Seminal vesicle agenesis: An uncommon cause of azoospermia

Abderrazak Bouzouita, MD;[*] Walid Kerkeni, MD;[*] Hassine Abouda, MD;[†] Mohamed Khrouf, MD;[†] Hanene Elloumi, MD;[†] Najla Mnif, MD;[§] Taieb Messaoud, MD;[¥] Amel Zhioua, MD;[†] Fethi Zhioua, MD;[†] Mohamed Chebil, MD[*]

[*]Urology Department, Charles Nicolle Hospital of Tunis, Tunisia; [†]Gynecology and Obstetrics Department, Medically assisted Procreation Unit, Aziza Othmana Hospital of Tunis, Tunisia; [§]Radiology Department, Charles Nicolle Hospital of Tunis, Tunisia; [¥]Biochemistry Department, Children Hospital of Tunis, Tunisia

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Abstract

Seminal vesicle malformations are a rare cause of obstructive azoospermia, often associated with other internal genitalia and upper urinary tract birth defects. We report 5 new cases of seminal vesicle agenesis in men presenting with hypospermia and azoospermia. Imaging showed seminal vesicle unilateral agenesis in all patients. The remaining seminal vesicle was hypoplastic in 3 cases, dilated in 1 case and with abnormally thick content in another case. Vas deferens agenesis was observed unilaterally in 2 patients and bilaterally in 2 other patients. No renal malformations were detected. Genetic study showed in all cases a 46 XY karyotype without any microdeletions. A single heterozygous cystic fibrosis transmembrane regulator gene mutation was diagnosed in 1 man, but not found in his partner. Intracytoplasmic sperm injection using sperm from a testicular biopsy was performed in 3 couples, without success.

Introduction

Male infertility due to internal genitalia anomalies is rare (2% of cases); it is related to obstructive azoospermia.[1] Seminal vesicle (SV) birth defects are part of these malformations occurring in internal genital organs derived from the Wolff mesonephric duct. SV congenital cysts are commonly reported, while there are few observations of SV agenesis.[2] SV unilateral agenesis is observed in 0.6% to 1% of cases, whereas the incidence of bilateral agenesis remains unknown.[3] These SV abnormalities are often associated with vas deferens agenesis and may also be accompanied by reno-ureteral malformations.[2,3] Internal genitalia agenesis is frequently observed with cystic fibrosis transmembrane regulator (CFTR) gene mutations,[3] which should be searched in each man, and his partner, presenting with related-azoospermia. Male infertility due to SV agenesis or hypoplasia has benefited from advances in semen collection techniques and medically-assisted procreation.

We report 5 new cases of obstructive azoospermia related to SV agenesis and detail their clinical, biological, radiological and genetic features.

Case report

Five patients presenting with azoospermia were referred to our centre. They were all North African and had a mean age of 35.6 years. No one had any personal or family history of cystic fibrosis. Female partners had a mean age of 31.2 years and they all had normal hormonal examination, pelvic ultrasound and hysterosalpingography. Couples had primary infertility lasting on average 3.8 years.

External genitalia physical examination found 2 normally placed testicles with normal size and consistence in all cases, except in 1 patient who had an undescended and small left testicle. Epididymis palpation was normal in 2 patients, and a nodular head was found in 3 patients. Vas deferens was not palpable bilaterally in 2 cases and unilaterally in 2 other cases. Semen analyses showed hypospermia (semen volume less than 1.5 mL) and azoospermia in all cases. The follicle-stimulating hormone (FSH) level was normal in all patients. Transrectal ultrasound and pelvic magnetic resonance imaging (MRI) found SV unilateral agenesis in all patients. The remaining SV was hypoplastic in 3 cases, dilated in 1 case and with abnormally thick content in another case (Fig. 1, Fig. 2).

