Saethre-Chotzen Syndrome (SCS)

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CBY
Overview: Saethre-Chotzen Syndrome

• Condition first described by Saethre in 1931 and Chotzen in 1932
• A.K.A...
  • Acro-cephalo-syndactyly type III; ACS3
  • Class A basic helix-loop-helix protein 38 (bHLHa38)
• 1 in 25,000-65,000 births
• Autosomal dominant
• Diagnosis: primarily by clinical findings
  • CT scan-standard for dx of craniosynostosis
• Cause: mutations/deletions in the TWIST1 gene located on chromosome 7p21.1
  • Official name: Twist family basic helix-loop-helix (bHLH) transcription factor 1
  • More than 80 mutations in TWIST1 gene identified in people with SCS
**TWIST1** gene

- Inhibits cell proliferation/maturation and
  - Haploinsufficient $\rightarrow$ craniosynostosis secondary to cell overproliferation and abnormal maturation
- Key role in mediating cell patterning during limb morphogenesis and development
  - *TWIST1-null* mice exhibit growth retardation of forelimb buds
- 63% single bp substitutions, 22% deletions, 8% insertions, 10% duplications
  - some were combination of deletion & insertion, or deletion & bp change
  - Deletions $\rightarrow$ 90% risk of developmental delay
  - Most SCS patients have normal intelligence

6-month old child with SCS/PSS [7]
FGFR

- Mutations in **fibroblast growth-factor receptor (FGFR)** also reported
- Defects in *TWIST* gene linked to mutations in *FGFR2*
  - but can also independently result in SCS
- Interaction between *TWIST* and *FGFR* genes during development
  - Components of same molecular pathway involved in modulation of craniofacial and limb development in humans
  - *TWIST* normally represses FGFR activity in osteoblast differentiation
    - *TWIST* loss of function → FGFR gain of function
- FGFRs lie downstream of *TWIST*
- *TWIST* mutation → ectopic expression of *FGFR2* at suture
Craniofacial Features

- Highly variable clinical spectrum
- Craniosynostosis of coronal, lambdoid, and/or frontal sutures
- Brachycephaly, acrocephaly, low-set hairline
- Facial asymmetry, septal deviation, thin long pointed nose, maxillary hypoplasia
- **Ptosis** of upper eyelids, strabismus, hypertelorism
- Malformed ears, mildly hard of hearing
- **Oral manifestations:** high arch or cleft palate, class III malocclusion, enamel hypoplasia

Owen has SCS & is up for adoption. [8]
Other Clinical Features

- Syndactyly & brachydactyly (fused & shortened digits, especially 2\textsuperscript{nd}/3\textsuperscript{rd} fingers/toes) in ~1/3 of cases
- Congenital heart malformations
- Short clavicles
- Short stature
- Vertebral fusion
- Moderate degree of mental retardation
  - larger deletions (3.5 to >11 Mb) $\rightarrow$ learning difficulties
  - smaller deletions (2.9 kb) $\rightarrow$ intellectually normal
Differential Diagnosis

- Robinow-Sorauf syndrome (TWIST1)
- Baller-Gerold syndrome (TWIST1)
- Muenke syndrome (FGFR3)
- Crouzon syndrome (FGFR2, FGFR3)
- Pfeiffer syndrome (FGFR1, FGFR2)
- Apert syndrome (FGFR2)
Treatment

- Multidisciplinary treatment approach – craniofacial reconstruction team
  - Pediatrician, orthopedist, surgeons, ENT/otolaryngologist, neurologist, dentist, ophthalmologist, etc.
- Optimal time for repair within 1st year of life
- Regular vision & hearing evaluations
- X-ray of neck bones recommended ~age 2
- Early intervention for intellectual disability/developmental delay
- Genetic counseling
Treatment Procedures

- First correctional cranial surgery should be ~6-9 mo of age
  - Prevent permanent deformation → insufficient space for brain to grow, increased intracranial pressure → damage
- Correction of limb abnormalities to improve function (e.g. webbed fingers/toes)
- Reconstruction of eyelid and nose

A. Patient 1, postoperative three-dimensional CT, AP view. B, Patient 1, postoperative three-dimensional CT, lateral view. C, Patient 1, 4 years postoperatively, AP view. D, Patient 1, 4 years postoperatively, postoperative lateral view. AP, anteroposterior; CT, computed tomography. [6]
Works Cited


Extra Photos
Peace Sign Syndrome (PSS) aka Y-craniosynostosis

FIGURE 2. A, patient 1, preoperative three-dimensional CT, AP view. B, Patient 1, preoperative three-dimensional CT, lateral view. C, Representative synostotic outline of the “peace sign”. AP, anteroposterior; CT, computed tomography.
Cohen Syndrome

CBY 579L
Vahid Khoshkam DDS
What is Cohen Syndrome?

Developmental delay
Small head size (microcephaly)
Intellectual disability
Weak muscle tone (hypotonia)
Cohen Syndrome

- Hypotonia, obesity, and prominent incisors
- Norio syndrome
- Obesity-hypotonia syndrome
- Pepper syndrome
- Prominent incisors-obesity-hypotonia syndrome
Features of Cohen Syndrome

Progressive nearsightedness (myopia)

Degeneration of the light-sensitive tissue at the back of the eye (retinal dystrophy)

An unusually large range of joint movement (hypermobility)
Facial features of Cohen Syndrome

Thick hair and eyebrows
Long eyelashes
Unusually-shaped eyes (down-slanting and wave-shaped)
A bulbous nasal tip
A smooth or shortened area between the nose and the upper lip (philtrum), and prominent upper central teeth.
How common is Cohen Syndrome?

