Comparison of Testicular Histopathology in Patients with Obstructive Azoospermia and Men with Normal Semen Analysis

Thesis

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List of Abbreviations:

ABP	Androgen binding protein
BM	Basement membrane
CAVD	Congenital absence of the vas deferens
CBAVD	Congenital bilateral absence of the vas deferens
CF	Cystic fibrosis
CFTR	Cystic fibrosis transmembrane conductance regulator
CUAVD	Congenital unilateral absence of the vas deferens
DNA	Deoxyribonucleic acid
EDO	Ejaculatory duct obstruction
FNA	Fine needle aspiration
FNAC	Fine needle aspiration cytology
FSH	Follicle stimulating hormone
G	Gauge
GnRH	Gonadotropin-releasing hormone
HPG	Hypothalamic-pituitary-gonadal axis
ICSI	Intracytoplasmic sperm injection
IVF	In vitro fertilization
LH	Luteinizing hormone
L-PGDS	Lipocalin-type prostaglandin D synthase
micro-TESE	Microdissection testicular sperm extraction
NOA	Non-obstructive azoospermia
OA	Obstructive azoospermia
ROS	Reactive oxygen species
SCOS	Sertoli cell-only syndrome
SCR	Sertoli cell ratios
TD	Tubular diameter
TESE	Testicular sperm extraction
TRUS	Transrectal ultrasonography
WHO	World health organization

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ABSTRACT

Objective: To compare testicular histopathology of patients with obstructive azoospermia due to different etiologies and at different levels of obstruction with testicular histology of normozoospermic men .

Materials and methods: This retrospective study involves reevaluation of testicular biopsy slides from 137 patients with obstructive azoospermia and compare them with testicular biopsy slides from 24 normozoospermic subjects. The patients were subdivided according to the etiology of obstruction into two groups: congenital and acquired; and according to the level of obstruction into three categories: intra-testicular, epididymal, and high obstruction. Both quantitative and qualitative evaluations were performed.

Results: The percentage of interstitial fibrosis was significantly higher in the obstructive patients compared with the control group (P = 0.004). Adjusted mean late spermatid score was found to be significantly lower in acquired obstruction compared with the control group (p = 0.028). On comparing acquired with congenital obstruction, the difference in the thickening of BM, interstitial fibrosis, and Johnsen score were found to be statistically significant in favor of congenital obstruction. When comparing each level of obstruction with one another, no statistically significant differences were found with reference to histopathological features, adjusted mean late spermatid score, and Johnsen score . However, the percentage of interstitial fibrosis was significantly higher in the obstructive patients on comparing each level of obstruction with the control group. The level of significance increases as the site of obstruction approaches the testis i.e. P = 0.002 (intratesticular), 0.005 (epididymal), and 0.018 (high obstruction).

Conclusion: It is concluded that acquired obstruction of the genital tract is associated with altered testicular architecture and spermatogenic damage.

Key words: obstructive azoospermia, quantitative and qualitative evaluation, adjusted mean late spermatid score, interstitial fibrosis, hydrostatic pressure.

INTRODUCTION

The prevalence of azoospermia, defined as complete absence of sperm from the ejaculate, is less than 1 % among all men and approximately 10-15 % among infertile men. Although azoospermia has many causes, approximately 40 % of cases result from obstruction in the ductal system (**Jarow, 1989**). It is assumed that azoospermia and infertility in these cases are simply due to obstruction and that spermatogenesis is quantitatively normal. However, the effect of vasectomy on spermatogenesis is controversial (**McDonald, 2000**). While vasectomy is one of the most popular forms of the male contraception in many countries (**Farley et al., 1993**), it is rarely done in many other countries including Egypt. Some earlier study results failed to show significant effects of vasectomy on spermatogenesis in humans (**Silber, 1979**), and in animals (**Lohiya et al., 1983; Flickingers et al., 1988; Peng et al., 2002),** other studies revealed significant effects in humans (**Gupta et al., 1975; Jenkins et al., 1979; Jarow et al., 1985; Shiraishi et al., 2003; McVicar et al., 2005**) and in animals (**Barratt and Cohen, 1988; Singh and Chakravarty, 2000; Kong et al., 2004**).

These controversial results may be due to several factors such as species or individual variation, study design, postoperative complications, postoperative time interval and the methodology used to determine the spermatogenic status (**Peng et al., 2002**). Some other researchers investigated the effect of the cause of obstruction (e.g. vasectomy, congenital absence of vas deferens, herniorrhaphy, hydrocelectomy, Young syndrome, and ejaculatory duct obstruction) on spermatogenesis and testicular histology(**Nistal et al., 1999)**. The effect of the duration of obstruction was also investigated although in small number of patients by Matsuda and his colleagues (**1996**).