Vas deferens agenesis was observed unilaterally in 2 patients and bilaterally in 2 other patients (Fig. 3). Moreover, no renal malformations were detected in kidney ultrasound. Genetic study, performed in all patients, showed a 46 XY karyotype without any microdeletions in all cases. However, a single heterozygous CFTR gene mutation was diagnosed in 1 man, but not found in his partner. This mutation was a

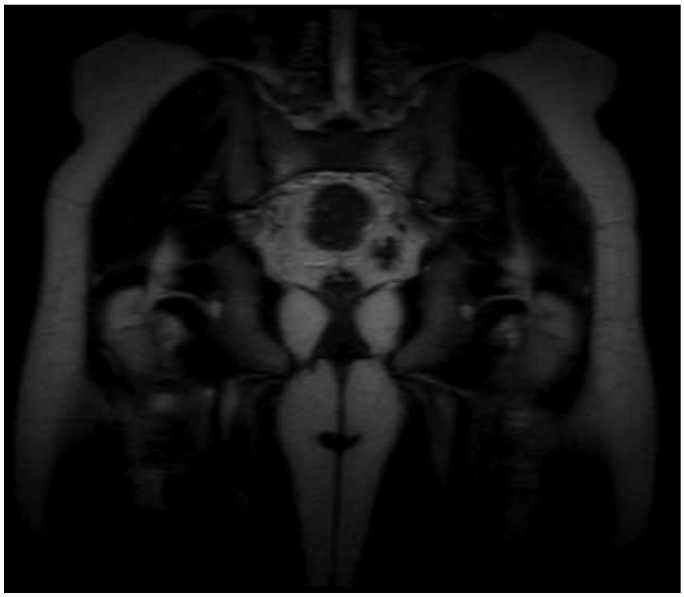

Fig. 1. T2 coronal magnetic resonance image: Right seminal vesicle agenesis.

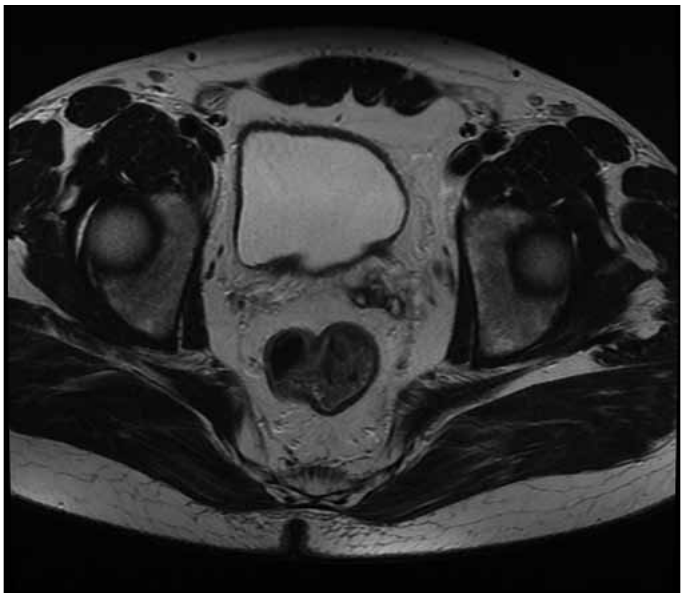

Fig. 2. T2 axial magnetic resonance image: Right seminal vesicle agenesis, left seminal vesicle hypoplasia with modified signal.

K1302R mutation with 5T polymorphism. Intracytoplasmic sperm injection (ICSI) using sperm from a testicular biopsy was attempted in 3 couples, twice in 1 couple, but without success (Table 1).

Table 1. Clinical, biological, radiological and genetic features of patients

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age (years)	39	43	36	31	29
CF personal or family history	No				
Physical examination					
Testicles	Normally placed, normal size and consistence				Undescended, small left testicle
Epididymes	2 nodules of the right epididymis head	Normal	Normal	Swollen head of the left epididymis	Nodular right epididymis head
Vas deferens	Bilaterally palpable, normal	Non palpable right vas deferens	Bilaterally non-palpable	Bilaterally non-palpable	-Non palpable right vas deferens -Swollen left vas deferens
Semen analysis	Hypospermia + azoospermia				
FSH (mU/mL)	2.24	2.05	3.5	1.63	1.89
Transrectal ultrasound + pelvic MRI	-Right seminal vesicle agenesis -Abnormally thick content of the left seminal vesicle	-Right seminal vesicle and vas deferens agenesis -Left seminal vesicle hypoplasia	-Right seminal vesicle agenesis -Left seminal vesicle hypoplasia -Right and left Vas deferens agenesis	-Right seminal vesicle hypoplasia -Left seminal vesicle agenesis -Right and left vas deferens agenesis	-Right seminal vesicle and vas deferens agenesis -Dilated left seminal vesicle and vas deferens
CFTR gene mutation	No	No	Heterozygous K1302R mutation with 5T polymorphism	No	No
Karyotype	46XY				
ICSI	2 unsuccessful attempts	Unsuccessful attempt	Unsuccessful attempt		

