

CHARGE syndrome

Also known as: CHARGE association, Hall-Hittner syndrome

Clinical Characteristics

CHARGE is an acronym for certain characteristics of the syndrome: Coloboma of the iris, Hear defects, Atresia (choanal), Retarded growth and development, Genital abnormalities, Ear anomalies and/or swallowing problems. Not all individuals with CHARGE syndrome have each of these manifestations, but these and others are commonly found. Coloboma (notching) of the iris may be unilateral or bilateral, as may choanal atresia. Heart defects include conotruncal anomalies, AV canal defects, and aortic arch anomalies. Genital abnormalities include hypogonadotropic hypogonadism and cryptorchidism in males. Hyposmia or anosmia is often observed, as is unilateral or bilateral facial palsy, due to cranial nerve dysfunction. Other features occasionally seen include orofacial clefts, tracheoesophageal fistula, autistic-like behaviors, attention-deficit hyperactivity disorder, and an increased pain threshold.

CHARGE Syndrome and Hearing Loss

Ear anomalies and hearing loss are found in 70-90% of individuals with CHARGE syndrome. The loss can range from mild to profound and may be sensorineural, conductive, or mixed. Sensorineural hearing loss is often associated with a Mondini malformation of the cochlea or hypoplasia of the auditory nerve. Its presence is sometimes predicted by facial paralysis. Conductive hearing loss is often due to malformed or absent ossicles, or absent or hypoplastic semicircular canals. These abnormalities are present in about 95% of patients and can lead to problems with balance, especially if vision is also compromised. Conductive hearing loss may fluctuate if middle ear disease occurs. Recurrent otitis media is common.

Natural History

CHARGE syndrome is diagnosed in both males and females and in all ethnicities. The prevalence of the syndrome is estimated to be between 1 in 8,500 and 1 in 12,000.

Infants with CHARGE syndrome have increased morbidity. Heart defects, central nervous system abnormalities, bilateral choanal atresia, and tracheoesophageal fistula appear to be the greatest contributors to a high infant mortality rate.

The four major diagnostic criteria are the "4 C's": choanal atresia, coloboma, characteristic ears, and cranial nerve anomalies. Heart defects are present in 75-85% of patients (the most common of which is tetralogy of Fallot), tracheoesophageal fistula in 15-20%. Swallowing and breathing problems can lead to gastroesophageal reflux and require special attention. Facial palsy is present in about 50% of patients, and coloboma of the eye(s) may cause light sensitivity in 80-90% of patients. 50-60% of males have some type of genitourinary issue, and 25-40% of all patients have some kind of renal

abnormality. Limb abnormalities are present in about one-third of affected individuals, and scoliosis is common. Babies with CHARGE syndrome are typically born at a normal length and weight, but growth retardation becomes evident later in infancy.

There are usually marked delays in the development of motor skills. Speech and language delays are also common due to issues with decreased hearing and/or vision. This does not necessarily mean that these children are cognitively impaired. Assessment of cognitive abilities is difficult, but it seems that at least half of all children with CHARGE syndrome have normal intellect. Many individuals are able to adapt well to their physical limitations and function as independent and contributing members of society. Severely affected individuals are not able to reproduce, but many mildly or moderately affected can and do. Some individuals with CHARGE syndrome exhibit autistic-like, repetitive, aggressive, obsessive-compulsive, and self-abusive behaviors. Some are diagnosed with attention-deficit hyperactivity disorder. These behaviors are often due to a frustration at being hindered in communication.

Genetics

The gene *CHD7* on chromosome 8 has been associated with CHARGE syndrome. It encodes a DNA binding protein involved in regulating early embryonic development. Mutations of this gene are found in 60-65% of individuals diagnosed with CHARGE syndrome. Most cases are thought to be sporadic, or due to new mutations. There is some evidence for autosomal dominant inheritance, but in general the recurrence risk for siblings of a person with CHARGE syndrome is 1-2% due to the possibility of a mutation in the germ cells of a parent.

Management

The diagnosis of CHARGE syndrome is made clinically. When performing genetic testing, cytogenetic testing should be done first, followed by molecular testing for genetic counseling purposes.

Initial evaluations following diagnosis should include a dilated ophthalmologic evaluation by a pediatric ophthalmologist, a cardiac evaluation, a nasal endoscopy and/or a CT scan to look for choanal atresia and/or stenosis, an evaluation for cleft palate, a cranial nerve function assessment, and evaluations for esophageal atresia/tracheoesophageal fistula. The initial ENT & audiologic evaluation should include BAER to evaluate hearing and a CT scan for middle and inner ear defects.

Intensive medical management and many surgical interventions may be required over the years. Management of each of the symptoms requires a great deal of coordinated care from a multidisciplinary team. Issues that must be addressed include: airway management, treatment for heart defects, swallowing and feeding difficulties, a renal evaluation, an endocrine evaluation, dental procedures (only to be performed under general anesthesia), chronic constipation, and behavioral issues.

Management of hearing loss should be appropriate to the individual. Hearing aids and hearing habituation should begin immediately. Bone conduction aids or an FM system

are often helpful. Cochlear implants have proven to be effective in patients with CHARGE syndrome, but there may be difficulties in placement due to bone anatomy or risk of damaging a facial nerve. Chronic serous otitis often requires the placement of PE tubes until adolescence. Any child with both significant hearing loss and vision impairment should be considered "deaf-blind" and receive proper educational services. It is suggested that these services begin as early as possible, even before the child has enrolled in school.

Regular ophthalmologic and audiologic evaluations are indicated, as are frequent dental examinations. If puberty does not occur in a timely manner, LH and FSH levels should be obtained by an endocrinologist, provided this has not already been done. A scheduled appointment with a geneticist and/or genetic counselor is also recommended.

Resources for Families

Statewide Genetics Program

Phone: 608-267-7148

Fax: 608-267-3824

Email: meyeram@dhfs.state.wi.us

Wisconsin First Step Hotline

Phone: 1-800-642-7837 voice/TTY

Website: www.mch-hotlines.org

Wisconsin Office for Deaf and Hard of Hearing

Phone: 1-608-266-3118 voice/TTY

Website: www.dhfs.state.wi.us/sensory

Regional Children and Youth with Special Health Care Needs Centers

Centers in Green Bay, Wausau, Milwaukee, Madison, and Chippewa Falls

Website: http://dfhs.wisconsin.gov/DPH_BFCH/cshcn/index.HTM

WI Chapter of Families for Hands & Voices

Phone: (920) 437-7370

Website: www.handsandvoices.org

Parent-to-Parent of Wisconsin

Phone: 1-888-266-0028

Email: rmathea@shsmh.org

Family Village online resource

Library Card Catalog of Disorders

www.familyvillage.wisc.edu

CHARGE Syndrome Foundation, Inc.

409 Vandiver Drive, Suite 5-104

Columbia, MO 65202

Phone: 573-449-4694 OR 1-800-442-7604

Email: marion@chargesyndrome.org

Website: www.chargesyndrome.org