

Detection of Intratubular Germ Cell Neoplasia among Azoospermic patients

Thesis

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List of Abbreviations

Ag nor	Argyrophilic nucleolar organiser region
AP-2 γ	Activator protein -2 gamma
Chk2	Checkpoint kinase
CDK	Cyclin-dependent kinase
CEACAM 1	Carcinoembryonic antigen - related cell adhesion molecule -1
CIS	Carcinoma in situ
DDR	DNA damage response
EC	Embryonal carcinoma
ESC	Embryonic stem cell
FCM	Flow cytometry
FISH	Fluorescence in situ hybridization
FSH	Follicle stimulating hormone
GCTs	Germ cell tumors
HLA	Human leucocyte antigen
HX-eosin	Hematoxylin. Eosin
ICSI	Intracytoplasmic sperm injection
IGF	Insulin growth factor
I (12p)	Isochromosome 12p
ITGCN	Intra tubular germ cell neoplasia
LM	low power microscope
LH	Luteinizing-hormone
NES1	Normal epithelial cell-specific 1
NSGCTs	Non seminomatous germ cell tumors
OCT 3/4	Octamer-3/4

PAS	Periodic acid schiff
PLAP	Placental alkaline phosphatase
RBM	RNA-binding motif
SCO	Sertoli cell only
TDS	Testicular dysgenesis syndrome
TESE	Testicular sperm extraction
TGCT	Testicular germ cell tumours
TM	Tumor microlithiasis
WHO	World health organization

Abstract

Intratubular germ cell neoplasia (ITGCN), is a pre-invasive precursor of testicular germ cell tumors, an increased risk of harbouring (ITGCN) has been reported in men with a history of cryptorchidism, in contralateral testes of men previously treated for unilateral germ cell tumor, in intersex patients, in men with extragonadal germ cell tumor and in infertile men so a testicular biopsy is necessary to diagnose (ITGCN) . Aim of the work: The aim of this retrospective study is to find the prevalence of ITGCN among testicular biopsies from azoospermic patients attending Kasr EL-Ainy Hospital between the years 2005 – 2007. MATERIAL AND METHODS: This retrospective study was done from patients underwent testicular biopsies on Kasr El-Ainy hospital for period (2005 - 2007), for each patient we recorded the age, duration of infertility, FSH level, fresh mount and pathology, every slide was examined under light microscopy 40x magnification for histological evaluation and the suspected cases of (ITGCN) according to WHO was recorded and there paraffin sections were treated with placental alkaline phosphatase (PLAP) stain, a classic immunohistochemical marker of ITGCN for evaluation. RESULTS: Among 415 patients, (ITGCN) examination was confirmed in 4 patients which is about (1%) of cases. CONCLUSION: for all patients at high risk of (ITGCN), PLAP stain should be routinely done to the testicular biopsy, this would allow earlier detection and proper management of such serious life threatening condition and all azoospermic patients undergoing TESE should be examined histopathologically and suspicious cases of CIS (ITGCN) should be evaluated by PLAP stain.

Key words:

- ITGCN
- TESE
- PLAP

INTRODUCTION

Intratubular germ cell neoplasia (ITGCN) is the uniform precursor of testicular germ cell tumors (GCTs), except for spermatocytic seminomas in elderly men and yolk sac tumors and mature teratomas in infants. There is some variability in the terminology of ITGCN; it has also been called carcinoma in situ (CIS), or testicular intraepithelial neoplasia. However, this is not an epithelial lesion, and thus the latter terms are not preferred **Huyghe et al., (2005)**

ITGCN can be found in testicular tissue adjacent to GCTs in approximately 90 percent of adult cases **Jacobsen et al., (1999)**, and is found in all groups at risk for testicular cancer, including men with cryptorchid testes, prior testicular cancer and individuals with abnormal sexual differentiation **Parkinson et al., (2003)**.

The prevalence of ITGCN in all groups at risk for testicular cancer and other populations mirrors that of GCTs, in the absence of in vitro or animal studies, has contributed significantly to the theory that ITGCN is the precursor of GCTs **Linke et al., (2005)**.

