Etiology of Azoospermia in a Military Population

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Abbreviations and Acronyms

AZF = azoospermia factor

CBAVD = congenital bilateral absence of vas deferens

CFTR = cystic fibrosis transmembrane conductance regulator

EDO = ejaculatory duct obstruction

FSH = follicle-stimulating hormone

KS = Klinefelter syndrome

NOA = nonobstructive azoospermia

OA = obstructive azoospermia

SCOS = Sertoli-cell only syndrome

SSR = surgical sperm recovery

T = testosterone

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Study received Naval Medical Center San Diego local institutional review board approval.

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Purpose: Male infertility is commonly seen at urology clinics and 10% to 20% of infertile males are found to be azoospermic. Azoospermia is classically categorized as nonobstructive or obstructive. This classification tailors the evaluation, diagnosis and proper treatment. We performed a retrospective study to provide an updated etiology of azoospermia in patients in the United States in a universal health care model.

Materials and Methods: We retrospectively reviewed the records of men with azoospermia who presented to our institution between 2004 and 2012. Laboratory data were analyzed, included semen analysis, follicle-stimulating hormone, luteinizing hormone, testosterone, semen fructose and genetic studies. Patients underwent scrotal exploration as indicated for testis biopsy and sperm extraction.

Results: We reviewed 139 outpatient records. Nonobstructive azoospermia was diagnosed in 99 men (71%), including 33 (34%) identified with Sertoli-cell only syndrome. Other etiologies included an idiopathic cause in 25 cases (26%), Klinefelter syndrome in 9 (9%), maturation arrest in 9 (9%), Y chromosome microdeletion in 5 (5%), cryptorchidism in 4 (4%), trauma in 4 (4%), exogenous testosterone supplementation in 4 (4%) and other genetic disorders in 6 (6%). Obstructive azoospermia was identified in 40 men (29%), of whom 16 (40%) had congenital bilateral absence of the vas deferens. Other etiologies included an idiopathic cause in 11 cases (28%), an iatrogenic condition due to a surgical cause in 5 (13%), ejaculatory duct obstruction in 3 (8%), trauma in 1 (3%), retrograde ejaculation in 1 (3%), vas deferens occlusion in 2 (5%) and unilateral absence of the vas deferens in 1 (3%).

Conclusions: This study delineates the etiology of azoospermia in men with universal access to care.

Key Words: testis; azoospermia; infertility, male; etiology; military personnel

Azoospermia can be a disturbing problem for couples with male factor infertility. The etiology of the condition ultimately determines treatment and fertility outcomes. The incidence of azoospermia in the general male population is estimated to be around 2%.[1] Azoospermia is found in approximately 20% of all males evaluated for infertility.[2]

The full evaluation of the male with azoospermia can be costly and cumbersome, which can preclude complete evaluation. Several diagnostic tests are available to determine the cause of the condition. The AUA

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(American Urological Association) Best Practice Statement on the male with azoospermia outlines guidelines for evaluation.[3] Previous reports of the etiology of azoospermia in the United States came from tertiary infertility clinics where fees for services are common. The military health care system provides a unique environment in the United States since complete infertility evaluations can be offered to patients without direct cost to the patient. This system allows for a unique perspective on the etiology of azoospermia in a male population with universal access to medical care.

Males with azoospermia are classically subcategorized as having NOA or OA. By definition those with NOA have intratesticular defects in sperm production and those with OA have normal spermatogenesis with impaired or blocked sperm transport from the testes to the urethra. The diagnosis is made by physical examination and laboratory analyses. It is necessary to identify the correct etiology of azoospermia to determine the prognosis, treatment options and likelihood of successful SSR.

Knowledge of the prevalence of the various azoospermia etiologies is essential to evaluate and counsel infertile males. We report a study of azoospermia etiologies.