It has been diagnosed in fewer than 1,000 people worldwide. More cases are likely undiagnosed.
Inheritance of Cohen syndrome

This condition is inherited in an autosomal recessive caused by an abnormal gene located on chromosome 8 at 8q22-q23.
Affected Populations by Cohen Syndrome

- Cohen syndrome affects males and females in about equal numbers.
- It appears to occur more frequently in people of Finnish or Ashkenazi Jewish descent.
Other signs & Symptoms of Cohen Syndrome

- Unusual increased extension (hyperextensible) of the joints, narrow hands and feet with long fingers and toes, a single crease (simian) on the palms of the hands, and deformities of the knees, elbows, and spine.

- Undescended testicles in males (cryptorchidism), delayed puberty, and mild to moderate mental retardation are also symptomatic of this rare disorder.
Standard therapies of Cohen Syndrome

- Treatment of Cohen syndrome may include surgery to correct facial deformities, visual problems, webbed fingers and/or undescended testicles. Genetic counseling may be of benefit for patients and their families. Other treatment is symptomatic and supportive.
Pierre Robin Sequence

Wijdan Alsaedi

Advanced Operative Program
In 1923, a physician named Pierre Robin described a newborn child with an abnormally small lower jaw (mandible), large tongue and breathing problems.
Pierre Robin Sequence

is a condition of facial difference characterized by severe underdevelopment of the lower jaw (retrognathia), a downward or backward-positioned tongue (glossoptosis), respiratory obstruction, and usually a cleft palate.
Why is Pierre Robin called a sequence and not a syndrome?

the underdeveloped lower jaw begins a sequence of events, which leads to the abnormal displacement of the tongue and subsequent formation of a cleft palate.
Causes

- The exact cause of PRS is not known.
- External factors, which crowd the fetus and interfere with the growth of the lower jaw, may contribute to PRS.
- Certain neurological conditions which lead to decreased jaw movement in utero, can also restrict jaw growth.
- Some studies demonstrate there may be a genetic basis for PRS.
Symptoms

- Significantly arched palate
- Smaller jaw as compared to the face
- Jaw positioned significantly backwards in the mouth
- Tongue appearing larger in size
- Cleft palate
- Recurring ear infection
Diagnosis

• By examining the infant and NOT by special diagnostic tests
Chances of having a baby with PRS

- The overall incidence is low, (one in 8,500 to 14,000) births.

- **Equally** common in males and females.

- Higher incidence of PRS in **twins**, which may be due to crowding in the uterus, thereby restricting growth of the mandible.
Syndromes associated with PRS

- PRS can be seen in other syndromes including Stickler and Velocardiofacial syndromes.

- Stickler syndrome is the most common syndrome associated with PRS. It occurs in 10 to 30 percent of cases.

- Velocardiofacial syndrome is associated with PRS in approximately 10 percent of cases.
Problems associated with PRS

- Feeding difficulties
- Respiratory problems
Feeding difficulties

- Babies with *minor* degrees of PRS can learn to feed with specially adapted nipples and bottles such as the Haberman Feeder, the Meade Johnson Cleft Palate Nurser, or a regular nipple with a larger opening.
Feeding difficulties

- For infants with more severe PRS, the risk of aspiration (inhaling fluid into the lungs) during feeding can be high.

- The baby may struggle to move milk to the back of the throat and swallow, while trying to breathe.

- In this case significant calories for weight gain can be lost.

- A feeding tube (nasogastric tube) may be inserted into the nose and down into the stomach.
• Children who require long-term feeding assistance may need a gastric tube surgically inserted through the abdominal wall into the stomach.

• Many children with PRS outgrow their feeding problems when the mandible grows more sufficiently (one to two years of age).
Respiratory problems

- Because of the small, recessed jaw found in children with PRS, the tongue tends to fall backwards when the child is placed on his/her back.

- When the tongue falls backwards it blocks off the throat and obstructs breathing.
Respiratory problems

- For those infants with more severe respiratory obstruction, surgical procedures may be required to improve breathing.

- For children whose breathing obstruction is not relieved by prone positioning, a tongue-lip adhesion may be recommended.
Respiratory problems

- Some surgeons will perform a procedure called mandibular distraction.

- is a procedure involving surgically cutting the lower jaw and placing either an internal (in the mouth) or external (through the skin) device.

- This device can be slowly adjusted to lengthen the jaw and theoretically pull the tongue out of the back of the throat.
• Infants with this condition should NOT be put on their back, to prevent the tongue from falling back into the airway.
• Feeding must be done very carefully to avoid choking and breathing liquids into the airways.
Treatment

- In some cases the mandible or the jaw develops so significantly that by the time the baby turns 5 to 6 years old the conditions looks normal.
- Children who do not undergo such significant development may have to undergo surgical treatment at the jaw.
- If any cleft palate is experienced it should also be closed through surgical procedures.
- It is essential for a child with cleft palate to be timely examined by speech pathologist as these children are at risk of developing defective or delayed speech issues.
References

- DJ Plast Reconstr Aesthet Surg. What is 'Pierre Robin sequence'? Breugem CC1, Mink van der Molen AB.2009 Dec;62(12)
- The treatment of micrognathia with obstruction by a plastic operation. Lyon Chir. 1956. 52:420-31
- http://www.craniofacial.net/pierre-robin-sequence-dallas/
Thank You