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Abstract Topic: - Prenatal, perinatal and developmental genetics

Abstract Title: - Novel homozygous non-synonymous mutations in NEB and a hemizygous mutation in OFD1 identified in an aborted fetus from a family with a history of miscarriages

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Aims: - To diagnose the genetic basis of fetal loss by clinical exome sequencing and offer genetic counselling based on the findings.

Methods: - Genomic DNA was extracted from aborted fetus tissue, peripheral blood leukocytes of the couple, siblings, and the couple's parents. Trio-clinical whole-exome sequencing was performed for the fetus and the parents. The identified genetic mutations in NEB, OFD1, and SLCO2A1 were confirmed by Sanger sequencing.

Results: - Clinical whole exome sequencing identified mutations in NEB, OFD1, and SLCO2A1 genes. We identified a homozygous non-synonymous mutation in exon 6 (c.367C>T; p.Arg123Cys) and 133 (c.20279A>G; p.Asp6760Gly) of the NEB gene in the fetus but the consanguineous couple were heterozygous for the same. We also identified a non-synonymous hemizygous mutation in exon 10 of the X-linked gene OFD1 (c.1035G>T; p.Lys345Asn) in the fetus however, the father was negative while the mother showed heterozygosity for this mutation. Besides, we found a non-synonymous homozygous mutation in exon 8 of the SLCO2A1 gene (c.1105G>T; p.Gly369Cys) and the couple showed heterozygous mutation. Sequencing analysis further revealed that the mutations were inherited from the couple's parents.

Conclusions: - Our study elucidated the genetics behind the miscarriage and aided the couple in deciding the best course of action for a successful full-term pregnancy.

Keywords: - Clinical whole exome sequencing identified mutations in NEB, OFD1, and SLCO2A1 genes. We identified a homozygous non-synonymous mutation in exon 6 (c.367C>T; p.Arg123Cys) and 133 (c.20279A>G; p.Asp6760Gly) of the NEB gene in the fetus but the consanguineous couple were heterozygous for the same. We also identified a non-synonymous hemizygous mutation in exon 10 of the X-linked gene OFD1 (c.1035G>T; p.Lys345Asn) in the fetus however, the father was negative while the mother showed heterozygosity for this mutation. Besides, we found a non-synonymous homozygous mutation in exon 8 of the SLCO2A1 gene (c.1105G>T; p.Gly369Cys) and the couple showed heterozygous

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