

Klippel-Feil Syndrome

Abstract

Klippel-Feil syndrome (KFS) is a congenital condition brought on by a genic mutation that mostly affects the spine. Patients with KFS commonly present with a short neck, low hair line and limited mobility in the neck. There are many other symptoms associated with KFS such as fused vertebrae, stenosis in the spine, extra bone growth and the rare occurrence of lesions. Many of the problems associated with KFS occur later in life such as loss of sensory and motor control in the limbs caused by gradual stenosis in the spine or shifting in unstable vertebral joints causing pressure on the nerves. KFS is uncommon (1 in 40000 to 42000), and is only evident in patients who have received the genetic anomaly from both parents. KFS is divided into three categories depending on how many vertebrae are fused and where they are in the spine.

Introduction

Klippel-Feil syndrome (KFS) is an unusual skeletal malformation also known as synostosis of the cervical spine.¹ KFS is characterized by the fusion of at least two cervical and/or thoracic vertebrae. It occurs in around 1 in 42 000 births worldwide and is a congenital cause of difficult airway.² KFS is thought to be caused by a mutation in either the MEOX1 gene or the GDF6 and GDF3 genes.^{3,4} The syndrome can be random or inherited through the family line and is most commonly known for the failure of normal segmentation resulting in the fusion of the mesodermal somites during 3rd and 8th weeks of embryonic development.⁴

Patients with KFS usually present with; short neck, low hairline, and fusion of the cervical spine. Less than 50% of patients will have all three of these clinical features. These abnormalities are usually present from birth but there are symptoms and repercussions of these conditions that may not show themselves until the patient is older. Commonly patients with

synostosis of the cervical spine complain of head and neck pain, radiculopathy, and decreased range of motion in the neck.⁵

Classifications

According to Klippel and Feil, the syndrome can be divided into three different classifications based mainly on where the spinal fusions are located:

Type I: Cervical and upper thoracic spinal fusion. There can be two or more groups of vertebrae fused together or multiple vertebrae fused into one large bone.

Type II: One or two interspace fusions, often associated with hemi vertebrae and occipitioatlantal fusion

Type III: Both cervical and lower thoracic or lumbar fusions.⁴

These different classifications are based on the different areas of bone fusion but they all have related soft tissue issues that may not all fit in two these three types. Some soft tissue problems such as neuropathy and pain are found in all three classifications.

Case Study 1

Klippel-Feil syndrome is a congenital condition characterized by a lack of development in the cervical spine. Some of the symptoms of KFS are; short neck, low posterior hair line and limited head movement. According to Bayrakli et al⁶, KFS only seems to have anomalies in the growth of bone in the cervical region in humans. There is, however, evidence that it affects bone in the thoracic spine also. This view is not shared by everyone. There are, however, no signs that there is a lack of brain development in patients with KFS.

These conditions are caused by a failure of the vertebrae to separate completely during development. Bayrakli et al⁶ explain their findings on KFS2, a recessive subtype of KFS. Their

research shows that a mutation in the MEOX1 gene on the chromosome 17q21.21 is the root cause of these malformations. Genetic testing on children of a family with a consanguineous marriage or a marriage between two people who share a similar bloodline who both had KFS2 and were found to have this same mutation in the MEOX1 gene.

Findings showed that the parents and several of the unaffected members of the family displayed none of the symptoms where the seven family members with this condition all had the same mutation. In addition to the short neck, low posterior hair line and limited head movement, 3D images from CT as well as full spine images from MRI showed bony ankyloses or fixation between the atlas and occipital bone, fusion between C1 and C2 and omovertebral bone between the scapula and the vertebrae which is responsible for a condition called Sprengel's deformity. Research with these family members as well as mice showed that two genes, MEOX1 and MEOX2 were critical and that MEOX2 would compensate for the lack of MEOX1 in the muscle development but not in bone growth. The mice in the study showed bone anomalies throughout the entire spine but in humans the symptoms were only found in the cervical spine according to Bayrakli et al.⁶

The test showed that genetic mutations as small as a change in one nucleotide can cause one amino acid substitution in a protein and produce symptoms such as the bone anomalies in KFS2 when those mutations are amplified down a genetic line through consanguineous relationships. It also showed that a mutation in the MEOX1 gene is the prime cause of these mutations. They found other mutations in the same group but the MEOX1 was the only gene to effect the bone changes that were so evident in CT and MRI. While the test was running several other families with the same KFS2 syndrome were discovered and added to the study. To assure

the veracity of their findings Bayrakli et al⁶ studied 100 unrelated subjects and found no sign of the gene mutation in any of them.

