotide variations and detection of small insertion-deletion with the GATK and snpEff programs, respectively. Only one clinically relevant *PCCA* gene variant was confirmed by unidirectional Sanger sequencing of an end-point polymerase chain reaction (PCR)-derived 250 bp fragment containing exon 23 of the *PCCA* gene (Figure 1A). Annotation was carried out using the Alamut Visual 2.14 software

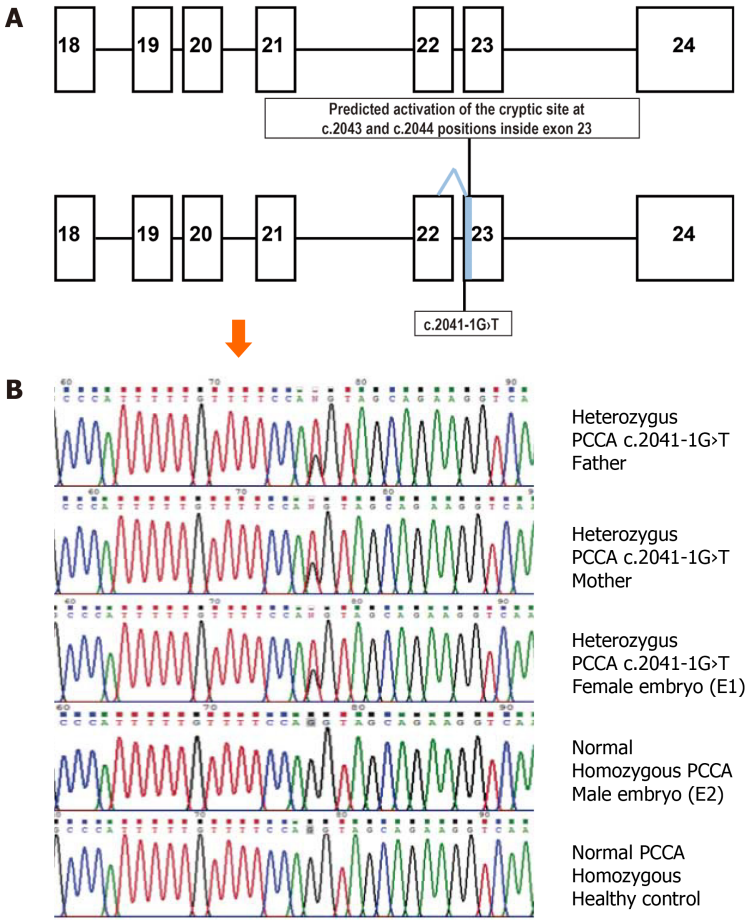

Figure 1 Propionyl-CoA carboxylase alpha subunit (*PCCA*) gene variant in the present family. A: Schematic representation of the intron 22-exon 23 boundary of the *PCCA* gene and the predicted *in silico* generation of a possible cryptic acceptor site; B: Partial electropherograms (only forward strands are shown) of the intron 22-exon 23 region of the *PCCA* gene (NG_008768.1 and NM_000282.3) in both parents and embryo E1 demonstrated a heterozygous genotype for the likely pathogenic variant c.2041-1G>T. The G-to-T transversion predicts an abolished splicing acceptor site in the *PCCA* intron 22. A wild-type *PCCA* genotype was noted for embryo E2 as well as in the healthy control included in the analysis. Sanger sequencing was performed, in triplicate, for the PGT-M assays.

(SOPHIA GENETICS, Lausanne, Switzerland).

FINAL DIAGNOSIS

Both parents were found to be asymptomatic heterozygotes for the same pathogenic *PCCA* gene variant (Figure 1B), c.2041-1G>T (NM_000282.4; ClinVar:RCV000802701.1; dbSNP:rs1367867218). According to the *in silico* evaluation by the Splice Site Finder-like, MaxEntScan, NNSPLICE, and GeneSplicer programs, including the Splicing Prediction Module of Alamut Visual 2.14 software, this variant eliminates the natural acceptor splicing site of intron 22 and possible activation of a cryptic acceptor splicing site inside of exon 23 (positions c.2043 and c.2044; Figure 1A).

