INTRODUCTION

CCD (also known as cleidocranial dysostosis) is an autosomal dominant disorder that affects most prominently those bones derived from endochondral and intra-membranous ossification, such as the cranium and the clavicles. It is a rare disease, with all ethnic groups being equally affected. The most prominent clinical findings are abnormally large, wide-open fontanelles at birth (that may remain open throughout life), mid-face hypoplasia, abnormal dentition, clavicular hypoplasia and hand abnormalities. The phenotype may vary from isolated dental anomalies to fully manifesting disease, even amongst individuals in the same family. Penetration is high.

Diagnosis is based on clinical and radiographic findings that include a skeletal survey of the cranium, thorax, pelvis, spine, long bones, hands and feet. It can also be diagnosed by ultrasound examination in the offspring of an affected parent as early as 14 weeks gestation.

Other conditions share some characteristics with CCD. It is therefore important to confirm the clinical diagnosis with a molecular diagnosis. This then enables family testing or prenatal diagnosis to be carried out (although the latter is not often requested). A negative test result in an affected individual may indicate that an alternative diagnosis should be considered. A karyotype may be appropriate as abnormalities of 8q22 have been seen in rare individuals.

The service is funded by the National Commissioning Group for Highly Specialised Services (HSS) for referrals from England, Scotland, Wales and Northern Ireland.

TESTING AND REFERRALS

All diagnostic samples should be accompanied by a completed clinical questionnaire & consent form (click here)

The aim is to provide a joint Molecular and Clinical service, and Professor Andrew Wilkie (+44 (0)1865 222619) is available for advice. We test:

- Clinically affected patients
- Relatives of clinically affected patients in whom a mutation has been identified
- Prenatal testing is available in cases where a mutation has been identified. These must be discussed with the laboratory and arranged in advance.

REFERRALS

From Clinical Genetics, Paediatrics, Craniofacial clinics, Dysmorphologists. Prenatal testing is only accepted from Clinical Genetics and / or Prenatal Diagnosis.

STRATEGY

Family tests: When a mutation has been identified in a family the individual is tested only for the familial mutation. For new cases: About 70% are due to mutations of RUNX2, and up to 13% are due to microdeletions of the gene.

TECHNICAL INFORMATION

Mutation analysis: Bidirectional fluorescent sequencing of RUNX2 exons 0-7.
MLPA: dosage across all exons of the craniofacial genes TWIST1, ALX1, ALX3, MSX2, RUNX2 and EFNB1 and at 3 exons of ALX4. CCD has been reported in association with deletions of the RUNX2 gene.

TARGET REPORTING TIMES: Supraregionally funded by HSS for referrals from the UK

Diagnostic: 8 weeks
Familial Mutation test: 10 days
Prenatal testing: 3 days

N.B. Details are correct for the date of printing only – last updated 11/06/2015