Signs and Symptoms

There are many less common conditions associated with KFS that include; deformities of the skull, face, spine, and extremities, as well as abnormalities of the genitourinary, cardiac, respiratory, auditory or central nervous system.⁷ Some abnormalities associated with the skeletal system are cervical ribs and the existence of omevertebral bone. Omevertebral bone is rib-like bone that fuses a vertebral lamina with one of the scapula² (see **Figure 1**). This extra bone growth can be surgically removed.

Though x-ray and CT are the most utilized modalities used in the diagnosis of KFS, Magnetic Resonance Imaging (MRI) and Ultrasound can be very useful in identifying soft tissue problems that may trouble a KFS patient. As an example; an MRI of a 31 week gestation fetus showed a large occipital meningoencephalocele, no kidney on the left side and marked dilation of the duodenum. After birth sonograms showed a left pelvic kidney posterior to the bladder and the meningoencephalocele was able to be surgically repaired. The use of MRI can also establish the absence of cervical disks indicating these vertebral fusions in KFS.⁸

Patients with KFS can also be found to have Sprengel's deformity, a condition, seen well on x-ray, where the scapula sits higher on one side of the patient's back than the other. There are also cases where Sprengel's deformity is bilateral. This is believed to be caused by a lack of development before birth where the shoulder never drops completely down into its normal position on the neck.⁴ Sprengel's deformity causes difficulty in movement of the arms and shoulders.

Dermoid or epidermoid cysts have also been prevalent in patients with KFS causing neurologic deficits in different areas of the body depending on the location of the growth. Although these cysts are usually located in the posterior fossa, some have been reported extending from the posterior fossa down to the upper cervical spine and there have even been rare cases where they extend down to the upper thoracic spine.¹⁰ Patients with these cysts will present with extremity paresthesias associated with progressive paraparesis. These, as with other soft tissue issues are identified and diagnosed best with MRI and Ultrasound.

Challenges in Patient Care

Due to differences in anatomy, the care of Klippel-Feil patients can be difficult. A patient with limited range of cervical movement and vertebral instability can be at risk of neurological damage during laryngoscopy, intubation and positioning for surgery.² Minor trauma can make non-fused vertebral segments excessively mobile and unstable causing neurologic symptoms which may or may not be permanent.⁴ Most neurological manifestations are derived as a consequence of chronic compression of cervical spinal cord, pons, medulla, and stretching of cranial nerves.¹ Even the use of fiber optic intubation can be unsuccessful due to excessive angulation between the nasopharynx and glottis.⁹ The ability to view the airway and actually see the differences in anatomy can be highly valuable.

Though the symptoms associated with KFS are wide and varied, many of them can be successfully improved through surgery or avoided all together with special care of the patient. Problems with neuropathy and chronic pain can be alleviated by correcting the stenosis or realigning any vertebrae that may have shifted through surgical fixation. The joints between each vertebra in the body allow for only a slight amount of movement, so when a person moves their neck or turns their head, it takes the combined movements of all the joints in the neck for the

person to have a full range of motion. Because a KFS patient may have two or more vertebrae fused together the other vertebrae may be at risk of serious damage even with minor trauma. The non-fused joints in the spinal column may be forced to move beyond their individual range of motion. The results can be catastrophic. Even small movements involved in positioning a patient for surgery or an examination may cause damage to the spine, subsequently great care must be taken when handling a patient with KFS.

Due to the abnormal shape and anatomy, airway management in pediatric patients with KFS can be difficult for an anesthesiologist especially if the patient is unable or unwilling to cooperate. Numerous associated anomalies such as scoliosis, cleft palate, respiratory problems, deafness, genitourinary abnormalities, Sprengel's deformity, synkinesis (involuntary muscular movements), cervical ribs, and congenital heart diseases may further add to the difficulty.¹

The greatest difficulties with KFS lie in the secondary effects on the nervous system, which usually present with features of progressive cord and brain stem compression even with relatively minor trauma.⁴ For example; one patient developed a progressive slurring of speech, difficulty chewing and swallowing along with choking spells, weakness and atrophy of the thumb and index finger. His soft palate was sagging with absent gag reflex. All from a minor fall. Another patient showed low Compound Motor Action Potential in both facial nerves and denervation potentials in right upper limb suggestive of anterior horn cell disease. There are many more examples but cases such as these are very common.⁴