TREATMENT

After the *PCCA* genotype characterization and post-genetic testing counseling, both parents requested PGT-M for PA, along with PGT for aneuploidies (PGT-A). A single *in vitro* fertilization (IVF) cycle, embryo biopsy, and PGT were performed according to the standard protocols of the Ingenes Institute, as previously described[3,4]. The mother underwent one standard course of controlled ovarian stimulation with 1650 UI of Gonal (FSH, Merck, Darmstadt, Germany) and 375 UI of Merapur (Hmg Ferring Laboratories, Saint-Prex, Switzerland). After 36 h, 12 oocytes (10 were in Metaphase II) were retrieved with ultrasound guidance and were fertilized by intracytoplasmic sperm injection. Only morphologically optimal embryos were considered for PGT,

using the Istanbul Consensus Workshop Criteria on Embryo Assessment[3].

During day 5 of embryonic development, two embryos were determined to be of high-quality and were biopsied. Using micromanipulation, 4-7 cells from the trophectoderm were isolated and placed into a 0.2 mL PCR tube. Afterward, the embryos were cryopreserved using the vitrification technique[4]. The biopsies were subjected to Whole Genome Amplification (WGA, according to the manufacturer's protocol) using the SurePlex DNA Amplification System (Illumina Inc., San Diego, CA, United States). NGS (Veri-seq PGS Library Prep kit, Illumina Inc., San Diego, CA, United States) was performed and embryo ploidy assessment was obtained[4]. To determine the embryos' *PCCA* genotype, in triplicate, WGA-DNA samples were subjected to PCR amplification and Sanger sequencing assays, as previously employed for both parents. Samples from healthy adults and blank controls were included in all PCR and Sanger assays. The two embryos obtained were found to have a normal chromosome composition by PGT-A and were characterized as euploid. For PGT-M for PA, the first embryo (E1), which had a normal XX sex chromosome composition, was heterozygous for the pathogenic *PCCA* variant (NG_008768.1(NM_000282.3): c.2041-1G>T) and was diagnosed as a non-affected female PA carrier (Figure 1B). The second embryo (E2), which had a normal XY sex chromosome composition, was wild-type for the *PCCA* gene and was diagnosed as a non-affected male (Figure 1B). Both embryos were determined to be acceptable for transferred, after both parents agreed. The embryo implantation protocol consisted of endometrial preparation with Evorel 50 and Gonapeptil depot (Ferring Laboratories, Saint-Prex, Switzerland). Luteal phase support was carried out with Utrogestan (300 mg/day/vaginal).

OUTCOME AND FOLLOW-UP

Fourteen days after transfer, β-hCG serum levels were 168.0 mUI/mL, confirming a positive pregnancy. After 16 wk, an ultrasound exhibited a single gestational sac. The couple declined to confirm the *PCCA* genotype of the fetus by invasive diagnostic testing. Duo test was performed during week 11-13, which indicated a low risk of chromosomopathy during the 1st trimester. Also, a TORCH screen was performed, which was negative. Structural ultrasound and five following consultations showed that the baby was healthy throughout the pregnancy. A healthy newborn male was delivered after 38 wk of pregnancy (weight: 4080 g, length: 49 cm, APGAR 9/9). The newborn's metabolic screening demonstrated a normal acylcarnitine profile. Moreover, none of the typical symptoms for PA were noted in the subsequent days after birth. When this article was submitted, the child was four months of age and has not presented with any symptoms of PA.

DISCUSSION

Here, we report a couple that underwent preconception counseling, pre- and post-genetic testing counseling, subjected to IVF and PGT-M to avoid the high probability of bearing an affected PA offspring. The preventive reproductive approach was successful and the couple was able to conceive a healthy newborn. As reported with other potentially fatal organic acidemias, the poor clinical prognosis of PA justifies providing preconception genetic counseling and preventive reproductive options, like PGT-M, to at-risk couples[5]. Monogenic disorders have been estimated to occur in about 0.36% of births[6]. These Mendelian diseases can be identified in embryos belonging to at-risk couples through PGT. At present, different technologies are available to directly search for specific mutations for a highly accurate genetic diagnosis of potential embryos. PGT-M has been performed with sequencing verification for 234 pathogenic genetic variants; however, this approach increases the cost and time to complete. As pointed out before, NGS strategies applied to PGT-M allow identifying pathogenic variants located across the genome, including those responsible for "rare disorders", like organic acidemias[5]. However, this approach is an expensive and time-consuming testing that does not appear to be an affordable option for couples where a specific pathogenic genotype has been previously identified. Therefore, the most straightforward approach is to perform PGT-M to identify the pathogenic genotype from IVF-generated euploid embryos[4]. Indeed, here, our technique presents as an alternative to prenatal diagnosis and avoids termination of a pregnancy in the case of a compromised fetus. Moreover, the cost associated with the methodology presented here can significantly reduce the patient's