Some previous studies compared testicular biopsies from patients with obstructive azoospermia with postmortem testicular biopsies (**Bermudez et al., 1994; Nistal et al., 2003**) or testicular tissues obtained from men who underwent castration due to malignancy of the prostate (**Rajalakshmi et al., 1993**). The present study, on the other hand, has the advantage of using the testicular biopsies from normozoospermic men. For such cases we used the technique of wide bore needle testicular biopsy as was previously described (**Fahmy et al., 2004**). This procedure is less invasive and can provide enough sperm for ICSI and sufficient tissue for histopathological examination.

Aim of the work:

The aim of this study is to compare testicular histopathology of patients with obstructive azoospermia due to different etiologies and at different levels of obstruction with testicular histology of normozoospermic men .

Chapter (I)
(spermatogenesis)

Spermatogenesis

Organization of The Testes:

The testes are ellipsoid in shape, and engulfed by a Capsule (tunica albuginea) of strong connective tissue (**Middendroff et al., 2002**). Thin fibrous septa divide the parenchyma of the testis into about 370 conical lobules. The lobules consist of the seminiferous tubules and intertubular tissue, containing groups of endocrine Leydig cells and other cellular elements (Fig. 1). Each seminiferous tubule arises and ends at the rete testis (**Roosen-Runge and Holstein, 1978**).

The seminiferous tubules are the site of sperm production. Each seminiferous tubule is about 180 µm in diameter; the height of the germinal epithelium measures 80 µm, and the thickness of the peritubular tissue is about 8 µm (**Davidoff et al., 1990**). The germinal epithelium consists of cells at different stages of development. These cells are located within the invaginations of Sertoli cells which are connected by tight junctions separating the germinal epithelium in a basal and an adluminal compartments. These specialized zones, the so called 'tight junctions' form the blood testicular barrier of the testis (**Holstein, 1999**).

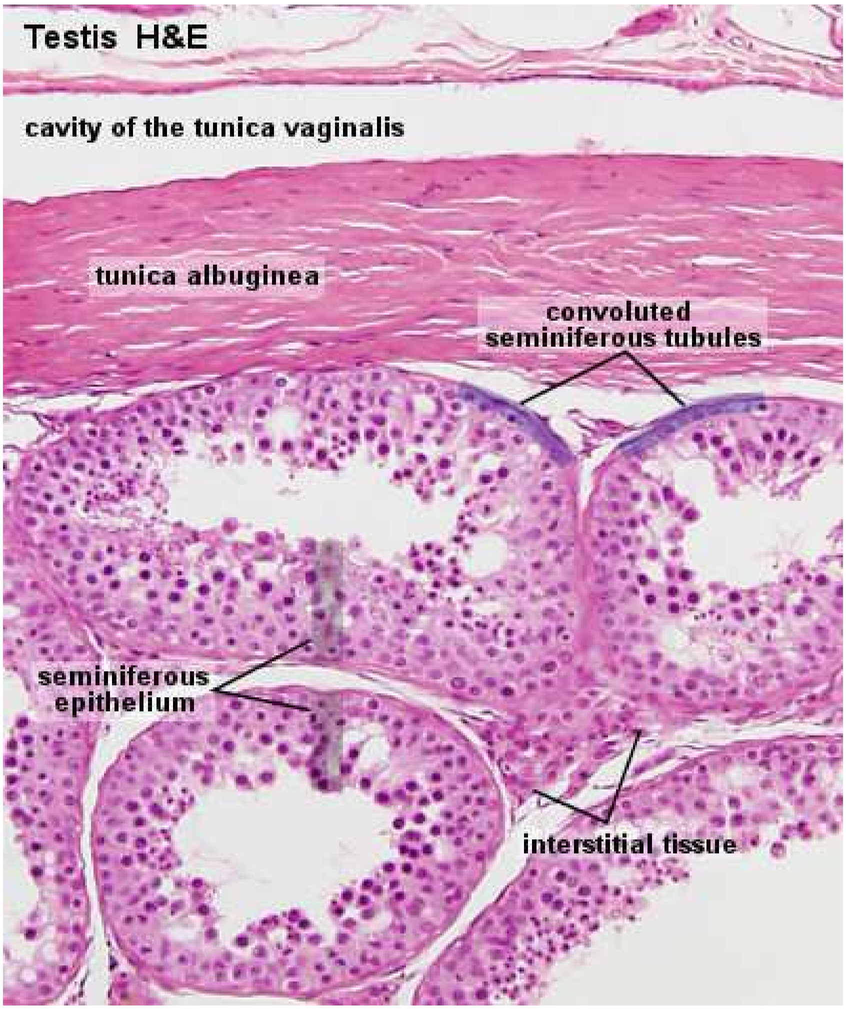

Fig. 1: Normal histology of human testes
This image at:embryology.med.unsw.edu.au/.../BGDlabXYXX_8.htm

