



## Andrology and Fertility

## Azoospermia in a Male with Klippel–Feil Anomaly

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## ABSTRACT

Müllerian-duct aplasia, renal agenesis, and cervical somite dysplasia (MURCS) is a rare genetic disorder. Previously thought to be exclusive in females, there have now been a small number of case reports describing a male analogue. We describe a patient with obstructive azoospermia and Klippel–Feil anomaly.

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## Introduction

Müllerian-duct aplasia, renal agenesis, and cervical somite dysplasia (MURCS) was first described in 1979 by Duncan et al.<sup>1</sup> This rare disorder was previously thought to be exclusive in females but there have been a few number of case reports describing a male analogue of azoospermia, renal anomalies and segmentation abnormalities of the cervicothoracic spine and renal anomalies.<sup>2–4</sup> We describe a patient with obstructive azoospermia and Klippel–Feil anomaly.

## Case report

A 27-year-old male was referred for work up for male factor infertility. His partner's fertility work up had been deemed normal. He had been diagnosed at an early age with Klippel–Feil Syndrome and had undergone cervical spinal fusion at a young age. Hypospadias was surgically corrected in infancy.

A semen analysis showed borderline low semen volume, normal pH suggesting presence of prostatic and seminal vesicle secretions and azoospermia. Physical exam was pertinent for a circumcised phallus with mildly hypospadias meatus, bilaterally descended testicles, 18 mL bilaterally, bilateral absence of vas deferens and bilateral hypoplastic epididymis. Follicle stimulating hormone, total testosterone, free testosterone and estradiol were 1.2 IU/L (normal range 1.3–19.3 IU/L), 240 ng/dL (normal range 240–950 ng/dL),

6.0 ng/L (normal range 5.05–19.8 ng/dL), 16.2 pg/mL (normal range 10–40 pg/mL), respectively. A renal ultrasound confirmed presence of bilateral kidneys. Based on physical exam findings and semen analysis patient was diagnosed with obstructive azoospermia.

Patient underwent a testicular biopsy and sperm extraction on 11/01/2016. His diagnostic testis biopsy showed normal spermatogenesis. The testicular sperm extraction showed 6 vials at 0.5 mL preserved with good number and good apparent quality of sperm. Patient was counseled on the potential for In-vitro fertilization.

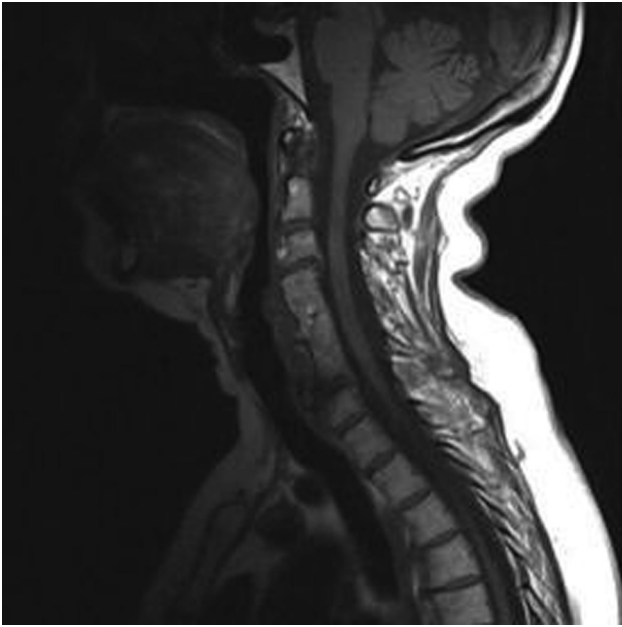
## Discussion

Klippel–Feil anomaly was first described in 1912 by Klippel and Feil. It is described as the fusion of two or more cervical vertebrae, short neck, limitation of head movement, and low posterior hairline (Fig. 1).<sup>5</sup> This anomaly has been described scarcely in the literature in association with MURCS (Müllerian-duct aplasia, renal agenesis, and cervical somite dysplasia). MURCS was first described by Duncan et al in 1979. It is a developmental disorder present at birth that primarily affects the reproductive and urinary systems. MURCS association is predominately seen in females, although males can also have this condition as well.

Kidney development begins with the earliest embryonic stage of the kidney, the Pronephros, a vestigial structure that disappears by the 4th week of embryonic life, giving rise to the Mesonephros, the main excretory organ from embryonic weeks 4–8. During this stage in embryonic development, the embryo is sexually undifferentiated, with the potential to give rise to either male or female structures from two primitive ducts, the Wolffian and Mullerian.

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**Figure 1.** Non-segmentation (block vertebrae) seen here involving the C4–C6 segments with prominent degenerative change in the adjoining motion segments. Yochum T, Rowe L; *Essentials of Skeletal Radiology* 3rd ed., vol 1 2005 Lippincott pub.

The Wolffian (mesonephric) ducts lie medially while the Mullerian (paramesonephric) ducts lie laterally.<sup>6</sup>

In the presence of XY chromosome, the SRY gene on the Y chromosome activates differentiation of the gonads into testes through the action of testis-determining factor. After development of the testes, Leydig and Sertoli support sexual differentiation by producing testosterone, to further development of Wolffian ducts, and Mullerian inhibiting substance, inducing destruction of the Mullerian structures, respectively. In the absence of the SRY gene, female development proceeds. The Mullerian ducts develop into the female internal structures – fallopian tubes, uterus, and upper part of the vagina while the Wolffian ducts degenerate.<sup>7</sup>

In males, the Wolffian ducts becomes the epididymis, vas deferens, and seminal vesicles. Both males and females with MURCS association can have absent or abnormally formed reproductive

organs. This typically manifests as absence of the vas deferens in males, as in our patient, and absence of the fallopian tubes in females. Additional phenotypic expression can include kidney abnormalities, short stature, fused spinal bones in the neck and upper back, and hearing loss.

There have been four case reports to date describing males with MURCS.<sup>2–4,8</sup> Each case report involved males presenting with azoospermia. Fifty percent of the cases had unilateral renal agenesis. Hormone evaluation was normal in two of the cases while another case had an elevated FSH. Testicular biopsy was performed on two of the four males. One case showed normal spermatogenesis. While the other case showed abnormal spermatogenesis of the right testicle and presence of Sertoli cells only in the left testicle. Other anomalies were noted including anal atresia, cryptorchidism and bilateral seminal duct agenesis.

## Conclusion

There have been several causes of MURCS that have been postulated including teratogen exposure in utero but these have not been confirmed. This rare syndrome and the role it plays in infertility will need to be further studied.

## Conflicts of interest

No conflicts of interest.

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