CONDITION

Classic type pfeiffer syndrome

Learn about classic type, or type 1, Pfeiffer syndrome, including skull and limb differences, genetic causes, diagnosis, treatment, and long-term follow-up.

WHAT IT IS
Rare genetic condition affecting skull and limb growth

BODY SYSTEM
Bones, face, hands and feet

MAIN SYMPTOMS
Short wide head, flat midface, broad thumbs, broad big toes

WHAT CAUSES IT
Inherited or new genetic change

HOW IT IS DIAGNOSED
Skull CT and genetic testing

MAIN TREATMENT
Craniosynostosis surgery and multidisciplinary supportive care

CAN IT BE CURED?
No, treatment manages individual problems

IS IT AN EMERGENCY?
Sometimes, with severe difficulty breathing

LONG-TERM OUTLOOK
Generally milder with possible serious complications

Overview

Classic type Pfeiffer syndrome, also called type 1 Pfeiffer syndrome, is a rare genetic condition that affects the growth of the skull, face, hands, and feet. It is present from birth.

In this condition, some of the joints between a baby's skull bones close too early. These flexible joints are called sutures . Early closure is known as craniosynostosis . It can change the shape of the head and limit the space available for the growing brain.

Classic Pfeiffer syndrome also causes broad thumbs and big toes. They may angle away from the other fingers or toes. Some people have partial joining, called syndactyly, between certain fingers or toes.

"Classic" or "type 1" is a historical clinical label. It generally describes a milder pattern than

Pfeiffer syndrome types 2 and 3. People with classic Pfeiffer syndrome do not usually have the cloverleaf-shaped skull associated with type 2, and intellectual development is often typical. However, the condition varies from person to person. Some children still develop important concerns involving pressure inside the skull, breathing, hearing, vision, or dental alignment.

Early assessment matters because skull and airway problems can affect health and development. Care is usually coordinated through a craniofacial team that includes specialists in skull surgery, brain and nerve surgery, genetics, hearing, eye care, breathing, dentistry, and child development.

Symptoms

The features of classic Pfeiffer syndrome may be noticed at birth or during early infancy. Their severity can differ even among relatives with the same genetic change.

Common skull and facial features include:

Shallow eye sockets may cause the eyes to project forward. The eyelids may not fully protect the eye surface in more affected children. This can lead to dryness, irritation, or injury to the clear front layer of the eye, called the cornea.

The thumbs and big toes are usually broad and may point away from the other digits. Fingers and toes may be short. Mild joining of the soft tissues between digits can occur. These differences do not always interfere with walking or hand use.

Some children have hearing loss. This is often related to repeated middle-ear fluid or differences in the ear structures. Hearing difficulties can affect speech development if they are not identified and treated.

A small midface and narrow nasal passages can contribute to noisy breathing, snoring, or obstructive sleep apnea. Sleep apnea means that breathing repeatedly becomes reduced or stops for short periods during sleep. Signs may include restless sleep, pauses in breathing, mouth breathing, daytime tiredness, or behavior and attention difficulties.

Craniosynostosis can sometimes lead to raised pressure inside the skull. Possible signs include persistent or worsening headaches, repeated vomiting, unusual sleepiness, changes in vision, or loss of previously gained developmental skills. Babies may be irritable or feed poorly. These symptoms have many possible causes, but they require medical assessment.

- An unusually short and wide head caused by early fusion of skull sutures
- A tall or prominent forehead
- A flat or underdeveloped middle part of the face

- Widely spaced or prominent eyes
- A small upper jaw, which can make the lower jaw appear prominent
- Crowded teeth or an abnormal bite

Causes and risk factors

Classic Pfeiffer syndrome is caused by a disease-causing change, also called a pathogenic variant, in either the FGFR1 or FGFR2 gene. These genes provide instructions for proteins called fibroblast growth factor receptors. The proteins help control how bone cells grow and mature.

A pathogenic variant can make signaling through one of these receptors overly active. Skull bones may then mature and join too early. The same altered signaling affects development of the face, hands, and feet.

Pfeiffer syndrome follows an autosomal dominant inheritance pattern. This means one altered copy of the gene is enough to cause the condition. A person with Pfeiffer syndrome has a 1 in 2 chance of passing the familial genetic variant to each child, regardless of the child's sex.

Some people inherit the variant from an affected parent. In others, it begins as a new genetic change in the egg or sperm or shortly after conception. This is called a de novo variant. Parents generally did not cause the condition through anything they did during pregnancy.

Family members with the same variant can have different features. Genetic test results cannot always predict exactly which medical concerns a child will develop.

Diagnosis

Diagnosis begins with a medical history and physical examination. A clinician looks at the head shape, facial structure, thumbs, fingers, big toes, and other joints. The child's head growth and development are also reviewed.

Craniosynostosis must be distinguished from positional flattening, which can develop when a baby regularly rests on the same part of the head. Positional flattening does not involve early fusion of skull sutures. A clinician experienced in infant head shape can often recognize the difference, but imaging may be needed.

Low-dose computed tomography, or CT, can show which skull sutures have fused and help surgeons plan treatment. Some centers use ultrasound in young infants when appropriate. Because CT uses radiation, the care team considers whether the information is necessary and

uses techniques intended to limit exposure.