Testicular ITGCN may be diagnosed in several different clinical scenarios:

- In the contralateral testis of a man with a GCT.
- In the testis of a man who presents with an extragonadal GCT.
- In a cryptorchid testis (regardless of orchidopexy) or in the normal contralateral testis.
- In the testes of infertile men.
- In dysgenetic gonads

A multitude of additional risk factors or undetermined relative importance have also been described, including testicular atrophy, microlithiasis, low birth weight, Down syndrome, and gestational estrogen excess **Rajpert et al., (2006).**

The CIS cells can be detected in the adjacent parenchyma of most invasive tumors, and are more frequently associated with nonseminomatous germ cell tumors (NSGCTs) than with seminomas **Oosterhuis et al., (2003).**

Aim of the work

The aim of this retrospective study is to find the prevalence of ITGCN among testicular biopsies from azoospermic patients attending Kasr EL-Ainy Hospital between the years **2005 – 2007**.

Study design: Retrospective study

Normal histology of the testis

The testes of most mammals are located extra-abdominally in the scrotum. This is actually a temperature controlling device. In most mammals spermatogenesis proceeds evenly and smoothly at an optimal temperature slightly below the core body level. The role of the scrotum is to maintain that temperature.

When the ambient temperature drops, the testes are pulled up by muscular action towards the warmth of the body cavity, and when it rises, the muscle relax, allowing the testes to descend and remain cool. Almost all terrestrial mammals have extra-abdominal testes **Handelsraan et al., (1985).**

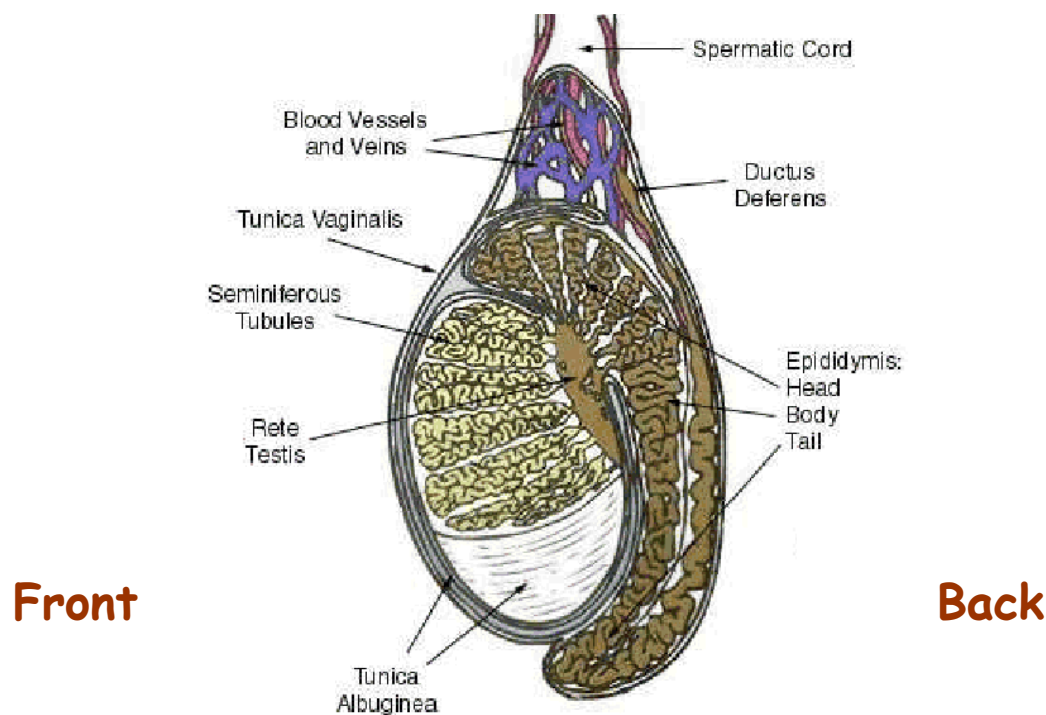


Figure (1): Shows Testes (single testis) Scott, (2000).