Basilar invagination caused by cranial migration has been known to cause progressive quadriparesis and actually increase tone in all four limbs. MRIs of KFS patients with basilar invagination, or upward movement of the C2 vertebra, have revealed large fourth ventricular lesions, some extending from the region of foramen magnum to the posterior third ventricular

and posterior interhemispheric regions. In one case, the space available for the spinal cord at the foramen magnum was only 3.4 mm.¹¹

Case Study 2

A 47-year-old female was seen for progressive gait disturbance or problems in her normal gait pattern while walking. She had been diagnosed with KFS at 1 year of age. Two months before visiting the physician, the patient developed bilateral lower extremity paresthesias (tingling or burning) along with progressive paraparesis (weakness).¹⁰ She had the traditional short webbed neck, low occipital hairline, and restricted neck mobility. However, she did not complain of any neurological deficits in her upper extremities.

On examination the patient showed signs of bilateral proximal paresis or partial inability to move in the iliopsoas and quadriceps muscles with marked patellar hyperreflexia, a condition that can include uncontrolled switching.¹⁰ The patient also had loss of position and vibration sensation in the distal lower extremities including the ankles but not all the way to the knees. She exhibited decreased pin-prick sensation on the left half of her body from the clavicle down and on the right from the lower thorax down. During testing the patient had difficulty with tandem gait, falling to either side, while finger-nose-finger testing stayed steady.¹⁰ Plain cervical x-rays showed fusion of all vertebral bodies from C2 down to T6. (see **Figure 2**) No notable instability was seen at occiput-C1 or C1-C2 a problem which is often found with KFS.

Computed tomography (CT) images confirmed the fusion of the cervical vertebrae and showed a circumscribed lesion lying behind the fourth ventricle and extending down to the T1 vertebrae. In the posterior fossa, the lesion blocked the foramen of Magendie, an opening in the roof of the fourth ventricle of the brain that creates a passage for cerebrospinal fluid, resulting in secondary obstructive hydrocephalus.¹⁰ Magnetic resonance imaging (MRI) showed a

craniocervical mass that measured 3.2 cm by 8.4 cm. The lesion deformed the medulla, displacing it caudally.

The patient was then prepared for surgery. During preparation of the sub-occipital region, a small dimple located below the occipital region was found. A craniectomy and cervical laminectomy was performed to expose the lesion.¹⁰ The normal anatomy of the patient was then found to be distorted, the posterior parts of the cervical spine down into the thoracic spine, including the C2-T6 spinous processes, laminae and facet joints were fused into one mass of bone.¹⁰ After performing a laminectomy and opening the dura, a large cystic mass with yellowish fluid, hair and keratin debris was found, and diagnosed as a dermoid tumor.¹⁰ These can be found to have hair, soft, tissue, bone and even teeth.

X-rays done during the first week after the surgery showed no instability in the vertebrae. Six years later the patient was said to be doing well and symptom-free. No evidence of tumor recurrence was found on follow up MRI studies.

Several neuronal tissue anomalies have been found in KPS patients including: diastematomyelia, syringomyelia, agenesis of the corpus collosum, meningocele, cervical occult spina bifida, intramedullary lipoma, extradural hemiangiolipoma. However, intracranial or spinal tumors with KFS are rare.¹⁰

Interesting Facts

Some research has been done with the purpose of diagnosing historical figures who may also have suffered with KFS. One study claimed that the famous Egyptian pharaoh of the 18th dynasty – Tutankhamun or King Tut may have had KFS. The hypothesis was rejected in another study from a group while assessing the skull and cervical spine radiographs to determine the cause of death, but controversy on the subject still exists.³

Conclusion

While Kippel-Feil syndrome is a congenital condition and has no cure, the prognosis is not grave. There are a wide and varied number of symptoms associated with KFS that can be cured or repaired through surgery. The neural deficits and chronic pain that some patients experience can be greatly lessened even if the symptoms appear to be quite severe. People with KFS are at higher risk of injury even in situations that would otherwise be inconsequential. Though rare, it is crucial that KFS is diagnosed and caution should be taken in the treatment and care of these patients. Due to the differences in shape and anatomy of patients with KFS some procedures that may be routine with another patient can prove difficult. Studies have shown that KFS is a genetic, though rare condition, and tends to run through family lines although it can, in rare cases, occur in a patient that has no family history of the condition. It doesn't always present itself in every generation and even if one sibling demonstrates symptoms, the rest of the family may be symptom free.

