Klippel-Feil syndrome

In 1912 Maurice Klippel and André Feil described a syndrome that is now called Klippel-Feil syndrome (KFS).[1]

What causes Klippel-Feil syndrome? (Aetiology)[1]

Klippel-Feil syndrome (KFS) is caused by a failure in the normal segmentation with fusion of the cervical vertebrae during the early weeks of fetal development. Klippel-Feil syndrome is a rare skeletal anomaly characterised by abnormal fusion of two or more vertebrae.[2]

KFS is thought to be the result of a genetic mutation in one of the following genes:

- Growth differentiation factor (GDF) 6 or 3 (autosomal dominant). The GDF genes are both associated with the transforming growth factor beta (TGF-β) family of proteins. GDF6 is associated with growth and maturation of bone and cartilage, whereas GDF3 is known to play a role in ocular and skeletal development.
- Mesenchyme homeobox (MEOX) 1 (autosomal recessive). The MEOX1 gene has been shown to play a significant role in somitogenesis; and MEOX1 mutations have displayed similar Klippel-Feil findings in mice.

Any of the cervical vertebrae can be involved but the most common fusion is of C2-C3. There are three types of KFS:

- KFS 1: autosomal dominant; caused by mutation in the GDF6 gene on chromosome 8q22.
- KFS 2: autosomal recessive; caused by mutation in the MEOX1 gene on chromosome 17q21. C5-C6 fusion is more likely to be an autosomal recessive disorder.

- KFS 3: autosomal dominant; caused by mutation in the GDF3 gene on chromosome 12p13.

KFS has also been shown to be associated with numerous skeletal defects and other anomalies.

- Common skeletal findings include Sprengel deformity (congenital elevated scapula) and scoliosis.
- Other defects include anomalies within the urogenital system, cardiovascular system and deafness.

A widely held concern regarding fused segments amongst the cervical vertebrae, is the resultant pressure or increased force on the adjacent mobile segments. It has been postulated that subsequent hypermobility of these adjacent segments could lead to advanced degenerative changes causing cervical myelopathy and neurological injury.

Classification

There are three types of cervical vertebral fusion:

- **Type I** is massive fusion of many cervical and upper thoracic vertebrae into bony blocks.
- **Type II** is fusion at only one or two interspaces, although hemivertebrae, occipito-atlantal fusion and other anomalies might also occur.
- **Type III** is both cervical fusion and lower thoracic or lumbar fusion.

Since Feil's first classification of KPS into these 3 types (I – III), other classification systems have been advocated to describe the anomalies, predict the potential problems, and guide treatment decisions.[3]

Klippel-Feil syndrome epidemiology

It is believed that KFS occurs in 1 out of 42,000 births.[4]

However, the true incidence of this condition has not been properly assessed and may vary between populations. In addition, not all cases are recognised. One study found the prevalence of Klippel-Feil syndrome amongst 831 paediatric patients, who underwent cervical CT imaging over a 3-year period, was 1.2%. [1]

Klippel-Feil syndrome symptoms (presentation)

Clinical presentation is varied because of the many associated syndromes and anomalies that can occur. Presentation may occur at any time in life, often as an incidental finding.

The 'clinical triad' findings, which are short neck, low posterior hairline and a limited cervical range of motion, only occur in around 50% of people with KFS. [4]

- Upper cervical spine involvement tends to present at an earlier age than involvement of the lower cervical spine.
- Decreased range of movement of the neck is the most consistent finding with loss of rotation being more pronounced than loss of flexion and extension.
- A low hairline occurs in 40-50%.
- About 20% have neurological problems. These may be produced by hypermobility. Some patients present with pain. Scoliosis may be congenital or acquired and affects around 60%. Sometimes there is a compensatory scoliosis. High cervical abnormalities can cause acute spinal cord compression following comparatively minor trauma.
- Synkinesia is mirror movement of the upper extremity, in which patients are unable to perform a movement of the right hand without performing the same movement of the left hand. This is disabling in everyday activities. It may be improved with therapy and usually improves with age.
- Associated abnormalities may include scoliosis, spina bifida, anomalies of the kidneys and the ribs, cleft palate, respiratory problems and heart malformations. There may also be abnormalities of the head and face, skeleton, genitals, muscles, brain and spinal cord, arms, legs and fingers.

- Many and varied abnormalities of the renal system have been reported in as many as a third of cases.
- Torticollis and facial asymmetry affect between a quarter and a half of all those who have KFS.
- Cardiovascular anomalies occur in 15-30% of cases. The most common problem is ventricular septal defect.
- Less common associations include congenital limb deficiencies, craniosynostosis, ear abnormalities and hearing impairment, and craniofacial abnormalities.

Investigations[1]

The extent of investigation will depend upon the age of presentation, the nature of the problem and other confounding issues. It may be part of assessing the need for surgery to stabilise the neck. Such surgery carries risks, and intubation for anaesthesia can be dangerous.

- Anteroposterior (AP) and lateral views of the cervical spine are basic. If abnormalities are present, careful assessment of the atlanto-occipital joint is required. Various other views may be required.
- CXR may show cardiac abnormalities or fusion of ribs.
- CT scan can be very useful at the base of the skull, especially if abnormalities are unilateral.
- MRI scan is useful to assess the spinal canal and any abnormalities of the spinal column, such as syringomyelia.
- Ultrasound is used for imaging of the urinary tract. Intravenous pyelogram (IVP) may also be required.
- All children should have an assessment of hearing.

Klippel-Feil syndrome treatment and management

Because of the varied severity and associated complications, the management is very variable and individually based.

Musculoskeletal management varies from modification of activities to extensive spinal surgery.

- Associated abnormalities - eg, cleft palate and/or heart or renal anomalies - may require surgical correction.
- Management of hearing impairment when required.
- Avoidance of trauma is important. A person with no neck may seem an ideal candidate for the front row of a scrum but this would be extremely dangerous.
- Genetic counselling may be required.
- Cervical deep muscle strengthening has been shown to improve the stability of the hypermobile cervical spine and also help to decrease mechanical stress applied around the spine, thereby alleviating pain. [5]

Surgery

Surgical intervention may be required in a variety of situations:

- Fusion anomalies and the difference in growth potential between the two sides of the spine can make deformity progressive.
- Instability of the cervical spine requires fixation. Instability of the cervical spine can develop between two sets of fusion anomalies separated by a normal segment.
- Neurological deficits or persistent pain require surgery.
- Development of a compensatory curve in the thoracic spine may require surgical intervention or bracing.
- Symptomatic spinal stenosis may require decompression and fusion.

One review found that the prevalence of patients with Klippel-Feil syndrome requiring surgery was 18.5%, with the majority undergoing posterior cervical surgery. [6]

NB: Careful pre-operative examination and preparation for difficult airway management are important for these patients, especially those with micrognathia. [7]

Prognosis

The prognosis for KFS depends on the specific associated anomalies.

Further reading

- Menger RP, Rayi A, Notarianni C; Klippel Feil Syndrome. StatPearls, Sept 2022.

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