# Saethre-Chotzen syndrome

Saethre-Chotzen syndrome is a genetic condition characterized by the premature fusion of certain skull bones (craniosynostosis). This early fusion prevents the skull from growing normally and affects the shape of the head and face.

Most people with Saethre-Chotzen syndrome have prematurely fused skull bones along the coronal suture, the growth line that goes over the head from ear to ear. Other parts of the skull may be malformed as well. These changes can result in an abnormally shaped head, a high forehead, a low frontal hairline, droopy eyelids (ptosis), widely spaced eyes, and a broad nasal bridge. One side of the face may appear noticeably different from the other (facial asymmetry). Most people with Saethre-Chotzen syndrome also have small, rounded ears.

The signs and symptoms of Saethre-Chotzen syndrome vary widely, even among affected individuals in the same family. This condition can cause mild changes in the hands and feet, such as partial fusion of the skin between the second and third fingers on each hand and a broad or duplicated first (big) toe. Delayed development and learning difficulties have been reported, although most people with this condition are of normal intelligence. Less common signs and symptoms of Saethre-Chotzen syndrome include short stature, abnormalities of the bones of the spine (the vertebra), hearing loss, and heart defects.

Robinow-Sorauf syndrome is a condition with features similar to those of Saethre-Chotzen syndrome, including craniosynostosis and broad or duplicated great toes. It was once considered a separate disorder, but was found to result from mutations in the same gene and is now thought to be a variant of Saethre-Chotzen syndrome.

## Diagnosis

present a new and unique pattern of sutural fusion “peace sign synostosis” (PSS) characterized by synostosis of the metopic, bicoronal, and sagittal sutures and associated with abnormalities of the TWIST1 gene known to be associated with Saethre-Chotzen syndrome (SCS). To do so, we performed a retrospective review of patients with bicoronal, metopic, and at least partial anterior sagittal synostoses at the Children's Hospital of Philadelphia and Seattle Children's Hospital. Patients' demographics, genetic analysis, perioperative and clinic notes were reviewed. Five patients were identified with PSS and abnormalities of TWIST1 consistent with SCS. One patient, with the longest follow-up of 7 years, underwent 5 intracranial procedures and required a ventriculoperitoneal (VP) shunt. The remaining 4 patients underwent posterior cranial vault distraction as the initial procedure, followed by anterior cranial vault remodeling. Two patients required a VP shunt. To conclude, synostosis of the metopic, bicoronal, and sagittal sutures (PSS) appears to be associated with SCS and produces a characteristic skull morphology that can be readily identified on physical examination. Early data suggest a high rate of reoperation, increased necessity for a VP shunt, and potential complications. Of note, this novel phenotype had not been previously observed at our respective institutions, reported in the literature, or observed in association with TWIST1 abnormalities as described in association with SCS [1)].

# Case series

All patients born with Saethre-Chotzen syndrome between January 1992 and March 2017 were included. Evaluated parameters included occipital frontal head circumference (OFC), fundoscopy, neuroimaging (ventricular size, tonsillar position, and the presence of collaterals/an abnormal transverse sinus), polysomnography, and ophthalmological outcomes. The relationship between papilledema and its associated risk factors was evaluated with Fisher's exact test.

Results: Thirty-two patients (21 females, 11 males) were included. Median (SD) age at first surgery was 9.6 months (3.1mo) for patients who were primarily referred to our center (range: 3.6-13.0mo), the median (SD) age at last follow-up was 13 years (5y 7mo; range: 3-25y). Seven patients had papilledema preoperatively, which recurred in two. Two patients had papilledema solely after first surgery. Second cranial vault expansion was indicated in 20%. Thirteen patients had an OFC deflection, indicating restricted skull growth, one patient had ventriculomegaly, and none developed hydrocephalus. Eleven patients had emissary veins, while the transverse sinus was aberrant unilaterally in 13 (hypoplastic n=10 and absent n=3). Four patients had mild tonsillar descent, one of which was a Chiari type I malformation. Four patients had obstructive sleep apnoea (two mild, one moderate, and one severe). An aberrant transverse sinus was associated with papilledema (p=0.01).

Interpretation: Single one-stage fronto-orbital advancement was sufficient to prevent intracranial hypertension for 80% of our patients with Saethre-Chotzen syndrome. Follow-up should focus on OFC deflection and venous anomalies [2)].

# Case reports

A 15-month-old male patient with typical clinical features of SCS in addition to developmental delay, which is a rare complication in SCS. He showed a de novo 0.9-Mb microdeletion in 7p21, in which TWIST1, NPMIP13, FERD3L, TWISTNB, and HDAC9 were included. In comparison with previously reported patients, HDAC9 was suggested to contribute to developmental delay in SCS patients with 7p21 mirodeletions [3)].

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An 11 day-old-girl was transferred to our hospital for surgical treatment of craniosynostosis. Either her fam- ily history or intrauterine growth was not remarkable. In addition to craniofacial deformities such as brachy- cephaly due to bicoronal craniosynostosis, high-arched palate, inferiorly positioned ears and midfacial defor- mity, she was accompanied with cardiovascular anom- alies including patent foramen ovale, patent ductus arteriosus, pulmonary artery stenosis as well as low anal atresia. She underwent general anesthesia for suture craniotomy at the age of one month. After induction of general anesthesia with sevoflurane and confirming adequate mask ventilation, fentanyl and rocuronium were administered. Direct laryngoscopy revealed Cormack-Lehane grade to be 1, followed by orotracheal intubation with a 3.5 mm uncuffed tube. A diagnosis of Saethre-Chotzen syndrome was made at the age of six months based on the result of genetic test She underwent general anesthesia for additional three times for fronto-orbital advancement, removal of the destruction devices and perineal anoplasty at 11, 15 and 16 months, respectively, which was performed uneventfully. She has no physical development disor- ders, with delay in language development at the age of 27 months [4)].

[1)]

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3)

Shimbo H, Oyoshi T, Kurosawa K. Contiguous gene deletion neighboring TWIST1 identified in a patient with Saethre-Chotzen syndrome associated with neurodevelopmental delay: Possible contribution of HDAC9. Congenit Anom (Kyoto). 2018;58(1):33-35. doi:10.1111/cga.12216
4)

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