The peritubular tissue (lamina propria of seminiferous tubules) consists of about five layers of myofibroblasts with intermingled connective tissue ground substance. These cells cause peristaltic contractions of the tubules assisting transport of the immotile spermatozoa to the rete testis (**Holstein et al., 1996**).

Spermatogenesis:

Spermatogenesis is a tightly controlled biological process in which male germ stem cells undergo sequential phases in the seminiferous tubules to become mature spermatozoa (Fig. 2). It starts at puberty and continues throughout life. Spermatogenesis can be divided into three major phases: proliferation and differentiation of spermatogonia (spermatocytogenesis), meiosis, and spermiogenesis (**de Kretser et al., 1998**).

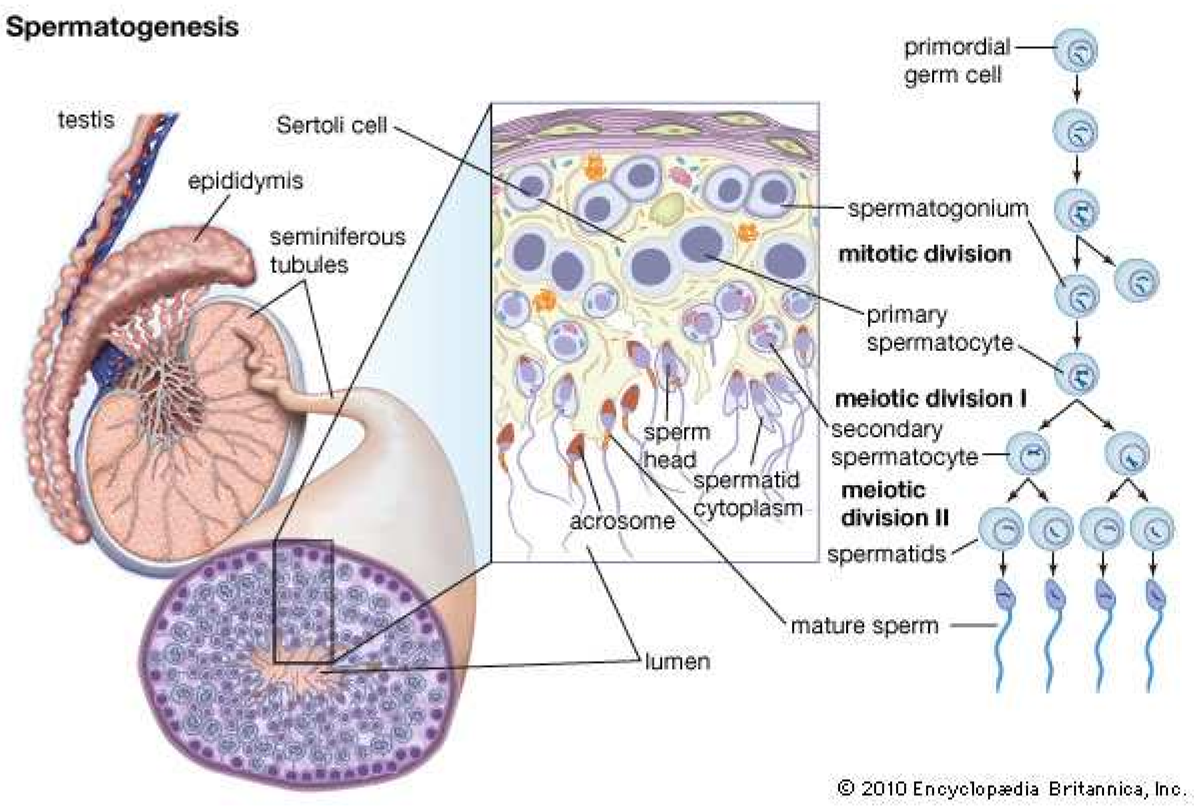

Fig. 2: Sequential phases of spermatogenesis <http://www.britannica.com/EBchecked/topic-art/559418/143155/>.