Background

CHARGE association/syndrome (A/S) has emerged as one of the most common causes of deaf-blindness in children. The diagnosis of CHARGE A/S is based on the clinical assessment of distinguishing features (Table 1). It is a complex and difficult condition to manage, often presenting with physical anomalies at birth (choanal atresia, cyanotic heart disease, tracheo-esophageal fistula), which require corrective surgery. Twenty years ago, many patients did not live past infancy; however, today, with advances in technology and treatment, more children are reaching late childhood and adolescence. This increase in life expectancy has afforded researchers a better understanding of the medical, behavioural, and developmental issues associated with CHARGE A/S. As a consequence, many of these issues can be more easily managed, and some even prevented, with early intervention and careful long-term follow-up. Data from the first six months of the Canadian Paediatric Surveillance Program (CPSP) has enabled a more accurate estimation of the Canadian incidence of CHARGE A/S, which is thought to be closer to 8/100,000, based on data from the Atlantic region.

Management and long-term follow-up

The treating physician should coordinate a multidisciplinary team of paediatric subspecialists and paramedical experts to address all aspects of care for the patient with CHARGE A/S.

Developmental delay

Early signs of developmental delay are not determinants of poor outcome or mental retardation. The deaf-blind child with CHARGE A/S should receive education appropriate for dual-sensory impairment within the first few months of life, allowing the child to benefit from experts in audiology, speech therapy, otorhinolaryngology and ophthalmology. Auditory brainstem evoked potentials are recommended before discharge from the neonatal unit.

Growth deficiency/delayed puberty

Growth deficiency begins shortly after birth, and may be due to illness, hospitalization, and/or feeding difficulties, with little catch-up over time. Consequently, adolescents with CHARGE A/S are in the lower percentiles on growth charts.
Endocrine problems resulting from delayed or incomplete puberty include irregular menses, the absence of secondary sexual characteristics and an increased risk for osteoporosis. Consequences are psychological as well as medical.

A low serum LH/FSH in the first few months of life indicates a defect in the hypothalamic-pituitary-gonadal axis (causing hypogonadotrophic hypogonadism). If not already tested at infancy, a child should be tested at 13-14 years of age or before the onset of puberty, since a random LH/FSH measurement is unreliable in children between infancy and puberty.

**Feeding difficulties**

Feeding difficulties are commonly severe and are likely caused by multiple cranial nerve anomalies. Dysfunction of cranial nerves IX and X causes velopharyngeal/laryngeal incoordination resulting in serious difficulties in swallowing. Anosmia and ageusia may be the result of the dysfunction of cranial nerves I and VII, respectively.

Many children require gastrostomy/jejunostomy feeding and may find the transition to oral feeding difficult. A team of specialists, including a dietician, a gastroenterologist, an occupational therapist and a speech language pathologist, will help overcome these feeding difficulties.

**Scoliosis**

Scoliosis occurs in CHARGE A/S individuals, but is underreported. Because scoliosis tends to progress during accelerated growth, the patient should be monitored closely during periods of growth spurts and growth hormone supplementation. Expertise from a physiotherapist and an orthopedist are valuable in the management of this condition.

**Ophthalmological problems**

Retinal detachment can be a consequence of chorioretinal (posterior) colobomata and can be provoked by trauma such as eye-poking. A patient with photophobia can use tinted glasses and a brimmed hat to alleviate sensitivity to light.

**Neurological problems**

Late-onset seizures and migraines have been reported in CHARGE adolescents. Neurological problems may also present in unusual ways, such as behavioural outbursts. A thorough neurology assessment, including radiological imaging (CT/MRI), may rule out other causes.

**Behavioural profile**

Many older CHARGE A/S patients exhibit specific behaviours such as: difficulty in initiating activities, social detachment, aggression and behavioural outbursts, self-abuse, sleeping difficulties, poor self-esteem regarding facial appearance, and tactile defensiveness.
Psychological/co-morbid issues
Other common diagnoses in CHARGE individuals include obsessive-compulsive disorder, pervasive developmental disorder, attention deficit disorder and hyperactivity, depression, and anxiety. Psychological/psychiatric evaluations, educational specialists’ expertise and judicious pharmacotherapy are often essential for successful management of one or more co-morbid diagnoses.

