

Genitourinary Anomalies Associated with Klippel-Feil Syndrome

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ABSTRACT: Of thirty-nine patients with Klippel-Feil syndrome, twenty-five (64 per cent) had significant genitourinary-tract anomalies demonstrated by intravenous urogram and physical examination. The incidence of these anomalies in Feil's three types of the syndrome was essentially the same, unilateral renal agenesis being the most common. A routine intravenous urogram is indicated in patients with this syndrome.

In 1912, Maurice Klippel and André Feil¹⁶ described the syndrome of a short neck, limitation of neck motion, and low posterior hairline. Dubreuil-Chambardel first used the now familiar eponym in 1921⁷.

Many associated anomalies of the musculoskeletal, neurological, cardiovascular, respiratory, and genitourinary systems have been described since that time^{4,6,8,11,12,13,14,16,17,18,19,20,21}. However, of the more than 200 papers about this subject, only a few documented the coexistence of severe renal anomalies^{15,17,20}.

This study of genitourinary anomalies associated with Klippel-Feil syndrome was stimulated by the unexpected death of a friend of one of us (W. B. M.). He was a thirty-year-old man with this syndrome, agenesis of the left kidney, chronic renal failure, and acute cardiac decompensation. Shortly thereafter a child with Klippel-Feil syndrome, admitted to Children's Hospital in Pittsburgh for an unrelated problem, was found to have a single mid-line pelvic kidney by intravenous urography.

Materials and Methods

All patients admitted to Children's, Presbyterian-University, and the Oakland Veterans Administration Hospitals in Pittsburgh from 1955 to 1973 whose diagnosis included Klippel-Feil syndrome were analyzed. They had been admitted for reasons other than Klippel-Feil deformity, in most instances their chief complaint being congenital scoliosis, Sprengel's deformity, or congenital heart disease. All told there were thirty-nine patients whose diagnosis of Klippel-Feil syndrome was based on the findings on anteroposterior, lateral, and oblique roentgenograms of the cervical and thoracolumbar spine. All patients with typical findings were included in the study regardless of associated anomalies.

Feil's original classification¹⁰ was used. His three types may be defined as follows:

Type I is a block fusion of all the cervical and upper thoracic vertebrae;

Type II is a fusion of one or two pairs of cervical vertebrae, frequently the second to the third or the fifth to the sixth, and is the most common type, although it usually goes unrecognized because there are no symptoms and the neck appears normal¹⁴;

Type III combines the anomalies of Type I or Type II with either lower thoracic or lumbar intervertebral fusions.

The records of thirty of the thirty-nine patients contained no report of an intravenous urogram. These patients were contacted and examined by at least one of us. Out-patient intravenous urograms were also obtained. The remaining nine patients had had an intravenous urogram as part of the evaluation of their other anomalies which included scoliosis, diastematomyelia, and myelomeningocele. It was not possible to examine these patients personally. One patient was dead, and the other eight had moved out of the area.

All patients with significant renal anomalies demonstrated by intravenous urogram were referred to the urological service for further evaluation.

Results

Our series included twenty-one Type-I, four Type-II, and fourteen Type-III anomalies. Of the four Type-II lesions, three were discovered when cervical roentgenograms were obtained after a neck injury, and one was associated with bilateral Sprengel's deformity.

The ages when the diagnosis of Klippel-Feil syndrome was made ranged from one day to sixty years, the median age being three years. Excluding the five patients who were more than eight years old, the average age was 2.9 years, which is consistent with the average reported in the literature¹².

The female-to-male ratio in this series was 1.8 to 1.0, unlike the equal sex distribution recorded in the literature¹².

Of the thirty-nine patients, twenty-three (59 per cent) had significant upper urinary-tract anomalies demonstrated by intravenous urogram, but only one of the twenty-three had symptoms suggestive of a renal anomaly. This female patient had a Type-III Klippel-Feil anomaly and was admitted with flank pain and anuria. An emergency intravenous urogram demonstrated unilateral renal agenesis with an obstructing renal calculus. The remaining twenty-two patients had no symptoms suggestive of a renal anomaly. One patient with a Type-I anomaly also had vaginal agenesis with a bicornuate uterus. Two others, one having a Type-I anomaly

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TABLE I

INCIDENCE RATES OF VARIOUS GENITOURINARY ANOMALIES ASSOCIATED WITH THE KLIPPEL-FEIL SYNDROME IN THE PRESENT STUDY COMPARED WITH THOSE STATED IN THE LITERATURE IN NORMAL RANDOM POPULATIONS

Genitourinary Anomaly	Present Study	Literature
Unilateral renal agenesis	282:1000	0.70:1000
Malrotation of kidney	205:1000	0.37:1000
Renal pelvic and ureteral duplication	154:1000	6.20:1000
Simple renal ectopia	128:1000	1.25:1000
Renal dysgenesis	51:1000	1.20:1000

with cryptorchidism, and the other, a Type-III lesion with hypospadias, had no renal anomalies. The combined total incidence of genitourinary anomalies was, therefore, 64 per cent.

The genitourinary anomalies in this series included unilateral renal agenesis, malrotation of the kidney, renal pelvic and ureteral duplication, simple renal ectopia, renal dysgenesis, hypospadias, cryptorchidism, and vaginal agenesis and bicornuate uterus.

