Case Report

Charge Syndrome

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A 2 yrs old female born at term presented to us with poor vision, inability to close her eyes since birth and enucleation of left eye at 1 month of age. On examination left orbit and socket were shrunken after enucleation. There was bilateral lid coloboma on medial half with symblephron and ankyloblephron formation. Extra ocular movements were reduced due to conjunctival and corneal adhesion to the upper lid. There was right corneal opacity due to ankyloblephron and limbal vascularization along with exposure keratopathy, associated with conjunctival congestion. There was right lower lid ectropion. There was no uveal coloboma; lens was clear with good fundal glow. She had multiple other congenital anomalies associated with CHARGE syndrome.

In 1981, the term CHARGE was created to describe a birth defect that had been recognized in children. CHARGE stands for: Coloboma (eye), heart defects of any type, atresia (choanal), retardation (of growth and/or development), genital anomaly and ear anomaly. It was recommended that diagnosis of the syndrome be based on the presence of four of these physical features. Since then, physicians have recognized that this definition and rule for diagnosis do not take into account many other physical characteristics of CHARGE syndrome, or the fact that some children with the syndrome did not meet the criteria for diagnosis. In addition, a gene associated with CHARGE syndrome has been identified on chromosome 8. CHARGE syndrome occurs in approximately 1 in 10,000 births worldwide, and usually the infant is the only child in the family with the syndrome. We describe a case of charge syndrome associated with coloboma and ankyloblephron formation in Pakistani population.

CASE REPORT

A 2 years old female child born at term with normal delivery presented to us with poor vision, epiphora, and inability to close her eyes since birth. Enucleation of left eye had been done at 1 month of age for a congenital cystic eyeball. On examination her left orbit and socket were shrunken. There were bilateral upper lid colobomas on medial half with ankyloblephron formation. Extra ocular movements were reduced due to conjunctival and corneal adhesion to upper lid. Right corneal opacity was present due to ankyloblephron. Limbal vascularization along with exposure

keratopathy was present which was associated with conjunctival congestion. There was right lower lid ectropion. There was no uveal coloboma; lens was clear with good fundal glow.

Multiple other systemic congenital anomalies were seen on investigation. Abdominal ultrasound showed congenital adrenal hypoplasia. Echocardiography showed atrial septal defect. Brainstem auditory evoked potentials (BAEP) showed bilateral decreased hearing sensation. CT brain showed normal midline structures with no hydrocephalus but a small cyst was seen in the frontal horn. Her serum cortisol was 5.6 ug/dl(N=6 - 8.6ug/dl), plasma ACTH was 23.2 pg/ml (N=46 pg/ml), serum aldosterone was 61.7 ng/dl (N=4 - 31 ng/dl), serum progesterone was 4.9 ng/ml (N=<2 ng/ml), serum sodium was 140 mmol/L (N=136-148 mmol/L), serum Potassium was 5.4 mmol/L (N=3.6 - 5.0 mmol/L), hemoglobin was 15.2 gm/dl, neonatal TSH was 2.5 mmol/L (N=0.01-6.3 mmol/L), blood glucose was 48 mg/dl (N=80-160 mg/dl), PT was 9.3 sec, APTT was 41.8 sec.

The patient had been treated previously with artificial tears and lubricating ointments. Dilating drops were being used to dilate the pupil beyond the central corneal opacity to improve vision. We operated on the patient's right eye for the release of ankyloblephron from conjunctiva and cornea. The defect of conjunctiva was closed with advancement flaps. The edges of coloboma were made raw and the upper lid defect was closed by anchoring of tarsal plate to medial canthal tendon medially after releasing the lid laterally using reverse tenzel flap. Postoperatively lagophthalmos decreased with improved extra ocular movements. There was vascularization of the cornea over the area of ankyloblephron release. Keratoplasty is planned at a later stage.

DISCUSSION

CHARGE is not an association, but a syndrome. It is characterized by very specific developmental anomalies of the optic vesicle, otic capsule, midline CNS structures, and upper pharynx which result from abnormal differentiation, setting, interaction, and migration of neural crest cells which extends from the third to ninth week gestation[1].

CHARGE syndrome can now be considered the leading cause of deaf blindness in infants and children, although there are differences in the severity of the expression of clinical features. Diagnosis of CHARGE syndrome is based on the physical symptoms the child has. The three most important symptoms are the 3 C's: coloboma, choanal atresia, and abnormal semicircular canals in the ears**.** There are other major symptoms, such as the abnormal appearance of the ears that are common in CHARGE syndrome but less common in other conditions. Some symptoms, such as a heart defect, may also occur in other syndromes or conditions, and thus may be less helpful in confirming a diagnosis. An infant suspected of having CHARGE syndrome should be evaluated by a medical geneticist who is familiar with the syndrome[2-3].

