

Case Report: Fibrodysplasia Ossificans Progressiva

Using Karyomapping for Successful Preimplantation Genetic Diagnosis

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Introduction

Fibrodysplasia ossificans progressiva (FOP) is a rare autosomal dominant condition that leads to significant disability and morbidity, characterised by the formation of heterotopic hard tissues within connective tissues.¹ Following the identification of the mutation in the ACVR1/ALK2 gene, it is now possible to mitigate the risk of inheritance by using in vitro fertilization (IVF) with preimplantation genetic testing for monogenic disorder (PGT-M). For this condition, Karyomapping and “phasing analysis” can be used to identify the inheritance of the high-risk FOP allele.²

Objective

To report the world’s first case of a healthy infant born following in vitro fertilisation (IVF) and preimplantation genetic diagnosis (PGD) using karyomapping for fibrodysplasia ossificans progressiva (FOP)

Case Report

- A 30-year-old female with FOP presented to the Centre for Reproductive and Genetic Health, London with her partner seeking fertility treatment to ensure she achieved pregnancy with an embryo unaffected by FOP.
- The couple underwent IVF and PGD with Karyomapping.
- The outcome measure is a live birth of a healthy child, not a carrier of the gain of function mutation on chromosome 2 typical of FOP cases.

Discussion

- A **multi-disciplinary team approach** was utilised in the planning of this case, considering the additional risks of oocyte retrieval, pregnancy and childbirth in women with FOP.
- The oocyte retrieval was covered with a **5-day course of prednisolone** to reduce the risk of a localised inflammatory reaction which could result in subsequent heterotopic ossification.
- This was subsequently weaned down with reducing doses every 2 days.
- The patient underwent uncomplicated oocyte retrieval, yielding 12 mature oocytes.
- Following ICSI, ten 2 PN zygotes were cultured, and six underwent trophoectoderm biopsy and vitrification 5-6 days after retrieval.
- **PGD via Karyomapping revealed 4 out of 6 (66.7%) of blastocysts were not carriers of the FOP-allele.**
- In total the patient had 3 separate embryo transfers. She successfully achieved pregnancy following the third embryo transfer, which went to 37 weeks’ gestation, and delivered by Caesarean section.
- **The baby was born in excellent condition and is unaffected by FOP.**

Conclusion

IVF/ICSI and PGD using karyomapping can successfully be used to identify embryos carrying the FOP allele.

Figure 1: Guidance for specialists managing FOP patients during the preconception, antenatal and intrapartum periods



MDT: Multi-disciplinary Team, IVF: In Vitro Fertilisation, ICSI: Intracytoplasmic Sperm Injection, SNP: Single Nucleotide Polypeptide, USS: Ultrasound Scan, GTT: Glucose Tolerance Test, GDM: Gestational Diabetes, FOP: Fibrodysplasia Ossificans Progressiva

References

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Declaration of interests

No competing interests. For more information, please email sughashini.murugesu@nhs.net