Klippel-Feil Syndrome "Plus"
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Abstract
We report a case with Klippel-Feil (KFS) syndrome associated with hypertelorism, microtia, Sprengel deformity, hand and feet deformities, scoliosis, clinical manifestations of Klippel-Trenaunay syndrome, other anomalies, and severe arterial hypertension secondary to renal artery stenosis. This patient underwent for surgical revascularization unsuccessfully, we have hypothesized that for patients with KFS and unilateral renal artery stenosis medical treatment with ACE inhibitors can provide more benefits than surgery or percutaneous transluminal angioplasty. In order to get better results in the management of this patients all underlying problems should be proper identified before send patient for any kind of surgery, it is important to bring this problems to the anesthesiologist's attention for a very careful manipulation of the neck and head during induction of anesthesia. The final results will be strongly related with the capacity of management of the underlying cardio-respiratory, renal, and nervous system problems but the family physician should decide in which order of priority surgical or medical intervention should be done. We propose the term of Klippel-Feil syndrome "Plus" for those patients with cervical vertebral fusion and many other associated deformities rather than to add another eponym to the long lists that already exist. From our knowledge this is novel combination no previously reported to the medical literature.

INTRODUCTION
Maurice Klippel and Andre Feil described Klippel-Feil syndrome (KFS) independently, in 1912. Later, Feil (1919) classified the syndrome in three different categories as follow: Type I (40%) is present when are fusion in most of the vertebral bodies. Type II (45%) is present when the fusion of 1 or 2 vertebrae occurs, fusion of C2-3 is dominant and fusion C5-6 is recessive, when there are associated thoracic and lumbar spine anomalies, then is type III (12%). KFS type IV (3 %) has been proposed for associated sacral agenesis.

Those cervical anomalies are due a failure of normal segmentation of cervical somites during the third and eight weeks of gestation. The incidence and prevalence of KFS have not been established and its etiology in spite of a great variety of hypothesis such as genetic, vascular, global fetal insult etc. remains unknown. Most of the patients present with decrease flexion and extension of the neck and almost complete inability to rotate the neck that is short on examination, and a low hairline is also observed. Various mechanisms of neural complications have been studied in the literature: medullary abnormality, spinal instability, narrowing of the cervical canal, and vascular dysfunction. Sometimes neurological problems due to craniocervical junction anomalies like Arnold Chiari malformations type I, platybasia, or basilar invagination can be seen. Other common problems associated to KFS are: scoliosis (60%), spinal bifida, cleft palate, ptosis of the eyes, Duane's eye contracture, lateral rectus palsy, facial nerve palsy and cleft palate, syndactyly, hypoplastic thumb, supernumerary digits, hypoplasia of the upper extremity, cervical stenosis, C1-C2 hypermobility and instability, cervical dysraphism, diastematomyelia, intracranial tumors, spinal cord abnormalities (Syringomyelia 15%), traumatic paraplegia, deformity of Sprengel (36%), omovertebral bone, ear abnormalities, hearing loss (38%), torticollis and facial asymmetry (45%), craniofacial dysostosis, cardiovascular anomalies (interventricular septal defect: 20%) genito-urinary- Up to 65% to such as: hydronephrosis, renal ectopia, renal agenesis (most common), horseshoe kidney, double collecting system, bilateral tubular ecstasies.

Several types of combined malformations such as: KFS + frontonasal dysplasia + Sprengel deformity + widely spaced nipples + psotaxial hexadactily of the left foot, KFS +
malformations of laryngeal cartilages, KFS + microtia + conductive hearing loss + bilateral restriction to supination and elbow flexion of the forearms, KFS + Sprengel anomaly + omovertebral bone + thumb abnormalities + flexion-crease changes, KSS + vertebral dissection, KFS + cervicomedullary neuroschisis + mirror movements, KFS + hypogonadotropism-anosmia (Kallmann syndrome), KFS + deafness + ocular motility disturbances (abducen's paralysis and retraction or adduction (Duane's retraction) also known as cervico-oculo-acoustic or Wildervanck syndrome, Klippel-Feil syndrome + azoospermia + renal abnormalities (an analogue of MURCS), among others, can be observed.

Medical and/or surgical treatments are dependent upon the congenital anomalies present in the syndrome. Undiagnosed hidden anomalies are close related with poor prognosis.

We report a case with some of the before-mentioned anomalies plus renal artery stenosis (RAS). From our knowledge this is novel combination no previously reported to the medical literature.

