SAETHRE-CHOTZEN SYNDROME

Otherwise known as?

Saethre-Chotzen syndrome is also known by the following names:

1. Craniofacial Dysostosis – This term refers to the condition's primary feature, which involves differences in skull and facial bone development.
2. Craniosynostosis Syndrome, Type 3 – A term highlighting the fusion of cranial sutures (craniosynostosis) seen in the condition.
3. SC syndrome – An abbreviation used to refer to Saethre-Chotzen syndrome.

Signs & Symptoms

Saethre-Chotzen syndrome is a genetic condition that primarily affects the development of the skull, face, and hands. The severity of the symptoms can vary, but common signs and symptoms include:

1. Craniofacial Features

The most prominent features of Saethre-Chotzen syndrome are related to differences in skull and facial development, due to craniosynostosis (premature fusion of cranial sutures).

- Craniosynostosis: This is the premature fusion of one or more cranial sutures, which can cause a different skull shape. The coronal suture (running from ear to ear) is most commonly affected. This leads to a short, broad skull (brachycephaly) or a tower-shaped skull (scaphocephaly).
- Facial asymmetry: One side of the face may appear different from the other, often due to the premature fusion of sutures.
- Wide-set eyes (hypertelorism): The eyes may appear farther apart than usual.
- Low-set ears: The ears may be positioned lower than usual on the head.
- Beaked nose: The nose may have a more pronounced or "beaked" shape due to the impaired development of the nasal bridge.
- Mild ptosis: Drooping of the upper eyelid (often mild).

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2. Limb differences

- Syndactyly: A common feature of Saethre-Chotzen syndrome is the fusion of fingers and toes (syndactyly). This often affects the third and fourth fingers or toes.
- Short fingers and toes: Some individuals may have shorter fingers and toes compared to their peers.

3. Intellectual and Developmental Features

- Mild intellectual disability: While most people with Saethre-Chotzen syndrome have normal intelligence, some may have mild developmental delays or learning difficulties.
- Speech and language delays: Speech may be delayed, and some children may have difficulty with language skills.
- Motor development delays: There may be slight delays in gross motor skills, such as walking and coordination.

4. Other Physical Features

- Hearing loss: Some individuals with Saethre-Chotzen syndrome may experience mild to moderate hearing loss, often due to ear differences.
- Heart problems: In some cases, individuals may have mild congenital heart problems, though these are not present in every case.
- Skin differences: Patches of thickened skin (cutaneous syndactyly) may be present, especially between the toes.

5. Possible Other Features

- Early fusion of other sutures: In rare cases, other sutures may fuse early, leading to additional cranial differences.
- Cleft palate: A small number of individuals with Saethre-Chotzen syndrome may have a cleft palate, which affects the roof of the mouth.

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Causes

Saethre-Chotzen syndrome is caused by genetic mutations that affect the development of the skull, face, and other body structures. The underlying cause of Saethre-Chotzen syndrome is typically associated with mutations in the TWIST1 gene, which is located on chromosome 7.

1. Genetic Mutations in TWIST1

- TWIST1 Gene Mutation: Most cases of Saethre-Chotzen syndrome are caused by mutations in the TWIST1 gene. The TWIST1 gene encodes a protein involved in the development of bone and tissue during embryonic development. This protein plays an important role in the development of the skull, limbs, and face.
- Gene Function: TWIST1 is a transcription factor that helps regulate the expression of other genes involved in craniofacial and skeletal development. Mutations in this gene can disrupt normal growth and development of the cranial sutures, leading to craniosynostosis (premature fusion of the skull bones). This results in the characteristic different skull shape seen in Saethre-Chotzen syndrome.

2. Inheritance Pattern

Saethre-Chotzen syndrome follows an autosomal dominant inheritance pattern. This means that an individual only needs one copy of the mutated TWIST1 gene to be affected by the condition.

- Inheritance from an affected parent: If one parent has Saethre-Chotzen syndrome, there is a 50% chance of passing the mutated gene to each child, as only one copy of the mutated gene is needed for the condition to occur.
- De novo mutations: In some cases, Saethre-Chotzen syndrome may occur due to a new mutation (de novo) in the TWIST1 gene. This means the mutation is not inherited from either parent but occurs spontaneously in the child.