Table 1: Diagnostic features of CHARGE A/S with late-onset sequelae

<table>
<thead>
<tr>
<th>Features of CHARGE A/S</th>
<th>Later childhood / adolescent issues</th>
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<tbody>
<tr>
<td><strong>Major “4 C’s”</strong></td>
<td></td>
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<tr>
<td>Ocular coloboma</td>
<td>Photophobia; retinal detachment</td>
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<tr>
<td>Choanal atresia/stenosis</td>
<td>Facial growth problems, unilateral nasal discharge</td>
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<tr>
<td>Cranial nerve anomalies</td>
<td>Feeding/swallowing problems; hearing loss; facial palsy (appearance)</td>
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<tr>
<td>Characteristic ear anomalies</td>
<td>Progressive hearing loss; chronic middle ear infections; vestibular problems affecting balance / motor skills.</td>
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<tr>
<td><strong>Minor</strong></td>
<td></td>
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<tr>
<td>Cardiovascular malformations</td>
<td>Arrhythmias; angina</td>
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<tr>
<td>Genital hypoplasia</td>
<td>Pubertal delay, hormone replacement; fertility (unknown)</td>
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<tr>
<td>Cleft lip/palate</td>
<td>Cosmetic concerns; self-image</td>
</tr>
<tr>
<td>Tracheo-esophageal fistula</td>
<td>Reflux esophagitis; feeding/swallowing problems</td>
</tr>
<tr>
<td>Distinctive CHARGE faces</td>
<td>Cosmetic concerns; self-image</td>
</tr>
<tr>
<td>Growth deficiency</td>
<td>Growth hormone replacement</td>
</tr>
<tr>
<td>Developmental delay</td>
<td>Educational, behavioural, social adjustment</td>
</tr>
<tr>
<td><strong>Occasional</strong></td>
<td></td>
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<tr>
<td>Renal anomalies</td>
<td>Renal failure</td>
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<tr>
<td>Spinal anomalies</td>
<td>Scoliosis</td>
</tr>
<tr>
<td>Hand anomalies</td>
<td>Fine motor problems; cosmetic concern</td>
</tr>
<tr>
<td>Neck/shoulder anomalies</td>
<td>Self-image concern</td>
</tr>
</tbody>
</table>

* 4 major or 3 major and 3 minor features confirms diagnosis of CHARGE (Blake et al, 1998).

**Velocardiofacial syndrome** (VCFS) and **DiGeorge anomaly/sequence** (DGS) should be ruled out, using the FISH (fluorescent in situ hybridization) studies for 22q11 deletion. Clinical presentation of DGS includes thymic hypoplasia, hypocalcemia, and cono-truncal heart defects, whereas in VCFS, typical facial dysmorphic features and cleft palate are seen more commonly. These clinical features can overlap.
Bibliography


Puberty in CHARGE adolescents and CHARGE into the adolescent and adult decades. Abi Daoud M, Blake KD (Toronto 2002).

Scoliosis in CHARGE. Doyle C, Blake KD (in press).

Test your knowledge

1. All of the following statements are true, except:
   a) The incidence of CHARGE across Canada ranges from 3/100,000 to 8/100,000.
   b) CHARGE is now one of the most common causes of deaf-blindness.
   c) There is no known genetic marker for CHARGE.
   d) Endocrine dysfunction in CHARGE often results in micropenis in males, minor labial anomalies in females, and absence of secondary sex characteristics in both sexes.
   e) The major criteria for CHARGE include: choanal atresia, ocular coloboma, cranial nerve defects, and characteristic ear anomalies.
   f) Feeding problems in children with CHARGE are most often a result of tracheo-esophageal fistula and, thus, can usually be resolved early in life with surgery.

2. A child with ocular coloboma, choanal atresia, and characteristic ear anomalies, in addition to three of the minor criteria for CHARGE would:
   a) Unquestionably have CHARGE.
   b) Not have CHARGE.
   c) Not likely have CHARGE.
   d) Most likely have CHARGE, pending FISH test for 22q11 deletion.

3. (A) CHARGE adolescent issue(s) secondary to a cranial nerve anomaly would be:
   a) Sensorineural hearing loss.
   b) Continued feeding difficulty.
   c) Psychosocial issues related to general appearance (e.g., facial palsy).
   d) No sense of smell.
   e) All of the above.

4. Hypogonadotrophic hypogonadotropism and, hence, high probability of delayed puberty in CHARGE children can be indicated by serum LH/FSH:
   a) In the first 2-3 months of life.
   b) Between the ages of about 5-12.
   c) After about age 13-14 (pubertal age).
   d) a) and c).
   e) a) and b).
5. Behavioural or psychological issues present in CHARGE adolescents may result from:
   a) Frustration due to inability to communicate.
   b) Pain or discomfort associated with an underlying medical problem.
   c) Psychosocial maladaptation related to general physical appearance and self-image.
   d) A diagnosis of attention deficit disorder with hyperactivity (ADDH).
   e) All of the above.

6. Adolescents with CHARGE A/S, when compared to the general adolescent population, are more likely to demonstrate all of the following, except:
   a) Scoliosis  d) Seizures  g) Delayed puberty
   b) ADDH  e) Abdominal colic  h) Depression
   c) Migraine  f) Schizophrenia  i) Osteoporosis

7. All of the pictures below are individuals with CHARGE A/S; spot the similarities.

RESOURCES

CANADIAN PAEDIATRIC SURVEILLANCE PROGRAM

01/2003

Answers:
1-f, 2-d, 3-e, 4-d, 5-e, 6-f