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Figures

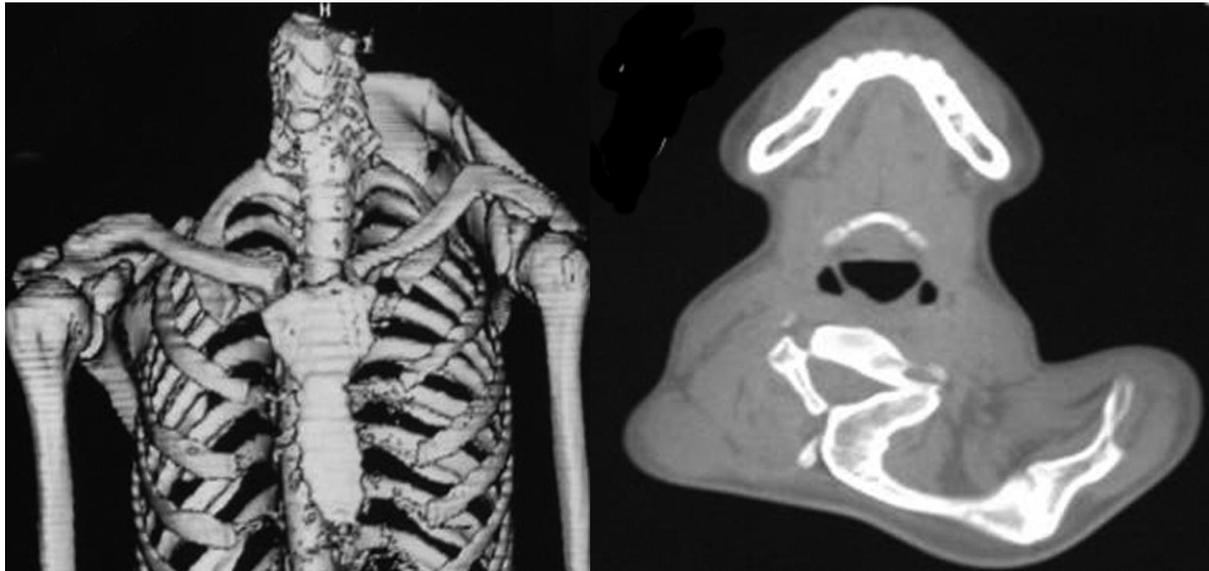


Figure 1. (a) A three dimensional CT scan of cervical spine and thorax confirmed fusion of C4-7 vertebrae with raised left scapula, (b) An omovertebral bar connecting left scapula to vertebral lamina. Images courtesy of: Ahuja V, Kazal S, Gombar S, Thapa D, Bahadur R. Glidescope® for predicted difficult airway in Klippel-Feil Syndrome. *J Anaesthesiol Clin Pharmacol* 2012;28(4):532-534,doi: 10.4103/0970-9185.101953.

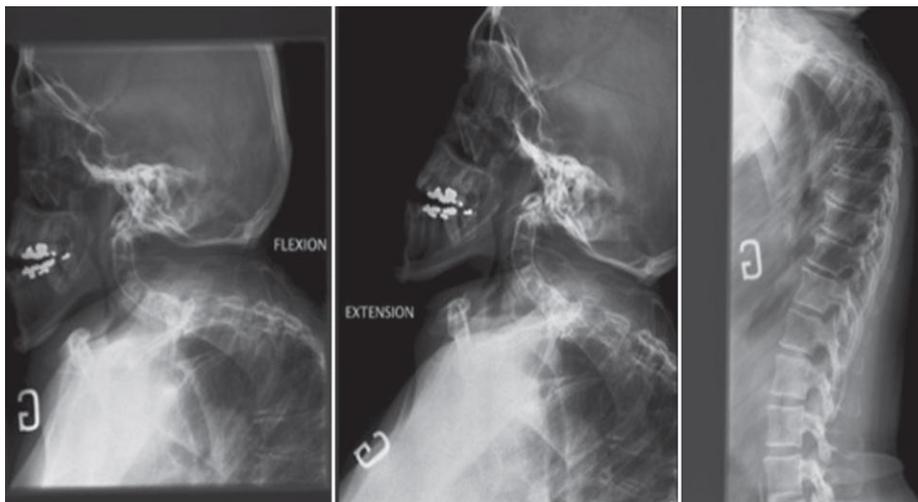


Figure 2. Radiographs of the cervical and thoracic spine demonstrating fused vertebral bodies from C2 down to T6. Significant kyphosis is also shown at the higher thoracic spine level, images courtesy of: McLaughlin N, Weil A, Demers J, Shedid D. Klippel-Feil syndrome associated with a craniocervico-thoracic dermoid cyst. *Surg Neurol Int* 2013;4(3):S61-S62,doi: 10.4103/2125-7806.109440.