3. Other Genetic Factors

While most cases of Saethre-Chotzen syndrome are due to mutations in the TWIST1 gene, rarely, other genetic changes or factors may contribute to the condition.

- Other genetic syndromes: In some cases, Saethre-Chotzen syndrome may be associated with other genetic syndromes or chromosomal differences, although this is less common.

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Testing & Diagnosis

The diagnosis of Saethre-Chotzen syndrome is based on a combination of clinical evaluation, genetic testing, and sometimes imaging. A multidisciplinary team of doctors, including geneticists, craniofacial specialists, and paediatricians, may be involved in the diagnostic process.

1. Clinical Evaluation

The first step in diagnosing Saethre-Chotzen syndrome is a thorough clinical assessment. A doctor will review the patient's medical history, family history, and physical features.

Clinical Features:

- Craniofacial differences: These may include craniosynostosis (early closure of sutures), wide-set eyes (hypertelorism), low-set ears, beaked nose, and facial asymmetry.
- Syndactyly (fusion of fingers or toes).
- Short stature and mild developmental delays.
- Speech and language delays.

Based on these features, a doctor may suspect Saethre-Chotzen syndrome, especially if the patient has the characteristic craniofacial features and limb differences.

2. Genetic Testing

The definitive test for Saethre-Chotzen syndrome is genetic testing to identify a mutation in the TWIST1 gene (located on chromosome 7). This gene mutation is responsible for the condition in the majority of cases.

Genetic Testing Steps:

- DNA sequencing: This test involves analysing the DNA to look for mutations or deletions in the TWIST1 gene. A mutation in this gene is the most common cause of Saethre-Chotzen syndrome.
- Chromosomal microarray: This test can detect larger chromosomal deletions or duplications that might affect the TWIST1 gene or other genes involved in craniofacial development.
- Familial testing: If a parent or close family member has already been diagnosed with Saethre-Chotzen syndrome, genetic testing can confirm whether the mutation is inherited or de novo (spontaneous).

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3. Imaging Studies

Imaging studies may be done to evaluate the skull, craniofacial features, and any associated skeletal differences.

- CT scans or MRI: These imaging tests can assess the extent of craniosynostosis (premature closure of skull sutures) and provide detailed information about the structure of the skull and facial bones. They can also help rule out other differences associated with craniofacial development.
- X-rays: X-rays may be used to assess the limbs for signs of syndactyly and to evaluate bone growth or other differences.

4. Family History and Genetic Counselling

Since Saethre-Chotzen syndrome follows an autosomal dominant inheritance pattern, genetic counselling can help assess the risk of passing the condition on to future children. A family history of craniofacial anomalies or syndactyly can suggest a genetic cause and may help in identifying other family members who may be affected.

5. Differential Diagnosis

Because the features of Saethre-Chotzen syndrome can overlap with other genetic conditions, the doctor may also need to rule out similar conditions, including:

- Crouzon syndrome
- Apert syndrome
- Pfeiffer syndrome
- Other craniofacial syndromes

To differentiate between these conditions, genetic testing, imaging, and clinical features must be carefully reviewed.

6. Follow-Up and Multidisciplinary Care

Once the diagnosis is confirmed, children with Saethre-Chotzen syndrome often require follow-up care from a multidisciplinary team that may include:

- Craniofacial surgeons to address craniosynostosis and any necessary surgeries.
- Genetic counsellors for family planning and understanding inheritance risks.
- Speech therapists to help with speech and language delays.
- Orthopaedic specialists for monitoring limb anomalies and evaluating the need for surgical treatment.
- Paediatricians to manage general health and development.

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Treatment

The treatment of Saethre-Chotzen syndrome typically involves a multidisciplinary approach that focuses on managing craniofacial differences, limb anomalies, and any associated developmental or health concerns. Treatment strategies are tailored to the individual's needs, and multiple specialists, such as geneticists, craniofacial surgeons, paediatricians, and therapists, are often involved.