CF: cystic fibrosis FSH: follicle-stimulating hormone; MRI: magnetic resonance imaging; CFTR: cystic fibrosis transmembrane regulator; ICSI: intracytoplasmic sperm injection.

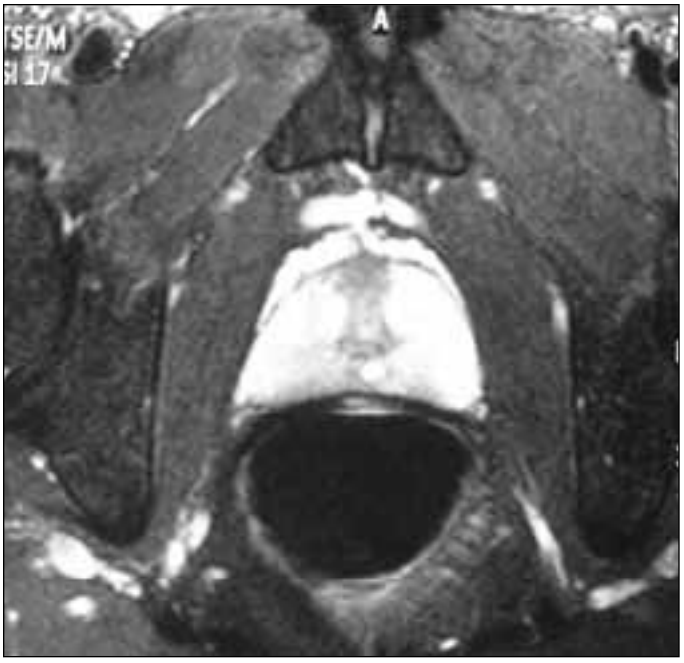

Fig. 3. Fat-Sat T2 axial magnetic resonance image: Bilateral vas deferens agenesis.

Discussion

A male factor, almost always marked by abnormal semen analysis, is responsible for 20% of couple infertility and contributes to infertility in 30% to 40% of couples.[4] SV malformations are relatively rare and poorly known, causing male infertility in 2% of cases.[1] They may be categorized into abnormalities of number (agenesis, fusion, duplication), maturation (hypoplasia), position (ectopia) or structure (diverticulum, cyst, communication with the ureter).[3] In all our patients, normal FSH level confirms, with hypospermia, the obstructive origin of azoospermia. Transrectal ultrasound is the gold standard for SV and internal genitalia assessment in cases of obstructive azoospermia.[5] Pelvic MRI is required when ultrasound is insufficient or when it shows a major ductal dilatation.[6] SV and vas deferens normally appear hyperintense on T2 due to the seminal fluid they contain in their light. All our patients had transrectal ultrasound then a pelvic MRI. Malformations of SV and vas deferens are intertwined. In fact, in patients with congenital bilateral absence of the vas deferens, bilateral SV agenesis was found in 23% to 43% of cases and unilateral SV agenesis in 27% to 50% of cases.[7,8] Also, patients with congenital unilateral absence of the vas deferens presented with ipsilateral SV agenesis in 71% to 90% of cases and contralateral SV agenesis in 20% of cases.[8,9] Among our 5 patients presenting with unilateral SV agenesis, 2 had ipsilateral absence of the vas deferens, 2 had bilateral vas deferens agenesis and 1 patient had 2 normal vasa deferentia. Moreover, it is well-demonstrated that if an embryological insult occurs before 7 weeks' gestation, when the ureteral bud separates from the mesonephric duct, SV agenesis may be associated with renal agenesis. Performing a renal ultrasound is therefore mandatory in cases of SV agenesis. No renal malformation was detected in our patients.

