Infertility

Embryology of the Absent Vas Supported by 2 Cases of Congenital Unilateral Absence of Vas With Varied Associations

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\textbf{A B S T R A C T}

Congenital absence of the vas occurs in up to 1% of men. Congenital unilateral absence of the vas deferens can be related to cystic fibrosis transmembrane conductance regulator mutations or in 79% of cases, renal agenesis. We present a case of each, diagnosed in children at operation for elective inguinal hernia repairs. One patient had associated ipsilateral renal agenesis with a normal cystic fibrosis screen. The other patient had an ipsilateral pelvic kidney and a mutation detected on cystic fibrosis screening. Current understanding of the embryology of the relationship between these defects would seem to be supported by our cases.

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\textbf{Introduction}

Congenital absence of the vas is estimated to occur in up to 1% of men. It may be associated with cystic fibrosis transmembrane conductance regulator (CFTR) mutations or in 79% of cases, renal agenesis.\textsuperscript{1} We present a case of each and discuss the current understanding of the underlying embryologic basis.

\textbf{Case presentations}

\textbf{Case 1: Unilateral absent vas and renal agenesis without CFTR mutation}

An 18-month-old boy underwent an elective left inguinal hernia repair. At operation, an absent vas and epididymis were identified (Fig. 1). He underwent renal ultrasound scanning and cystic fibrosis (CF) screening as follow-up and was found to have ipsilateral renal agenesis but no CFTR gene mutation.

\textbf{Case 2: Unilateral absent vas and pelvic kidney with CFTR mutation}

A 2-year-old boy also underwent elective left inguinal hernia repair. At operation, he too was noted to have an absent vas and epididymis. During follow-up, a renal ultrasound showed an ipsilateral pelvic kidney with normal contralateral kidney. Upper tracts were entirely normal. CF screening was performed. The CFEUV1 kit detected none of the most common 32 CF mutations in deoxyribonucleic acid from his lymphocytes but did show the patient had 1 copy of the 7T allele and 1 copy of the 9T allele at the intron 8 splice acceptor poly T polymorphism but not the 5T allele CFTR mutation. A sweat test was normal.

Laparoscopy was offered but declined by both families, as the outcome was not relevant to either child until they want to have children of their own. Radiological opinion in our center is that no form of imaging would be helpful at this age in assessing the presence of the contralateral vas and so was not offered. Ultrasound per rectum can be performed as an adult to assess the vas and seminal vesicles, as is protocol in an infertility clinic.

\textbf{Discussion}

CF is the most common autosomal recessive disease in Northern European Caucasians (1:1600). For individuals with no family history, the carrier frequency of CF is 1:25. The CF gene has been
localized to chromosome 7q31 and spans 250 kb genomic deoxyribonucleic acid which encodes a 1480 amino acid protein designated the CFTR.2

In some cases, particularly in those patients with an obstruction of their solitary vas deferens, congenital unilateral absence of the vas deferens (CUAVD) can also be related to CFTR mutations.3 Kolettis (2002) found 9 patients with CUAVD and an obstructed vas deferens at the inguinal or pelvic level, 8 of 9 (89%) had 1 CF mutation but no renal anomalies. These patients could therefore be viewed as having CFTR abnormalities that allow an intrinsically normal mesonephric duct to develop fully after the separation between the urinary and reproductive portions of the mesonephric duct. Other forms of CUAVD are simply mesonephric abnormalities unrelated to CF. In this same study, those patients with CUAVD and a completely patent vas deferens did not have any CFTR mutations but were more likely to have renal anomalies. Of these patients, 5 of 12 (42%) had an ipsilateral renal anomaly on the side of the absent vas deferens. These patients can be viewed as having an intrinsic defect in mesonephric duct development and morphogenesis.2 Men with CUAVD should therefore undergo CF testing and renal ultrasound, although it would be expected that the incidence of renal anomalies in men with a CF mutation would be low.7

Recently, the relationship between CFTR mutations and the congenital absence of the uterus and vagina (CAUV), which affects 1 in 5000 women, was examined on the rationale that the embryologic development of the mullerian ducts directly depends on the previous normal development of the wolffian ducts. Samples from 25 patients with CAUV were tested for the 33 most common CFTR mutations, including the 5T allele. The data suggested that it is unlikely for CFTR mutations to cause CAUV in women. Finding that CFTR mutations are associated with 80% of cases of congenital bilateral absence of vas deferens, a wolffian duct anomaly, but are not associated with CAUV, a mullerian duct anomaly, provides further evidence on the timing of CFTR damage in congenital bilateral absence of vas deferens. The effects of the CFTR mutations on the wolffian duct derivatives must occur after the ninth week of embryologic development, at a time when the wolffian and mullerian ducts have completely separated and are developing independently.4

Conclusion

Surgeons encountering an absent vas while undertaking a unilateral inguinal hernia repair must remember to assess the patient for other associated abnormalities such as CF and the “absent vas, absent kidney syndrome.” Donohue and Fauver5 indicated that unilateral absence of the vas deferens was associated with ipsilateral renal agenesis or other renal anomalies in more than 90% of men. Our cases add credence to the hypothesized lack of association between renal agenesis and the CFTR gene in patients with unilateral absence of vas deferens and the differing underlying embryology.

References

1. Rotman A. Congenital unilateral absence of the vas deferens. J Pediatr Surg. 2010;45:1925.
2. Mickie J, Milunsky A, Amos JA, Oates RD. Congenital unilateral absence of the vas deferens: a heterogeneous disorder with two distinct subpopulations based upon aetiology and mutational status of the cystic fibrosis gene. Hum Reprod. 1995;10:1728–1735.
3. Kolettis PN. The evaluation and management of the azoospermic patient. J Androl. 2002;23:293–305.
4. Radpour, Gourabi RH, Dizaj AV, Holzgreve W, Zhong XY. Genetic investigations of CFTR mutations in congenital absence of vas deferens, uterus, and vagina as a cause of infertility. J Androl. 2008;29:506–513.
5. Donohue RE, Fauver HE. Unilateral absence of the vas deferens. A useful clinical sign. JAMA. 1989;261:1180–1182.