Magnetic resonance imaging, or MRI, may be recommended when clinicians need more detail about the brain, fluid spaces, or the junction between the brain and spinal cord. MRI does not use ionizing radiation, although young children may need sedation to remain still.

Genetic testing can look for variants in FGFR1, FGFR2, and other genes associated with craniosynostosis. Testing may confirm the diagnosis, distinguish it from related syndromes, and provide information for relatives and future pregnancies. A genetic counselor can explain what the result does and does not show.

Additional assessment may include:

Prenatal ultrasound may sometimes identify craniosynostosis or unusual hand and foot features. If a familial genetic variant is known, prenatal or preimplantation genetic testing may be possible. These options are personal and are best discussed with genetics and maternal-fetal medicine specialists.

- Eye examination, including checks of the optic nerves and corneas
- Hearing testing and examination for middle-ear fluid
- Sleep assessment or an overnight sleep study
- Dental and orthodontic evaluation
- Developmental, speech, or learning assessment
- Measurement of head growth and monitoring for signs of raised pressure

Treatment and management

Treatment is based on the child's anatomy, symptoms, age, and development. There is no single treatment plan for everyone with classic Pfeiffer syndrome.

Craniosynostosis surgery creates space for brain growth and reshapes the skull. Depending on the child's age and which sutures are involved, surgeons may use an endoscopic procedure through small incisions or a more extensive reconstruction of the skull and forehead. Some children need more than one operation as they grow.

The operation and its timing are planned by a specialist craniofacial team. Families should receive an explanation of the expected benefits, surgical risks, recovery, and possibility of later procedures.

A child with prominent eyes may need lubricating eye treatments or other measures to protect the corneas. Surgery to move the forehead or midface forward may be considered when eye

protection, breathing, or facial growth requires it.

Airway treatment depends on the cause and severity of breathing problems. Options can include treatment of nasal obstruction, removal of enlarged tonsils or adenoids, positive airway pressure during sleep, or surgery to improve the airway. A sleep study helps the team judge how much obstruction is occurring.

Repeated middle-ear fluid may be managed with ventilation tubes. Hearing aids or other hearing support may be appropriate when hearing loss continues. Regular hearing checks are important because a child may not be able to describe a gradual change.

Dental and orthodontic treatment can address tooth crowding, an abnormal bite, and difficulties related to a small upper jaw. Jaw or midface surgery may be considered later, often after more facial growth has occurred, although severe breathing or eye concerns may require earlier action.

Most thumb and toe differences do not need treatment if they do not limit function. An orthopedic or hand specialist can assess pain, shoe-fitting problems, walking, or difficulty using the hands. Physical or occupational therapy may help with specific functional concerns.

Speech therapy, learning support, and developmental services should be provided when an individual assessment identifies a need. A diagnosis of classic Pfeiffer syndrome does not by itself mean that a child will have an intellectual disability.

Complications

Classic Pfeiffer syndrome is generally less severe than types 2 and 3, but complications remain possible.

Raised pressure inside the skull can damage the optic nerves and affect vision if it is not recognized. Pressure may result from limited skull growth, excess fluid around the brain, breathing-related changes, or a combination of factors.

Shallow eye sockets can leave the corneas exposed. Chronic exposure may cause pain, scarring, or reduced vision. Eye-muscle imbalance, known as strabismus, is also possible.

Midface underdevelopment can narrow the upper airway and contribute to obstructive sleep apnea. Untreated significant sleep apnea may affect daytime behavior, learning, growth, and heart or lung health.

Hearing loss may interfere with speech, language, school performance, and social interaction. Dental crowding and an abnormal bite can make chewing and oral hygiene more difficult.

Some children develop hydrocephalus, which is an abnormal buildup of fluid in the brain's fluid

spaces, or a Chiari malformation, in which part of the lower brain extends into the opening at the base of the skull. These problems are assessed and treated by neurosurgical specialists when present.

Multiple appointments, visible differences, or surgery can also affect emotional well-being. Age-appropriate explanations, school support, peer connections, and mental health care can be valuable parts of treatment.

Follow up

Long-term follow-up is usually provided by a craniofacial team. Visits may monitor head growth, skull shape, vision, hearing, sleep, breathing, dental development, speech, learning, and emotional health. The schedule changes with age and with the child's medical needs.

Routine follow-up is important even when a child seems well. Raised skull pressure, hearing loss, and sleep apnea may develop gradually and may not cause obvious early symptoms.

Contact the care team promptly for new or worsening headaches, repeated morning vomiting, changes in balance, declining school performance, developmental regression, increased snoring, breathing pauses during sleep, new eye pain, or changes in vision. These concerns are not always caused by Pfeiffer syndrome, but they deserve assessment.

Seek emergency care for severe difficulty breathing, blue or gray coloring, a seizure, sudden loss of vision, a serious eye injury, inability to close the eyelids over the eye, or a severe headache with repeated vomiting, confusion, or unusual difficulty waking.

As adolescents move toward adult care, follow-up may shift to adult craniofacial, dental, eye, hearing, sleep, and genetics services. Genetic counseling can help affected adults understand inheritance and reproductive options without directing personal decisions.

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