CASE REPORT

His family doctor refers a 15-years-old male patient to Neurology Out Patient Clinic. The referral doctor requested for this patient to be assessed for disability grand. The patient denied any complaint however is sent to admission because some physical anomalies were observed. The patient was born as the fourth child to healthy non-consanguineous parents. The family history was unremarkable. Pregnancy and birth were normal. When he was near the age of 4 years someone noticed a “funny elevation of the right shoulder” but no growth deficiency in stature is noticed. At admission his weight was 57 kg, his height 160 cm, and his head circumference 57 cm. On the face hypertelorism and mild micrognathia were observed, high narow palate, bilateral microtia (incompletely formed ear), short neck, and low hairline were also seen (Figure 1 with patient consent).

General examination also showed a remarkable chest asymmetry with Kyphoscoliosis, muscle wasting on the left arm, hand, and wide separation between 3rd finger and 4th finger (Figure 2). On the lower limbs: mild gigantism of the right big toe, lymphedema of the feet and port-wine stain and “birthmark” (cutaneous capillary malformations) were well defined, the nails and teeth were normal. He was well orientated and no language or speech problems were detected, recent memory and sensory attention were altered, and mild-moderate mental retardation were confirmed, motor system examination showed a decreased muscle power in proximal region predominantly with symmetrical hypotrophy on the left arm, and muscle wasting on the right suprascapular area. Apart from BP 170/129 mmHg, cardiorespiratory system showed unremarkable clinical findings. The inferior border of the liver is palpated at 4 cm below the right inferior costal margin.
Complementary exams showed: Normal full blood count, urea and electrolytes, glucose, creatinine, liver function tests, thyroid function tests, kidney function tests, were within normal limits. Radiographic studies showed vertebral fusion between C6-7, moderate scoliosis, Springer deformity, left omovertebral bone, on X-Rays of the craniocervical region, the superior border of C2 is 6 mm above Chamberlain’s line. CT Scan of the brain showed remarkable radiological signs of leucodistrophy in the cerebral hemispheres bilaterally. CT Angiography showed a right RAS (Figure 3); the patient is transferred to another hospital for surgical treatment where he died soon after operation.

ETHICAL CONSIDERATIONS

Informed consent was obtained and confidentiality retained.

DISCUSSION

Klippel-Trenaunay syndrome or Klippel-Trenaunay-Weber syndrome (KTWS), is generally accepted, when there are enlargement of the soft tissue, bony hypertrophy, port-wine stain, venous malformations and lymphatic abnormalities; in our patient we could not investigate arterio-venous fistulae by phlebography and arteriography because patient died before to do that. KTWS is an uncommon disease (around 310 cases have been published) due to a congenital malformation of the deep venous system with agenesis, hypoplasia or segmental atresia, the etiology is not clear however seems to be related with diffuse mesodermal abnormalities during fetal development and genetic mutations. In 1993, one patient with associated renal artery aneurysm is reported. We can not proof what relationship exist between KFS and KTWS, if there is any, but we know that KFS is associated to different other anomalies, reason why we prefer to nominate it as KFS “plus.” considering that it is an anecdotic coincidence.

Hypertelorism (Hp) presents as abnormal increase in distance between the eyes due to development arrest the greater wings of the sphenoid bone, which is sometimes associated to Sprengel deformity, and some other anomalies of the skull. It is often incorrectly diagnosed when a flat nasal bridge, epicanthal folds, external strabismus, widely spaced eyebrows, blepharophimosis, or some combination of these is present. Our patient presented a combination of anomalies not described in Greig's ocular hypertelorism.
syndrome and Hp in G, Opitz-G, or BBB syndrome combine
apert syndrome, and pfeiffer syndrome were also excluded.

present in stickler syndrome, Saethre-Chotzen syndrome,
retinal detachment, some degree of cleft palate, usually
Sheldon syndrome are can also be ruled out. Cataracts,
syndrome, Treacher-Collins syndrome, and freeman-
underdeveloped nose cartilage on the other, Miller
contracted muscles of the joints of the fingers and hands, and
of the lower eyelids for one side and a flat face, club feet,
Sequence is ruled out. In absent of cleft palate and drooping
spite of micrognathia), then Pierre Robin Malformation
were not related with oculoauriculovertebral dysplasia
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KIDNEYS
Abnormalities of the kidneys increase in frequency when
there are auricular deformities, particularly when the patient
is afflicted with other manifestations of facial
underdevelopment; many patients have hypoplasia or
vaginal agenesis, and abnormalities of their collection
systems. However, they can easily live with just one kidney,
to see patients with microtia and any life-
threatening renal consequences from these system
abnormalities is very uncommon, of course living with
extremely high diastolic hypertension has a different
prognosis. Cervical spine anomalies are more common in
microtic patients if other “midline defects” exist, such as
cardiac or renal disorders or cleft lip and palate but when
associated neurological symptoms are not present, the
frequency of these vertebral abnormalities are
underestimated. We considered that microtia in our patient
were not related with oculoauriculovertebral dysplasia
(Goldenhar’s syndrome) because he didn’t had cleft palate
and ocular dermoid among other differences. Because there
are not Cleft Palate, breathing problems and glossophtosis (in
spite of micrognathia), then Pierre Robin Malformation
Sequence is ruled out. In absent of cleft palate and drooping
of the lower eyelids for one side and a flat face, club feet,
contracted muscles of the joints of the fingers and hands, and
underdeveloped nose cartilage on the other, Miller
Syndrome, Treacher-Collins Syndrome, and Freeman-
Shelelson syndrome are can also be ruled out. Cataracts,
retinal detachment, some degree of cleft palate, usually
present in Stickler syndrome, Saethre-Chotzen syndrome,
Apert Syndrome, and Pfeiffer Syndrome were also excluded.