Bilateral or unilateral agenesis of the SV or the vas deferens is often associated with a variable form of cystic fibrosis. The clinical manifestations are caused by CFTR gene mutations. Depending on mutations and polymorphisms, alterations in the CFTR gene function are more or less significant and responsible for a large clinical variability ranging from multivisceral cystic fibrosis disease to isolated involvement of vas deferens and SV.[10] Therefore, it is reasonable to make a complete molecular analysis of the CFTR gene in cases of SV or vas deferens birth defects.

Conclusion

In our series, a K1302R mutation with 5T polymorphism was diagnosed in 1 patient. Thanks to techniques such as ICSI, patients with congenital agenesis of SV and/or vas deferens are now able to father children. In our series, an ICSI was performed without success in 3 couples. However, when a CFTR gene mutation is detected, there is an increased risk of cystic fibrosis in the child. Genetic counselling should therefore be provided to such couples and the partner should be also tested for CFTR mutations to determine the risk of cystic fibrosis in the child.

Competing interests: Dr. Bouzouita, Dr. Kerkeni, Dr. Abouda, Dr. Khrouf, Dr. Elloumi, Dr. Mnif, Dr. Messaoud, Dr. A. Zhioua, Dr. F. Zhioua and Dr. Chebil all declare no competing financial or personal interests.

This paper has been peer-reviewed.

References

1. Fontaine E, Jardin A. Anomalies des organes génitaux internes masculins et retentissement sur la fertilité. *Prog Urol* 2001;11:729-32.
2. Dubois R, Valvalle AF, Murat F, et al. Malformations des organes génitaux internes masculins issus du canal mésonéphrotique de Wolff. *Prog Urol* 2001;11:733-40.
3. Wu H-F, Qiao D, Qian L-X, et al. Congenital agenesis of seminal vesicle. *Asian J Androl* 2005;7:449-52. http://dx.doi.org/10.1111/j.1745-7262.2005.00058.x
4. Thonneau P, Marchand S, Tallec A, et al. Incidence and main causes of infertility in a resident population (1,850,000) of three French regions (1988-1989). *Hum Reprod* 1991;6:811-6.
5. Lotti F, Corona G, Colpi GM, et al. Seminal vesicles ultrasound features in a cohort of infertility patients. *Hum Reprod* 2012;27:974-82. http://dx.doi.org/10.1093/humrep/des032
6. Simpson WL, Rausch DR. Imaging of male infertility: Pictorial review. *AJR Am J Roentgenol* 2009;192:98-107. http://dx.doi.org/10.2214/AJR.07.7109
7. Schlegel PN, Shin D, Goldstein M. Urogenital anomalies in men with congenital absence of the vas deferens. *J Urol* 1996;155:1644-8. http://dx.doi.org/10.1016/S0022-5347(01)66152-4

8. Robert F, Bey-Omar F, Rollet J, et al. Relation between the anatomical genital phenotype and cystic fibrosis transmembrane conductance regulator gene mutations in the absence of the vas deferens. *Fertil Steril* 2002;77:889-96. http://dx.doi.org/10.1016/S0015-0282(02)02954-0
9. Hall S, Oates RD. Unilateral absence of the scrotal vas deferens associated with contralateral mesonephric duct anomalies resulting in infertility: Laboratory, physical and radiographic findings, and therapeutic alternatives. *J Urol* 1993;150:1161-4.
10. Boudaya M, Fredj SH, Haj RB, et al. Cystic fibrosis transmembrane conductance regulator mutations and polymorphisms associated with congenital bilateral absence of vas deferens in a restricted group of patients from North Africa. *Ann Hum Biol* 2012;39:76-9. http://dx.doi.org/10.3109/03014460.2011.642892

Correspondence: Dr. Walid Kerkeni, Urology department. Charles Nicolle Hospital of Tunis. Boulevard 9 avril 1938, Tunis 1006, Tunis; walidkerkeni@gmail.com