Pfeiffer syndrome

Pfeiffer syndrome is a genetic disorder 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. Pfeiffer syndrome also affects bones in the hands and feet.

Many of the characteristic facial features of Pfeiffer syndrome result from premature fusion of the skull bones. Abnormal growth of these bones leads to bulging and wide-set eyes, a high forehead, an underdeveloped upper jaw, and a beaked nose. More than half of all children with Pfeiffer syndrome have hearing loss; dental problems are also common.

In people with Pfeiffer syndrome, the thumbs and first (big) toes are wide and bend away from the other digits. Unusually short fingers and toes (brachydactyly) are also common, and there may be some webbing or fusion between the digits (syndactyly).

Pfeiffer syndrome is divided into three subtypes. Type 1, also known as classic Pfeiffer syndrome, has symptoms as described above. Most individuals with type 1 Pfeiffer syndrome have normal intelligence and a normal life span. Types 2 and 3 are more severe forms of Pfeiffer syndrome that often involve problems with the nervous system. The premature fusion of skull bones can limit brain growth, leading to delayed development and other neurological problems. In addition, individuals with type 2 or 3 can have fusion of the bones (ankylosis) in the elbow or other joints, limiting mobility, and abnormalities of the face and airways, which can cause life-threatening breathing problems. Type 2 is distinguished from type 3 by the presence of a cloverleaf-shaped head, which is caused by more extensive fusion of bones in the skull.

Frequency

Pfeiffer syndrome affects about 1 in 100,000 individuals.

Causes

Pfeiffer syndrome is most commonly caused by mutations in the *FGFR2* gene. Mutations in the *FGFR1* gene cause a small percentage of cases of type 1 Pfeiffer syndrome. Mutations in this gene have not been associated with type 2 or 3.

The *FGFR1* and *FGFR2* genes provide instructions for making proteins known as fibroblast growth factor receptors 1 and 2, respectively. Among their multiple functions, these proteins signal immature cells to become bone cells during embryonic development. A mutation in either the *FGFR1* or *FGFR2* gene alters the function of the respective protein, causing prolonged signaling, which can promote the premature fusion of skull bones and affect the development of bones in the hands and feet.

Inheritance Pattern

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Other Names for This Condition

- acrocephalosyndactyly, type V
- ACS V
- ACS5
- craniofacial-skeletal-dermatologic dysplasia
- Noack syndrome

Diagnosis & Management

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Pfeiffer syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1863356/

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22pfeiffer+syndrome%22+OR+%22craniosynostoses%22+OR+%22acrocephalosyndactylia%22

Other Diagnosis and Management Resources

- GeneReview: FGFR-Related Craniosynostosis Syndromes
  https://www.ncbi.nlm.nih.gov/books/NBK1455
- MedlinePlus Encyclopedia: Craniosynostosis
  https://medlineplus.gov/ency/article/001590.htm
- MedlinePlus Encyclopedia: Webbing of fingers or toes
  https://medlineplus.gov/ency/article/003289.htm

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Craniosynostosis
  https://medlineplus.gov/ency/article/001590.htm
- Encyclopedia: Webbing of fingers or toes
  https://medlineplus.gov/ency/article/003289.htm
- Health Topic: Craniofacial Abnormalities
  https://medlineplus.gov/craniofacialabnormalities.html

Genetic and Rare Diseases Information Center

- Pfeiffer syndrome
  https://rarediseases.info.nih.gov/diseases/7380/pfeiffer-syndrome

Additional NIH Resources

- National Institute of Neurological Disorders and Stroke: Craniosynostosis Information Page
  https://www.ninds.nih.gov/Disorders/All-Disorders/Craniosynostosis-Information-Page

Educational Resources

- Boston Children's Hospital
  http://www.childrenshospital.org/conditions-and-treatments/conditions/p/pfeiffer-syndrome
- Cincinnati Children's Hospital Medical Center: Craniosynostosis
  https://www.cincinnatichildrens.org/health/c/craniosynostosis
- Collaboration for Craniofacial Development and Disorders, Johns Hopkins University
  https://www.hopkinsmedicine.org/neurology_neurosurgery/centers_clinics/pediatric_neurosurgery/conditions/craniosynostosis/
- Headlines Craniofacial Support (UK)
  https://www.headlines.org.uk/medical-leaflets/HL7%20Pfeiffer%20Syndrome.pdf
- MalaCards: pfeiffer syndrome
  https://www.malacards.org/card/pfeiffer_syndrome
- Orphanet: Pfeiffer syndrome
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=710
- The Craniofacial Center, Dallas, Texas
  http://thecraniofacialcenter.com/pfeiffer.html

Patient Support and Advocacy Resources

- AmeriFace
  http://www.ameriface.org/
- Children's Craniofacial Association
  https://ccakids.org/
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/pfeiffer-syndrome/
- Resource List from the University of Kansas Medical Center
  http://www.kumc.edu/gec/support/craniofa.html

Clinical Information from GeneReviews

- FGFR-Related Craniosynostosis Syndromes
  https://www.ncbi.nlm.nih.gov/books/NBK1455

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28pfeiffer+syndrome%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- PFEIFFER SYNDROME
  http://omim.org/entry/101600

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