MATERIALS AND METHODS

W performed a retrospective study from 2004 to 2012 after receiving approval from the local institutional review board at Naval Medical Center San Diego. Subjects were identified based on an ICD-9 code consistent with azoospermia (606.0) using our outpatient records database. A total of 260 patients were assigned this specific ICD9 code. Excluded from study were 55 patients with previous vasectomy. Also excluded were 28 patients with incomplete charts, 20 with oligospermia and/or asthenospermia and 18 with no documented evidence of azoospermia other than the available ICD9 code. Subjects included active duty service members, dependents and retired service members who had universal access to medical care without payment for evaluations.

All patients were evaluated by 1 fellowship trained urological infertility specialist. Evaluation included a comprehensive history and physical examination, 2 separate semen analyses, hormonal analyses and genetic testing. Biopsy was offered to all patients for diagnostic and assisted reproduction purposes. Included in the data collection were patient age, semen analyses, semen fructose presence or absence and hormonal studies (FSH, luteinizing hormone, T, estradiol and prolactin). Physical examination findings were collected based on the presence or absence of testicular atrophy in 1 or 2 testes. Testicular atrophy was defined as testis size less than 4 cm. Genetic test results were collected, including full chromosomal analysis, Y microdeletion studies and CFTR gene studies. Results in patients who underwent testicular biopsies were also included. A total of 139 men met inclusion criteria and were included in analysis.

Men were placed in diagnostic categories by an infertility specialist. The diagnoses included in the NOA category were SCOS, KS, Y microdeletion, maturation arrest, testicular failure and other genetic disorders. The testicular failure group was further categorized as idiopathic or secondary to a history of undescended testis or exogenous anabolic steroid use. SCOS was based on testicular biopsy results. Men with KS had a 46,XXY karyotype. Known Y microdeletions were placed in the Y microdeletion category of AZFa, b, c or d. Men found to have another genetic disorder were placed in a separate category. Unknown causes of azoospermia were categorized as idiopathic.

In the OA category the diagnoses were CBAVD, trauma history and EDO. Men with positive CFTR findings or absent vasa deferentia on physical examination were placed in the CBAVD category. Patients with a history of trauma and normal FSH were categorized to have trauma. Unknown causes of OA were categorized as idiopathic.

RESULTS

The table lists results in the 139 subjects. NOA was seen in 99 cases (71%) and OA in 40 (29%). NOA results revealed that 33 men (34%) had SCOS, 25 (26%) had an idiopathic cause, 9 (9%) had KS, 9 (9%) had maturation arrest, 5 (5%) had Y microdeletions, 4 (4%) had a history of cryptorchidism, 6 (6%) had another rare genetic disorder known to cause infertility, 4 (4%) had exogenous testosterone use and 4 (4%) had a history of trauma (see table).

Etiology of NOA and OA in patients in current and previous studies

Etiology	No. Fedder et al (%)[5]	No. Jarow et al (%)[4]	No. Present Series (%)
NOA:	72	85	99
SCOS	—	37 (44)	33 (34)
Idiopathic	45 (63)	—	25 (26)
KS	6 (8)	3 (3)	9 (9)
Maturation arrest	—	20 (23)	9 (9)
Y microdeletion	9 (13)	—	5 (5)
Other genetic disorder	2 (3)	2 (2)	6 (6)
Undescended testis	—	—	4 (4)
Exogenous T	5 (7)	—	4 (4)
Trauma	—	—	4 (4)
Gonadotoxins	5 (7)	19 (22)	—
Mumps orchitis	—	4 (5)	—
OA:	28	49	40
CBAVD	12 (43)	16 (33)	16 (40)
Idiopathic	4 (14)	—	11 (28)
Iatrogenic (surgery)	2 (7)	1 (2)	5 (13)
EDO	—	3 (6)	3 (8)
Trauma	3 (11)	—	1 (3)
Retrograde ejaculation	—	—	1 (3)
Vas deferens occlusion	—	—	2 (5)
Unilat vas absence	—	—	1 (3)
Epididymitis	5 (17)	16 (33)	—
Young syndrome	—	1 (2)	—
Epididymal atresia	—	12 (24)	—
Epididymal	2 (7)	—	—