INFERTILE PATIENTS WITH Y-CHROMOSOME gr/gr DELETION and CONGENITAL BILATERAL ABSENCE OF VAS DEFERENS

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INTRODUCTION

An infertile man with Y-chromosome b1/b3 deletion presenting as normal spermatogenesis and congenital bilateral absence of vas deferens (CBAVD) has just been reported in the literature.[1] Genetic testing is routinely indicated at our center for non-obstructive azoospermia and severe oligozoospermia, including congenital absence of vas deferens. Therefore, we could detect 4 infertile men suffering from Y-chromosome gr/gr deletion with varying levels of spermatogenesis and CBAVD. Two recent large sample-sized studies at two centers of andrology and male infertility in Turkey, which were conducted on 500 azoospermic or severely oligozoospermic men (<5 x 10^6/mL) and 1616 infertile men, respectively, found no AZF deletion or chromosomal abnormalities in 35 and 114 patients with congenital absence of vas deferens.[2,3] These 4 patients could be likely first cases in the literature suffering from both gr/gr deletion and CBAVD.

PATIENTS

Four patients had typical seminal-fluid parameters of an obstructive azoospermia (low sperm volume and pH) due to CBAVD in association with bilateral seminal vesicle agenesis detected by transrectal ultrasound. Besides gr/gr deletion, risk factors for impaired spermatogenesis were also found, including heavy cigarette smoking and alcohol consumption in patient 1 and 2, history of mumps parotitis in patient 3, and varicoceles of the left testis and hypogonadism in patient 4. In patient 1 and 2, spermatogenesis was considered as normal as mobile spermatozoa could be easily aspirated via PESA technique. In patients 3 and 4, sperms were not found via PESA technique but could be extracted via TESE technique. Bilateral testicular biopsies showed severe hypospermatogenesis in patients 3 and 4.

Table 1. Patients' clinical characteristics and laboratory testing.

	Patient 1	Patient 2	Patient 3	Patient 4
Age (years)	32	30	30	27
Duration of infertility (months)	66	15	38	40
Testis volume (Right / Left) (mL)	15/17	17/18	20/15	15/13
Palpable bilateral vas deferens	Absent	Absent	Absent	Absent
Semen volume (mL)	1	1.5	0.4	0.7
Serum testosterone (ng/mL) LH (IU/L) FSH (IU/L)	3.14 2.35 3.75	5.21 4.84 2.55	3.20 3.62 3.83	2.44 6.35 9.51
Karyotype	46XY	46XY	46XY	46XY
Y-chromosome microdeletion	GR/GR	GR/GR	GR/GR	GR/GR
Risk factors for impaired spermatogenesis	Heavy smoking Beer drinking	Heavy smoking Beer drinking	Mumps	Palpable varicoceles at left testis
Hormonal therapy	No	No	No	Yes (hCG 5000 IU/week during 3 months)
Sperm retrieval technique	PESA	PESA	TESE	TESE
Testis histology	NA	NA	Mixed testicular atrophy Mean Johnsen score count 1 at right testis Mean Johnsen score count 1 at left testis	Mixed testicular atrophy Mean Johnsen score count 2 at right testis Mean Johnsen score count 2 at left testis

Because gr/gr deletion is also found in normozoospermic men and fertile men, its presence does not necessarily lead to male infertility. Systemic meta-analyses showed that gr/gr deletion is associated with the presence of oligozoospermia (<20 x 10^6/mL) rather than azoospermia. Therefore, at least one risk factor for impaired spermatogenesis must be added.[4,5]

At our center, a genetic examination for a CFTR mutation was not performed because we were not able to do a routine check of the CFTR gene, and patients had no past history of chronic bronchitis or sinusitis, which are typical symptoms of cystic fibrosis.

CONCLUSION

To our knowledge, these could be the first clinical cases in the literature describing the combination of Y-chromosome gr/gr deletion with CBAVD. More cases need to be accumulated to assess the effects of theses congenital anomalies on spermatogenesis.

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