Clinical Background and Genetics

- **Ellis-van Creveld syndrome (EvC)** is a very rare autosomal recessive chondrodysplasia (MIM: #225500).
- EvC is characterised by short ribs, polydactyly, growth retardation and ectodermal and heart defects. The skeletal features include shortening of the limbs, postaxial polydactyly, dysplastic nails and teeth and a range of dental anomalies. Congenital heart defects occur in 60% of affected individuals, usually an atrial septal or atrioventricular septal defect.
- EvC is caused by mutations in **EVC** and **EVC2**, however further genetic heterogeneity has been suggested.
- EvC is most prevalent in the Amish population of the USA. Birth prevalence in non-Amish population is estimated to be 0.7/100,000. Consanguinity has been reported in approximately 30% of cases (Ulucan *et al.*, 2008).
- Weyer’s acrofacial dysostosis (also termed Curry-hall syndrome) is a proposed autosomal dominant disorder that is allelic with EvC and is also caused by mutations in **EVC** and **EVC2** with variable expression.
- Clinical features include postaxial polydactyly with anomalies of the lower jaw and dentition, dysplastic nails and mild shortness of stature.
- NB. UKGTN dossier for EvC testing only. Referrals for Weyer’s acrofacial dysostosis are accepted if funding is available.

Service offered

- Full gene screen by direct sequence analysis of **EVC** and **EVC2**, sequenced in parallel in 43 fragments. Sensitivity 69% although detection rate may be higher.
- Deletion analysis is under consideration for development dependant upon the proportion of referrals without a detectable mutation.

Quality

- This is a UKGTN approved service. BGL participates in the EMQN DNA Sanger sequencing and UKNEQAS Pathogenicity of Sequence Variants external quality assurance schemes.

Referrals:

- Referrals are accepted nationally from clinical Geneticists only, providing that the UKGTN gate keeping criteria are met; please complete the UKGTN proforma found below.

Target reporting Time and Cost (where appropriate)

| EVC and EVC2 Full gene screen | 56 days | Please contact the laboratory for up to date prices |
| Carrier testing relatives for known mutation | 28 days |

Clinical Advice: If clinical discussion is required we would recommend contact with Dr Sarah Smithson, Consultant Clinical Geneticist, St Michael's Hospital, Bristol (Tel: 0117 342 5653).

References

UKGTN Testing criteria

Patient name:  
Patient postcode:  
NHS Number:  
Name of referrer:  
Title/Position:  

Disease: Ellis-van Creveld Syndrome  
Name of gene(s): EVC and EVC2  

Referrals will only be accepted from one of the following:

<table>
<thead>
<tr>
<th>Referrer</th>
<th>Tick if this refers to you</th>
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<tr>
<td>Consultant Clinical Geneticist</td>
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Minimum criteria required for testing to be appropriate as stated in the Gene Dossier

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<th>Criteria</th>
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<td>1. Patients with EVC Phenotype, isolated case or pedigree suggestive for autosomal recessive inheritance.</td>
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EVC is a multi-system disorder with main manifestation in the skeletal and cardiovascular systems. Growth is restricted and often there are problems with alignment of the legs and joints especially the knees. There are cosmetic issues such as frenulae in the mouth and additional digits which require surgical treatment.

Comments

If the patient does not fulfil these criteria and you still feel that testing should be performed please contact the Bristol Genetics Laboratory (Tel: 0117 414 6164) to discuss testing.