P-45 Pre-implantation genetic diagnosis (PGD) for genetic disorders in Saudi Arabia

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Saudi Arabian culture is highly consanguineous, with first-cousin marriages accounting for 60–70% of all marriages. The list of conditions for which PGD was performed is being extended rapidly. Single-gene disorders are a major health concern in the developing world including Saudi Arabia.
Given the difficulties in management of genetic disorders, reproductive options for families affected with genetic diseases in Saudi Arabia are often limited to PGD which is permissible under the law and religion whereas prenatal diagnosis with the intent of termination of pregnancy is neither widely practiced nor socially accepted, although it is accepted under certain conditions.
KFSH&RC has been offering PGD for monogenic and chromosomal disorders, since 2001. Over 300 pregnancies initiated for over 200 genetics disorders with a success rate of more than 90%.
In all these families PGD was undertaken using Whole Genome Amplification (WGA) which can be performed on a single cell. WGA is providing new opportunities in single-cell diagnosis like preimplantation genetic haplotyping (PGH) and microarray. The methods are so swift that chosen embryos can be replaced within the day, or cryopreserved for transfer in a later menstrual cycle if the parents so desire. A singleton pregnancy was achieved after transfer of one normal and one heterozygous embryo. Prenatal diagnosis by CVS confirmed a normal pregnancy.
Although there is no single ethical issue that unifies the field of genetics and PGD, informed consent, confidentiality and the potential for social harm and psychological distress are issues that physicians involved with testing should understand.

P-46 Preimplantation genetic diagnosis for glutaric aciduria type II

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Objectives: Glutaric aciduria type II, or multiple acyl-CoA dehydrogenase deficiency (MADD), is a rare metabolic disorder inherited in an autosomal recessive manner. The condition can be caused by mutations in at least 3 genes, including ETFA, ETFB, and ETFDH. When this potentially lethal disorder is known for its clinical and biochemical heterogeneity, mutation analysis will be an invaluable part of diagnosis. A dehydrogenase deficiency is mitochondrial organic acid disorder that impairs electron transfer flavoprotein (ETF) or ETF-ubiquinone oxidoreductase, and causes a defect in flavin metabolism or transport. The clinical features of patients suffering from MADD are rather heterogeneous. It ranges from lethal cases with neonatal anomalies to mildly affected individuals, presenting in childhood or adulthood with hypoglycemic, encephalopathy, and/or myopathy. There is evidence that the severity of the clinical phenotype, to some extent, depends on the location and nature of mutations in the genes encoding.
Material and Method: A PGD workup was performed initially on the parents' DNA and then tested on single cells. The female patient then underwent a cycle of IVF. Five embryos were suitable for PGD and the single blastomers were obtained by biopsy. Multiplex nested PCR analysis was performed for ETFDH gene c.1669G>A, p.E557K mutation, simultaneously with the linked polymorphic markers called D4S413, D4S2918, D4S2997, and D4S3351, all representing short tandem repeats (STR) associated with ETFDH gene located in 4th chromosome.
Results: The results show that there were 2 homozygous affected, 2 heterozygous and 1 normal genotype embryos. The normal embryo was transferred back to the patient and a singleton pregnancy was obtained. Amniocentesis confirmed the presence of the normal fetus.
Conclusion: These results show the feasibility of PGD for MADD, ETFDH gene. This technique could be applicable to families suffering from MADD, ETFDH gene mutation carriers as well since they share similar mutation and clinical manifestations.
Keywords: glutaric aciduria, ETFDH gene, PGD

P-47 Preimplantation genetic diagnosis for ARC syndrome

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Objectives: Arthrogryposis–Renal dysfunction–Cholestasis (ARC) syndrome is a rare multisystem disorder, which involves the kidney, liver, skin, and central nervous and musculoskeletal systems. Cardinal features of ARC include congenital joint contractures, renal tubular dysfunction, cholestasis, severe failure to thrive, ichthyosis, and a defect in platelet alpha-granule biogenesis. ARC syndrome is a rare autosomal recessive multisystem disorder caused by mutations in vacuolar protein sorting 33 homologue B (VPS33B) and VPS33B interacting protein.
Material and Method: A PGD workup was performed initially on the parents' DNA and then tested on single cells. The female patient then underwent a cycle of IVF. Five embryos were suitable for PGD and the single blastomeres were obtained by biopsy. Multiplex nested PCR analysis was performed for VPS33B gene c.1406-1 G>C mutation, simultaneously with the linked polymorphic markers called D15S127, D15S963, D15S996, and D15S2158, all representing short tandem repeats (STR) associated with VPS33B gene located in 15th chromosome.
Results: The results show that there were 3 homozygous affected and 1 heterozygous embryos. Genetic analysis could not be performed in the remaining one due to failed amplification. The heterozygous embryo was transferred back to the patient and a singleton pregnancy was obtained. Amniocentesis confirmed the presence of the normal fetus. Our patient gave birth and we confirmed the healthy birth.
Conclusion: These results show the feasibility of PGD for ARC Syndrome, VPS33B gene. This technique could be applicable to families suffering from ARC syndrome, VPS33B gene mutation carriers as well since they share similar mutation and clinical manifestations.
Keywords: ARC Syndrome, VPS33B gene, PGD

PGD & HLA

P-48 First successful preimplantation genetic diagnosis for β-thalassemia combined with HLA typing in China

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Objective: To perform preimplantation genetic diagnosis (PGD) of β-thalassemia combined with HLA typing for families designed to preselect unaffected embryos that were HLA antigen compatible with a sibling needing cord blood transplantation.