expenses, making the test accessible.

With embryo biopsies, a significant problem during analysis can arise if there is inadequate DNA or its concentration is very low. The signal can be improved by performing WGA. We have previously shown that using WGA-DNA, obtained by the fragmentation/amplification-based method, yields a suitable DNA template for the generation of small PCR fragments (250 bp aprox). Those fragments are successfully sequenced by the simple automated Sanger method to rapidly determine a specific embryo genotype for a single nucleotide change or other small pathogenic variants[4]. However, such assays must consider a false positive possibility due to the allele drop-out phenomena. As also noted in the recently reported PGT-M procedure performed with the WGA-DNA template obtained by isothermal genome amplification[4], in our triplicate Sanger sequencing assay, we were unable to document the allele drop-out phenomena. It would be necessary to carry out further validation studies to quantify the possibility of allelic amplification imbalances when PGT-M is based on WGA-DNA obtained by a fragmentation/amplification-based method.

The birth prevalence of PA across Asia-Pacific, Europe, and North America is 0.29, 0.33, and 0.33 per 100000 newborns, respectively[7], however, it is still unknown in Mexico. This disorder appears to be very rare for the Mexican population, as determined by at least two expanded neonatal screening reports applying an acylcarnitine profile[8.9], even though PA comprises around 7% of all detected inborn errors of intermediary metabolism in Mexican patients[10]. To date, in the Human Gene Mutation Database (http://www.hgmd.cf.ac.uk/), there are around 25 splicing defects responsible for PA. To the best of our knowledge, the c.2041-1G>T variant has not been reported in the literature as associated with PA. However, according to the gnomAD database, it is listed as an extremely infrequent allele, with only single heterozygous individuals identified in the Latino population (allele frequency 0.00002891). This feature contrasts with the consanguinity antecedent denied by the couple. Interestingly, both parents are of Mexican origin. However, they come from different states in Mexico, supporting the state of no endogamy in the couple.

Recently, the c.2041-1G>T variant has been reported in the ClinVar database as a likely pathogenic variant (RCV000802701.1), as it predicts to nullify the recognition of the natural acceptor splice site of *PCCA* intron 22. Another pathogenic variant, c.2041-2A>G, affects the same acceptor splicing site, conditioning exon 23 skipping in the mRNA but leads to a relatively mild PA phenotype with high residual PCC activity in fibroblasts. This is attributed to generating a small amount of normally spliced transcripts[11]. If the c.2041-1G>T variant also leads to exon 23 skipping, the resulting protein will lose a biotin-binding motif, leading to a non-functional PCC enzyme[11]. Possible residual exon 23 retention and the activation of the in silico predicted out-of-frame cryptic acceptor splice site inside exon 23 must be confirmed by further experimental assays to define the precise pathogenic effect of c.2041-1G>T and its possible genotype-phenotype correlation.

CONCLUSION

Here, we report the c.2041-1G>T variant of the *PCCA* gene classified as likely pathogenic and is associated with PA. Moreover, we show that using PGT-M coupled with IVF could be applied to avoid the transmission of PA in patients' descendances, which should decrease the potential of an unsuccessful pregnancy and increase the possibility of delivering a healthy baby. Lastly, we demonstrate the feasibility of using WGA-DNA templates for a low-cost, rapid, and accurate PGT-M for life-threatening disorders, like PA.

ACKNOWLEDGEMENTS

We are grateful to the participants of the study and to Ing. Lucero Cervantes Pozos for her editorial assistance. We also thank the technical support of Semper Genomics SA de CV.