Choanal atresia is present in 35-65 % of cases with CHARGE syndrome. The back of the nasal sinuses on one or both sides narrowed (stenosis) or doesn't connect with the back of the throat (atresia). Cranial nerve abnormality can also be seen in 90-100% which includes missing or decreased sense of smell, difficulty in swallowing in 70-90% of cases, facial paralysis (palsy) on one or both sides 50-90%. Heart defect are seen in 75 % of cases. The most frequent type is septal defect. Growth retardation is seen in 80 % of cases and is first detected when the infant fails to grow normally in the first six months of life. It is due to growth hormone deficiency. The child's growth tends to catch up after infancy. Mental retardation is seen in 70 %. IQ may range from normal to severe retardation. Underdeveloped genitals are seen 80-90% of males and 15-25 % of females. Ear abnormalities are seen in 95-100 % of cases in which ear is malformed. Problems in the inner ear, such as abnormal semicircular canals or nerve defects, may result in deafness (60-90%)[4].

Some of the problems include central nervous system disorders, pituitary abnormalities, swallowing difficulties, urinary tract malformations such as abnormal kidney shape or location, backup of urine from the bladder into the kidney (reflux), posterior urethral valves, cleft lip and/or palate, degeorge sequence (congenital absence of the thymus and parathyroid glands), facial features include square shape of the face and head, flat cheekbones, facial asymmetry, wide nose with a high bridge, omphalocele, tracheophageal fistula, esophageal atresia.

If the child has a suspected hearing problem the otolaryngologist and audiologist can evaluate the child to determine if there are surgical procedures and/or assistive listening devices that can be considered. Since these children often suffer from chronic otitis media (fluid in the middle ear), they need to be monitored on a regular basis. Additionally,

the teacher of the deaf and hearing impaired will be able to assist in making recommendations for educational modifications and strategies. A speech pathologist is also likely to be involved in helping the child with speech issues.

The cause of CHARGE is not known. It is not known to be related to illness, exposure to drugs or alcohol during pregnancy and typically it does not occur to more than one person in a family. It is very rare and cannot be predicted. It is important however, to discuss risks for passing CHARGE syndrome to future generations with a trained geneticist.

Children with CHARGE require a great deal of medical management. There are often numerous surgeries to repair heart defects, choanal atresia, the gastrointestinal tract, the esophagus, cleft lip or palate, etc. Although many of these procedures are done when the child is a newborn, some of the less life-threatening problems may not appear until later or may have to wait until later in the life of the child to be addressed. Children with CHARGE syndrome are often sickly, especially in the early years. They frequently experience colds that turn into pneumonia. Even conditions that would be minor in most children may become serious conditions for them.

A coloboma is a hole in one of the structures of the eye, such as the lens, eyelid, iris, retina, choroid or optic disc. The hole is present from birth and can be caused when choroid fissure fails to close up completely before a child is born. A coloboma can occur in one or both eyes. The incidence of coloboma is estimated at around 0.5 to 0.7 per 10,000 births, making it a relatively rare condition. Eyelid coloboma is a full-thickness defect of the eyelid. Although an eyelid coloboma can occur in many locations, the most common position is at the junction of the medial and middle third of the upper lid. No lid appendages or accessory structures are usually seen within the coloboma[5-6].

Some children with CHARGE have problems with visual acuity (either near or far-sighted) which usually can be corrected with glasses. However, some of these children may also have field losses which can cause problems for them in reading, travel, reading sign language or doing other visual tasks. A teacher of the visually impaired can help in making recommendations for educational modifications and strategies.

Corneal protection is the primary goal in the medical and surgical treatment of eyelid colobomas. Modalities that can be used either for small defects or for large defects awaiting definitive surgical therapy include artificial tears and ointment, moist chamber optical bandages, bedtime patching, dilating drops to improve vision due to central corneal opacity. The surgical procedure used depends on the size and the location of the defect[7].

If the eyelid coloboma is small and well managed with topical lubrication, then surgery may be delayed until later in childhood. Usually, it is corrected by direct closure. The edges of the defect are freshened with sharp incisions, and precise anastomosis is preformed. The lid margin is brought together using a 2-layer approximation of the tarsus and the skin. Lateral cantholysis and placement of near-far, far-near sutures may be necessary to minimize horizontal tension. If the eyelid coloboma is large; immediate surgical closure is usually needed to prevent corneal compromise[7]. A 2-stage reconstruction may be required for those defects that occupy greater than 40-50% of the lid. The surgical procedure used depends on the involved lid. In the lower lid the modified Hughes procedure is used which includes upper lid tarso conjunctival flap with retroauricular skin flap. Upper lid is constructed using modified Cutler-Beard procedure which includes lower lid tarso-conjunctival flap with retroauricular skin flap. Alternate techniques for either the upper lid or the lower lid include a semicircular flap from the lateral canthal area (Tenzel or modified Tenzel flap) and a full-thickness lid rotational flap[8-9].

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