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CHG. CHARGE Syndrome

NIHR BioResource – Rare Diseases study project

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Summary

CHARGE syndrome was first described in the early 1980's. The name CHARGE arises from an acronym made up of the first letter of some of the clinical features, namely:

C: Coloboma (eye defect)
H: Heart problems
A: Atresia choanae (blockage of nasal passages)
R: Retarded growth and/or development
G: Genital abnormalities
E: Ear abnormalities

It is now recognised that some unusual features (such as coloboma and choanal atresia) are more characteristic of CHARGE, with additional features also described such as cranial nerve abnormalities and defects of the semicircular canals. It is a rare condition, affecting around 1 in every 10,000 births, with boys and girls affected equally. CHARGE syndrome is a congenital condition (ie. children are born with it).

At least two thirds of children with a clinical diagnosis of CHARGE syndrome are found to have a mutation (change) in the gene CHD7; unlike other conditions many of these are unique mutations. CHD7 is an important gene involved in the early development of many organ systems in the developing fetus, which accounts for the wide number of clinical problems seen in CHARGE syndrome. However, in the majority of cases, it is not thought to be an inherited disorder passed on from parent to child, and is therefore unlikely to recur in further children within the family.

As CHARGE involves a large number of body systems, a multidisciplinary approach involving different specialists is required to ensure that the best treatments are given. The multidisciplinary team may include specialist input from genetics, endocrinology (hormones), ophthalmology (eyes), ENT (ear, nose and throat), cardiology (heart),

speech and language (including feeding), and psychology. Input from experts in visual impairment and developmental paediatricians, as well as from specialists in sleep disorders and neuropsychiatry, may also be required.

Collaborators:

- Birmingham Children's Hospital
- Royal Manchester Children's Hospital
- Great Ormond Street Hospital (GOSH)
- Moorfields Eye Hospital

We have support from the NIHR BioResource to gather a cohort of CHARGE patients. The main aim of this project is to gain a better understanding of the condition and why it happens. This will then help us improve the treatment for this highly complex condition which is associated with increased mortality and severe lifelong morbidity. To achieve these objectives, we will collect DNA samples and detailed phenotyping data from recruited patients.

Recruitment Criteria

Inclusion

Major abnormalities

1. Coloboma*: of iris, retina, choroid, disc; microphthalmia*
2. Choanal atresia: *unilateral/bilateral, membranous/bony, stenosis/atresia*
3. Characteristic ear abnormalities: *external ear (lop or cup-shaped), middle ear (ossicular malformations, chronic serous otitis), mixed deafness, cochlear defects*
4. Cranial nerve dysfunction: *facial palsy (unilateral or bilateral), sensorineural deafness and/or swallowing problems*
5. Hypoplasia of semicircular canals

Minor abnormalities

1. Genital hypoplasia: *males: micropenis, cryptorchidism; females: hypoplastic labia; both males and females: delayed, incomplete pubertal development*
2. Developmental delay: *delayed motor milestones, language delay, mental retardation*
3. Cardiovascular malformations: *all types, especially conotruncal defects (e.g., tetralogy of Fallot), AV canal defects, and aortic arch anomalies*
4. Growth deficiencies: *short stature, growth hormone deficiency*
5. Orofacial cleft: *cleft lip and/or palate*
6. Tracheoesophageal-fistula: *tracheoesophageal defects of all types*
7. Characteristic face: *sloping forehead, flattened tip* of nose