1. Craniofacial Surgery

A characteristic feature of Saethre-Chotzen syndrome is craniosynostosis, where the skull bones fuse too early, leading to a difference in head shape. Surgical intervention is often required to address these skull differences and prevent complications.

Key Surgical Treatments:

- Cranial Vault Reconstruction: This is the most common surgery for children with craniosynostosis due to Saethre-Chotzen syndrome. The goal of this procedure is to release the fused sutures in order to facilitate the growing brain to expand the skull and optimise facial growth. This is ideally done in infancy.
- Facial Surgery: In some cases, facial surgeries may be necessary to address facial asymmetry (uneven facial features). These surgeries may be done in the early years or later in life as the child grows.
- Orthognathic Surgery: If the child experiences issues with the alignment of the jaw, orthognathic surgery may be considered to improve bite and functionality of the mouth.

2. Limb Anomalies Treatment

Many children with Saethre-Chotzen syndrome have syndactyly, or the fusion of fingers or toes. Treatment for limb anomalies generally includes surgical separation of the fused digits.

Limb Treatment Options:

- Syndactyly Repair: Surgery is typically performed to separate the fused fingers or toes. This surgery is done to improve functionality and appearance of the hands or feet.
- Physiotherapy: After surgery, physiotherapy may be needed to help improve movement and dexterity in the affected limbs.

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3. Speech and Developmental Support

Children with Saethre-Chotzen syndrome may experience speech delays or developmental delays due to craniofacial differences or other aspects of the condition. Early intervention can be crucial for addressing these concerns.

Key Supportive Treatments:

- Speech Therapy: A speech therapist can help children with speech delays or difficulties in articulation due to cleft palate or oral motor issues. Therapy may begin early, around 1 to 2 years of age.
- Developmental Therapy: Children may benefit from early intervention programs that help with motor skills, language development, and social skills.
- Special Education Services: For children with learning disabilities or mild intellectual delays, special education services can provide tailored teaching strategies to meet the child's developmental needs.

4. Monitoring and Preventive Care

Children with Saethre-Chotzen syndrome may require ongoing monitoring to address any potential health issues and prevent complications.

Ongoing Care Includes:

- Regular Follow-Up with the Craniofacial Team: To monitor skull growth, facial development, and ensure the child's craniofacial surgery is effective.
- Hearing Tests: Due to potential hearing loss or middle ear problems, children may require regular hearing evaluations, especially if they have low-set ears or ear infections.
- Vision Monitoring: Some children with Saethre-Chotzen syndrome may have vision problems related to the shape of their skull or eyes, and regular eye exams may be necessary.
- Cardiac Monitoring: In cases where congenital heart problems are present, regular cardiac check-ups may be required.

5. Genetic Counselling

Given that Saethre-Chotzen syndrome is inherited in an autosomal dominant manner, genetic counselling is important for families. A genetic counsellor can provide information about the condition, the risk of having another child with Saethre-Chotzen syndrome, and explain inheritance patterns.

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7. Long-Term Follow-Up

Long-term care involves:

- Regular monitoring for any new health concerns or complications.
- Ensuring that the child receives continued speech therapy, educational support, and medical care as they grow older.

Did you know?

In Australia, approximately 1 baby per 100,000 births is diagnosed with Saethre-Chotzen syndrome.*

Saethre-Chotzen syndrome was first described by Swedish physician Hans Saethre in 1931 and later elaborated upon by German physician Otto Chotzen in 1939.

They recognized a pattern of craniofacial and skeletal differences in affected individuals, which was later linked to genetic mutations. The syndrome is now understood to be caused by mutations in the TWIST1 gene, affecting the development of bones and tissues.

References:

*Junaid, M., Slack-Smith, L., Wong, K., Bourke, J., Baynam, G., Calache, H., & Leonard, H. (2022). Epidemiology of Rare Craniofacial Anomalies: Retrospective Western Australian Population Data Linkage Study. J Pediatr, 241, 162-172.e169. https://doi.org/10.1016/j.jpeds.2021.09.060

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How we can support you:

- Care packs
- Financial assistance
- Family support coordinator
- Connection to other families