Disease NIPD for Apert syndrome

Introduction

Apert syndrome (MIM 101200) is a congenital disorder characterized primarily by craniosynostosis, midface hypoplasia, and syndactyly of the hands and feet with a tendency to fusion of bony structures. Most cases are sporadic, but autosomal dominant inheritance has been reported. Apert syndrome can be very severe and is easily distinguishable from other craniosynostosis syndromes. Two mutations in FGFR2 exon 8, c.755C>G (p.Ser252Trp) and c.758C>G (p.Pro253Arg), account for over 98% of reported cases.

Non-invasive prenatal genetic diagnosis (NIPD) is now possible using cell-free fetal DNA (cffDNA) in pregnancies at risk of Apert syndrome.

Referrals

All referrals should be made via a Clinical Genetics Department or Fetal Medicine Unit and will be accepted in either of the categories given below. If you wish to refer a case which does not fulfill these criteria please contact Professor Lyn Chitty (l.chitty@ucl.ac.uk) (Clinical) or Fiona McKay (Fiona.McKay@gosh.nhs.uk) (Laboratory)

1. At risk pregnancy
   - Paternal Apert syndrome OR
   - a previous pregnancy has been confirmed to have Apert syndrome, thus there is a very small risk of recurrence due to germline mosaicism
2. Abnormal ultrasound findings
   - Acrocephaly AND
   - Symmetrical syndactyly

Service offered

Targeted next generation sequencing (NGS) for p.Ser252Trp (c.755C>G), p.Pro253Arg (c.758C>G) and c.755_756delinsTT (p.Ser252Phe) mutations in FGFR2

Technical

Maternal EDTA blood is spun as soon as possible after collection, cffDNA is extracted from plasma. Molecular analysis is performed by PCR, followed by NGS (Illumina MiSeq). Amplification of fetal DNA will be confirmed using HLA markers, or ZFY-specific sequences.

Target reporting time

Results are normally available within 5 days of sample receipt.