OVERVIEW OF CHARGE SYNDROME FOR PHYSICIANS

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DIAGNOSIS & MANAGEMENT

The acronym CHARGE was proposed in 1981 by Pagon, et al.[1] Since then much has been learned, particularly about the influence of cranial nerve anomalies on major medical crises and long-term morbidity in CHARGE syndrome. Revised diagnostic criteria were published in a review for physicians in 1998.[2] Morbidity can be greatly diminished by understanding the interaction of these multiple anomalies. In particular, involvement of cranial nerves IX and X cause neurologic impairment of swallowing, leading to reflux and recurrent aspiration pneumonia. Addressing this problem could prevent many hospitalizations. When failure to thrive is present, one needs to take the swallowing difficulty into account along with possible lack of olfaction and the many other anomalies like heart disease which traditionally cause poor nutrition.

Each affected system is addressed in this CHARGE Parent Manual with particular caveats related to each specialty.

DEVELOPMENT

Older literature states that most, if not all, of these children are mentally retarded. ***That is not true.*** A majority of children with CHARGE have vision and/or hearing loss, which together can constitute the designation of "deafblindness" even when residual hearing and vision is present. Children who are deafblind are **"input-impaired,"** which means they need to learn alternative modes of communication and different ways to explore and interact with their environments. In addition many children have Mondini malformations which lead not only to hearing loss but also to vestibular dysfunction. The developmental effects are unusual motor milestones including a "five-point crawl" and delayed age of walking. Without congenital vision deficits and other anomalies, children with vestibular dysfunction (e.g. Usher Type I) walk on average at 18-24 months. Children with CHARGE who are multiply affected walk at 3-4 years. Clearly any infant who has delayed motor milestones, does not speak, and may not look you in the eye because of a macular coloboma will be considered mentally retarded. However, measuring output in such cases does not necessarily reflect true mental processing.

As more children are put into appropriate deafblind programs with adequate input, much improved output is being observed. Early diagnosis of vision and hearing loss is important but *referral to appropriate educational programming is vital.*

FINDINGS DESCRIBED BY THE ACRONYM

C- Coloboma (ocular)

Cleft affects the globe but not the eyelid. The coloboma can involve the iris, retina (with or without involving the macula) or disc. An upper visual field cut can range from insignificant to major.

Microphthalmos or even anophthalmos can be part of the coloboma spectrum.

C- Cranial nerve anomalies

I – the olfactory nerve may be involved with arhinencephaly. Lack of smell can have a major impact on feeding and, later, on socialization.

II – the ocular nerve is usually involved only if a coloboma involves the disc

VII - facial palsy is usually unilateral and present at birth. Facial asymmetry without facial palsy can also be seen as can asymmetric crying facies.
VIII – the acoustic nerve may be involved separate from malformations of the ear itself
IX & X – the major early problems poor or incoordinated swallowing with gastroesophageal reflux and aspiration pneumonia. These tend to improve over weeks, months or years.

H - Heart malformations

Any of the common types may be involved but tend to be of the conotruncal variety.
Vascular rings and aberrant subclavian arteries may cause tracheal compression.

A - Atresia or stenosis of choanae UL or BL, bony or membranous

R - Retardation of growth and/or development

Height and weight are usually normal at birth. Loss of growth milestones in the first two years is often associated with failure to thrive due to swallowing problems, heart disease, hospitalizations and recurrent illnesses.
Growth hormone deficiency may be present.
Developmental delay is due to many causes, the most important of which are vision and hearing loss combined with vestibular dysfunction due to anomalies of the inner ear. Acute medical illnesses and hospitalizations also contribute to the delays. Mental processing can be normal.

G – Genitourinary anomalies

Male genital anomalies include small penis, hypospadias, undescended testes
Female genital anomalies include small labia
Hypothalamic hypogonadism may account for the genital anomalies and delayed or absent puberty
Genitourinary problems also involve malformations of the kidneys and ureters (tubes to the bladder)

E - Ears anomalies: outer, middle, inner

Mixed hearing loss +/- vestibular dysfunction
Canals may be narrow
Acute and chronic otitis media is common
Anomalies of the middle ear ossicles may be present
Mondini defects vary in severity

OTHER FINDINGS

Floppy cartilage in ears and trachea
TE (tracheoesophageal) fistula
Esophageal atresia
Cleft lip/palate
DiGeorge sequence with poor immune response
High pain threshold
Resistance to some forms of anesthesia

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[1] Pagon RA, Graham JM, Zonana J, Young SL. Congenital heart disease and choanal atresia with multiple anomalies. J Pediatr 1981;99:223-227.

[2] Blake KD, Davenport SLH, Hall BD et al. CHARGE association: an update and review for the primary pediatrician. Clin Pediatr 1998;37:159-174.