REFERENCES

1 **Wongkittichote P**, Ah Mew N, Chapman KA. Propionyl-CoA carboxylase - A review. *Mol Genet*

Metab 2017; **122**: 145-152 [PMID: 29033250 DOI: 10.1016/j.ymgme.2017.10.002]
2 **Pena L**, Franks J, Chapman KA, Gropman A, Ah Mew N, Chakrapani A, Island E, MacLeod E, Matern D, Smith B, Stagni K, Sutton VR, Ueda K, Urv T, Venditti C, Enns GM, Summar ML. Natural history of propionic acidemia. *Mol Genet Metab* 2012; **105**: 5-9 [PMID: 21986446 DOI: 10.1016/j.ymgme.2011.09.022]
3 **Alpha Scientists in Reproductive Medicine and ESHRE Special Interest Group of Embryology**. The Istanbul consensus workshop on embryo assessment: proceedings of an expert meeting. *Hum Reprod* 2011; **26**: 1270-1283 [PMID: 21502182 DOI: 10.1093/humrep/der037]
4 **Neumann A**, Alcántara-Ortigoza MÁ, González-Del Ángel A, Camargo-Diaz F, López-Bayghen E. Diagnosis of Laron syndrome using monoplex-polymerase chain reaction technology with a whole-genome amplification template: A case report. *World J Clin Cases* 2019; **7**: 4029-4035 [PMID: 31832405 DOI: 10.12998/wjcc.v7.i23.4029]
5 **Habibzadeh P**, Tabatabaei Z, Farazi Fard MA, Jamali L, Hafizi A, Nikuei P, Salarian L, Nasr Esfahani MH, Anvar Z, Faghihi MA. Pre-implantation genetic diagnosis in an Iranian family with a novel mutation in MUT gene. *BMC Med Genet* 2020; **21**: 22 [PMID: 32013889 DOI: 10.1186/s12881-020-0959-8]
6 **Verma IC**, Puri RD. Global burden of genetic disease and the role of genetic screening. *Semin Fetal Neonatal Med* 2015; **20**: 354-363 [PMID: 26251359 DOI: 10.1016/j.siny.2015.07.002]
7 **Almási T**, Guey LT, Lukacs C, Csetneki K, Vokó Z, Zelei T. Systematic literature review and meta-analysis on the epidemiology of propionic acidemia. *Orphanet J Rare Dis* 2019; **14**: 40 [PMID: 30760309 DOI: 10.1186/s13023-018-0987-z]
8 **Torres-Sepúlveda Mdel R**, Martínez-de Villarreal LE, Esmer C, González-Alanís R, Ruiz-Herrera C, Sánchez-Peña A, Mendoza-Cruz JA, Villarreal-Pérez JZ. [Expand newborn screening using tandem mass spectrometry: two years' experience in Nuevo León, Mexico]. *Salud Publica Mex* 2008; **50**: 200-206 [PMID: 18516367 DOI: 10.1590/s0036-36342008000300003]
9 **Cantú-Reyna**, C, Zepeda, LM, Montemayor, R, Benavides, S, González, HJ, Vázquez-Cantú, M, Cruz-Camino, H. Incidence of inborn errors of metabolism by expanded newborn screening in a Mexican hospital. *J Inborn Errors Metab Screen* 2016; **4**: 1-8 [DOI: 10.1177/2326409816669027]
10 **Ibarra-González I**, Fernández-Lainez C, Belmont-Martínez L, Guillén-López S, Monroy-Santoyo S, Vela-Amieva M. [Characterization of inborn errors of intermediary metabolism in mexican patients]. *An Pediatr (Barc)* 2014; **80**: 310-316 [PMID: 24140120 DOI: 10.1016/j.anpedi.2013.09.003]
11 **Clavero S**, Pérez B, Rincón A, Ugarte M, Desviat LR. Qualitative and quantitative analysis of the effect of splicing mutations in propionic acidemia underlying non-severe phenotypes. *Hum Genet* 2004; **115**: 239-247 [PMID: 15235904 DOI: 10.1007/s00439-004-1147-1]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com