Unilateral renal agenesis or complete congenital absence of one kidney with the ureter absent or rudimentary⁵ was the most common anomaly in the present series, being associated with five Type-I, one Type-II, and five Type-III anomalies. Of the eleven patients with unilateral renal agenesis three had malrotation of their one kidney and one had vaginal agenesis and a bicornuate uterus.

Malrotation of the kidneys, or lack of proper mesial rotation as they ascend from the pelvis to their upper lumbar location during embryonic life⁵, was the second most common anomaly, occurring in eight of the thirty-nine patients.

Renal pelvic and ureteral duplication with two distinct renal pelves and ureters⁵ was demonstrated in six patients, four with Type-I and two with Type-III anomalies.

Simple renal ectopia, abnormal anatomical location of one or both kidneys⁵, was demonstrated in three patients, one with Type-I, one with Type-II, and one with Type-III anomalies. All five ectopic kidneys were unilateral, and were located in the pelvis: three on the left and two on the right. In the general population simple renal ectopia is three times more common on the left than on the right, and the pelvis is the most frequent ectopic site⁵.

Renal dysgenesis or hypoplasia with subnormal growth and function of the kidney⁵ was seen in one patient with Type-I and in one patient with Type-III anomalies.

As shown in Table I, the incidences of these renal anomalies were much higher in patients with Klippel-Feil syndrome than in a normal random population^{5,21}. These anomalies were associated with all three types of Klippel-Feil syndrome, being present in 62 per cent of the patients with Type I and 71 per cent of those with Type III, while two of the four patients with Type-II lesions had renal anomalies but no abnormalities of the lower genital tract. It is perhaps noteworthy that even though some authors have stated that Type-II lesions are not true Klippel-Feil

anomalies¹⁷, the findings in this series suggest that they, like the other two types, are associated with a high incidence of renal anomalies. However, the small number of patients with Type-II anomalies in this series prevents us from drawing any conclusions as to the true incidence of renal anomalies associated with this type.

Hypospadias, a congenital defect of the urethra in which the canal terminates ventral and posterior to the site of its normal opening⁵, occurred in one patient with a Type-III lesion and no associated anomaly of the upper urinary tract.

Cryptorchidism, imperfectly descended testes most frequently in the inguinal canals⁵, was found in one patient who had a left inguinal undescended testis with no associated renal anomalies and a Type-I lesion.

Vaginal agenesis, which is of urological interest primarily because of the high incidence of coexisting renal anomalies, unilateral renal agenesis being the most common⁵, was present in one patient with a Type-I defect. In addition to her vaginal agenesis she had unilateral renal agenesis and a bicornuate uterus.

Discussion

In the past the high incidence of genitourinary anomalies with the Klippel-Feil syndrome has been mentioned only briefly. Ramsey and Bliznak reported on two cases of renal agenesis, McElfresh and Winter performed intravenous urograms in fourteen patients finding two with renal agenesis and four with renal ectopia, and Hensinger and associates in a recent study of patients with Klippel-Feil syndrome noted that one-third had renal anomalies.

The axial skeleton differentiates from mesenchyme in serially arranged pairs of mesodermal somites. During the fourth week of fetal life, the ventromesial wall of each somite forms a pair of segmental sclerotome masses which eventually develop into the vertebrae incorporating the notochord and establishing the vertebral bodies.

During the same period, seven pairs of rudimentary pronephric tubules form as dorsolateral sprouts from segmentally arranged nephrotomes that border on the region of the future cervicothoracic junction. The distal ends of these tubules unite into paired longitudinal pronephric ducts which eventually perforate the cloaca. The pronephric tubules rapidly degenerate, while the paired pronephric ducts persist as the mesonephric or wolffian ducts. While the pronephric tubules are degenerating, the more caudal portion of the nephrogenic ridge forms the mesonephric tubules which connect the mesonephric duct¹.

At approximately thirty-five days of fetal development the distal portion of each mesonephric duct forms a ureteric bud which grows into surrounding nephrogenic tissue and becomes the definitive metanephros or adult kidney¹.

It is reasonable to assume in patients with Klippel-Feil syndrome that there was some insult to the pronephros, which lies between the seventh and fourteenth somites, the approximate area where the cervical spine develops, and that this insult caused faulty development of the spine and

some derangement in the adult genitourinary tract. In the case of renal agenesis, an insult occurring between the fifth and seventh week could result in complete arrest of development of the ureteric bud². Absence of the ureteric bud would account for agenesis of the kidney³. Renal dysgenesis could be explained on a similar embryological basis with incomplete arrest of the ureteric bud and metanephric development³.

Renal pelvic and ureteric duplication are probably produced during the fifth and sixth weeks of fetal life when the ureteral bud develops from the ventral division of the primi-

tive cloaca. Splitting of the ureteral bud results in duplication⁵. Simple renal ectopia is caused by failure of the kidney to ascend to its normal position during the seventh and eighth weeks of fetal life⁵.

From this brief review of the embryological development it is evident that the cervical vertebrae and genitourinary tract differentiate at the same time and in the same vicinity in the embryo. Therefore, an insult to the fetus between the fourth and eighth weeks of development could produce both genitourinary anomalies and the Klippel-Feil syndrome.

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