Because no evidence of ventricular septal defects and
conduction-system abnormalities were detected, we ruled
out Holt-Oram syndrome.

HYPERTENSION AND RAS
Inverse situation like postural hypotension in patient with
cervical cord compression (C2-C3) and selective damage of
the descending autonomic fibers due to craviocervical
anomaly and KFS, has been reported. 

Approximately one-fifth of the South African population has
hypertension; the national prevalence rate of 21 % is
equivalent to other industrialized countries and greater than
that many developing countries; nearly half South African
population still rural and much of the African urban
population now rapidly adopting Western lifestyle habits
therefore prevalence rates will increase with time. 

Prevalence of secondary hypertension remains unknown and
severe hypertension due to RAS and an associated KFS had
not been before-cited; to the best of our knowledge this is
the first report on this type of association in the medical
literature. Constriction of the renal artery leads to a cascade
of important hemodynamic and humoral events within the
affected kidney, stenosis of the renal artery reduces
perfusion pressure releasing rennin, augmenting intrarenal
angiotensin II production which increase systemic
vasoconstriction and aldosterone secretion

The optimal treatment for arterial hypertension due RAS is
controversial. Current treatment options are medical therapy
(angiotensin convertin enzyme inhibitors), percutaneous
transluminal angioplasty with or without stenting, and
surgical reconstruction. Renovascular hypertension must be
distinguished from RAS, in true renovascular hypertension,
the kidneys takes charge of the blood pressure and will do
what it takes to push blood pressure high enough to force
blood through the blocked artery. Some experts favor
surgical revascularisation because of occasional angioplasty
failure and the risk of deterioration of renal function after
angioplasty. Has been clearly established that for those
patients who have atherosclerotic RAS with normal or
mildly impaired renal function, primary angioplasty was not
more effective than antihypertensive drugs alone for
reducing blood pressure or limiting disease progression.

Has been accepted that angioplasty and stenting of stenosed
renal arteries normalizes renin secretion by both treated and
contralateral kidneys and improve the function of the treated
kidney but for young patients with non-atherosclerotic RAS
the chance for reducing blood pressure by angioplasty is and
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is not certain; considering that other vascular lesions could be present (Takayasu's disease) is not, however, when there is not coexisting renal parenchyma disease, when there is not progression to renal artery occlusion, no loss of renal mass, and no result in renal failure, those patients respond to angioplasty. Paulsen et al performed 591 renal angioplasties in 419 patients with significant renal artery stenosis with better results in patients with fibromuscular dysplasia and concluded: angioplasty can be done in selected patients.

Because renovascular hypertension remains despite surgery, although antihypertensive consumption declines some authors have postulated that uncorrected media/lumen ratio in resistance arteries does not cause hypertension. Surgical reconstruction of the stenosed renal artery take time under anesthesia and the patient's body is forcibly moved in turning maneuvers including the head and neck for inducing anesthesia therefore risk of provoke complications increase with, mainly in those patients who the 100 % of underlying problems had not been previously identified. It is important to realize that if the congenital anomalies are picked up at an early stage, the damage is less harsh during any intervention. Although the following situation has not been reported yet, if any patient with bilateral renal artery stenosis (ACE inhibitors are contraindicated) undergo for surgery then anesthetic consideration should be discussed, for patients with KFS and unilateral renal artery stenosis the treatment of choice is medical with ACE inhibitors until proven otherwise. We also propose the term of Klippel-Feil syndrome “plus” for those patients with cervical vertebral fusion and other associated deformities rather than to add another eponym to the long list that already exist.

ACKNOWLEDGMENTS

The authors wish to acknowledge Mrs. Lourdes Margarita Guillermina Valdes Perez for her contributions.

References

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