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Screening of gene detection of monogenic inherited disorder in an infertile population in Henan Province: an autosomal recessive disorder carried by maple syrup urine disease

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Key words: *monogenic inherited disorder; gene detection; maple syrup urine disease; infertile population; Henan Province*

Maple syrup urine disease (MSUD) is a rare autosomal recessive genetic disease with a low incidence. The incidence of this disease in newborns worldwide is approximately 1/185,000 [1].

A 27-year-old Chinese woman was presented in our hospital. The patient's husband was 27 years old. They had lived together for two years without pregnancy. The menstruation of this patient was irregular (4–5/30–45 days), with a moderate amount and mild dysmenorrhoea. Karyotype analysis revealed 46, XX in female; 46, XY, 22ps + in male. In April 2016, 18 eggs were obtained using a short-acting regimen. However, the quality of the embryos was poor. Two grade III embryos were transplanted in the fresh cycle, and one frozen blastocyst was used for clinical pregnancy. However, the foetus stopped development and labour was induced at the fifth month of pregnancy, and gene detection was not carried out. In 2018, a long-acting method was adopted to help the pregnancy in the follicular period. Hence, 13 eggs were obtained, two fresh cycles were transplanted, and one cleavage embryo and one blastocyst were frozen, without pregnancy. In July 2019, a long-acting method was applied again to help the pregnancy in our hospital. Hence, 12 eggs were obtained, but the quality of the embryos remained poor. One embryo of grade III did not lead to pregnancy. After obtaining informed consent, 110 kinds of monogenic inherited disorders were detected. The studies involving human participants were reviewed and approved by the Ethics Committee of the Second Affiliated Hospital of Zhengzhou University. Written informed consent was obtained from the participant for the publication of this case report (including all data and images).

After obtaining an informed consent from the patient, 3 mL of peripheral blood was collected, and an EDTA anticoagulant was used to prepare the genomic DNA for high-throughput sequencing analysis.

The DNA was extracted from the peripheral blood. First, the DNA sample of the patient was randomly interrupted to sequence the exons of the BCKDHA gene (9 exons), BCKDHB gene (10 exons), DBT gene (11 exons), DLD gene (14 exons), and the adjacent regions. After DNA amplification, high-throughput sequencing was directly performed. Then, the sequencing results were compared with the data of the BCKDHA gene (nm), BCKDHB gene (nm), DBT gene (nm), DLD gene (nm), SNP database, HapMap database, 1000 human genome database, and other public databases, in order to obtain the suspicious mutation sites.

Next, Sanger sequencing was performed to verify the DNA samples. Po1yPhen 2 software was used to predict the function of the missense mutation.

The results of high-throughput sequencing revealed that exon 6 of the BCKDHB gene has a deletion: exon 6: c.718delc, which was confirmed by the Sanger sequencing (Fig. 1).

MSUD is a metabolic disease caused by the lack of branched-chain α-ketoacid dehydrogenase (BCKD) complex, which belongs to autosomal recessive genetic disease [2]. More than 265 genes have been reported to cause BCKD complex enzyme mutations in the world [3]. Carrying out gene screenings for the infertile population would help to decrease the birth of children with specific genetic diseases and

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eliminate the related genetic risks for other members of the carrier's family.

Conflict of interests

The authors have no conflicts of interest to disclose.

Statements of ethics

The study was conducted ethically in accordance with the World Medical Association Declaration of Helsinki and was approved by Ethics Committee of the Second Affiliated Hospital of Zhengzhou University. Written informed consent was obtained from the participant for the publication of this case report (including all data and images).

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Competing interests

None declared.

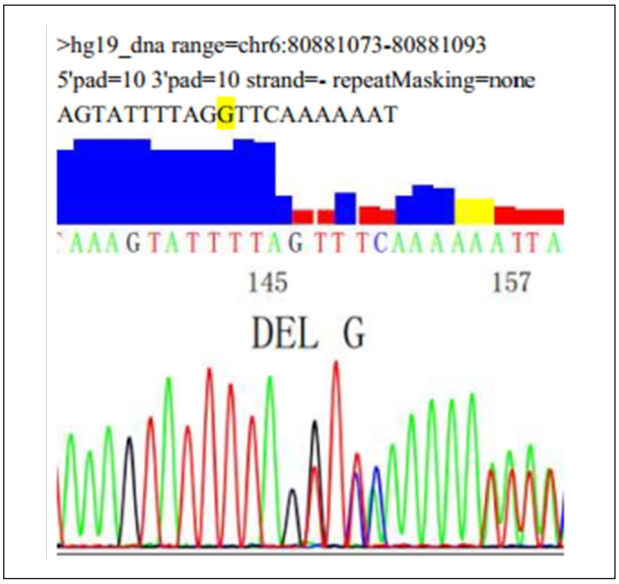

Figure 1. *High-throughput sequencing of BCKDHB gene*

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