

Clinical Pathologic Correlation

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VGH Urology Grand Rounds

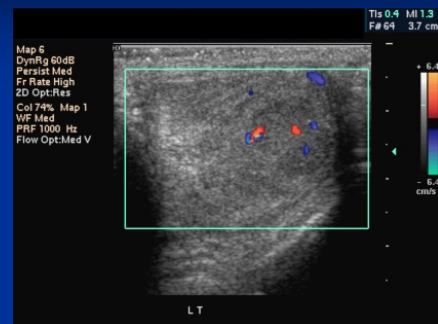
Case

- 28 yo male
- Married, no children, university student
- Left testicular mass x 1 month
- UBC Student Health Service, ABX
- Scrotal U/S

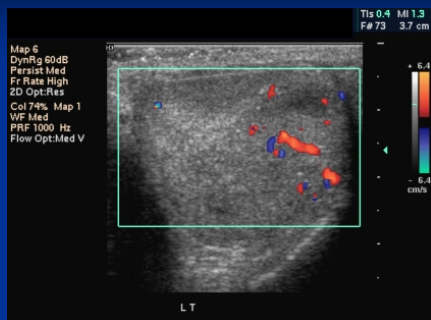
Scrotal U/S



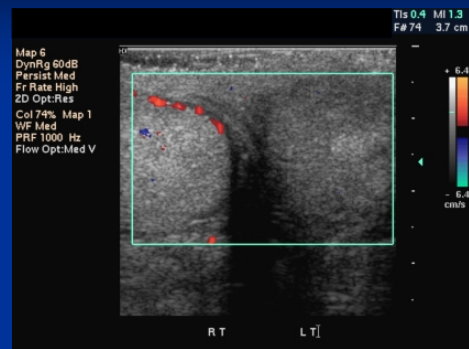
Scrotal U/S

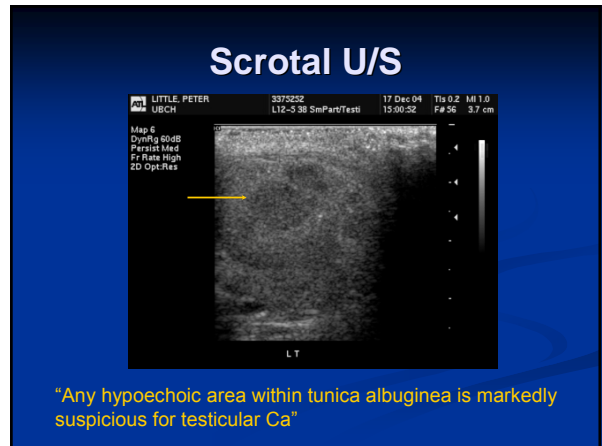
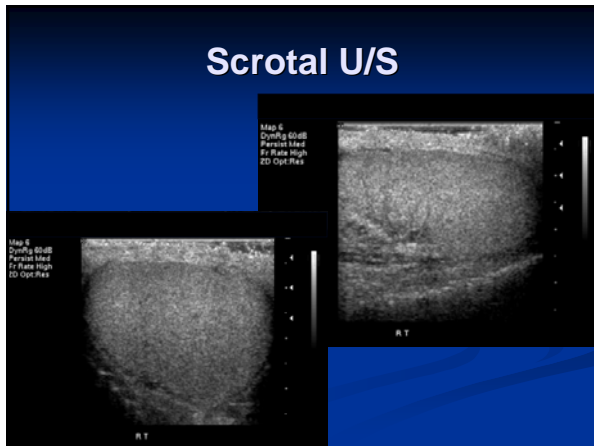


Scrotal U/S



Scrotal U/S





Ddx intratesticular lesion

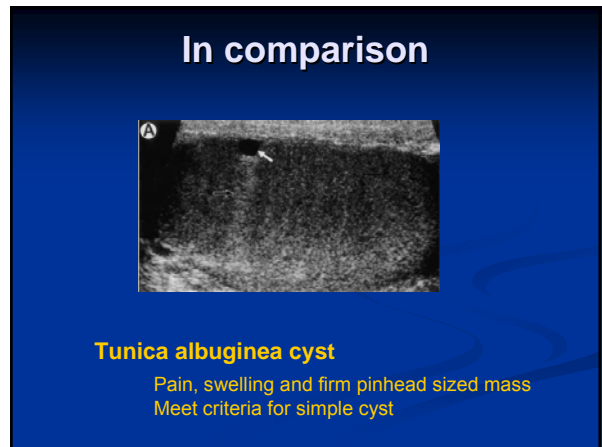
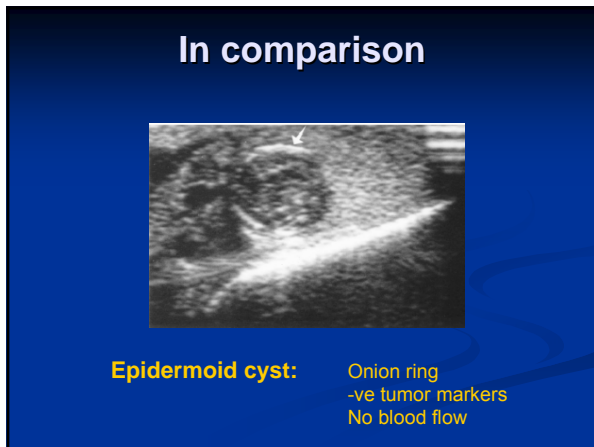
Benign:

- Epidermoid cyst
- Tunica albuginea cyst / simple cyst
- Cystic ectasia of rete testis
- Intratesticular varicocele
- Adrenal rest tumor
- Splenogonadal fusion
- Leydig cell hyperplasia
- Pick's adenoma
- Fibroma, angioma, neurofibroma, leiomyoma
- Granuloma (TB, shisto, malakoplakia)
- Infection or infarct (mumps, syphilis, W. bancrofti)
- Hematoma

Ddx intratesticular lesion

Malignant:

- Germ cell tumors
 - Seminoma
 - NSGCT (YS, embryonal, teratoma, chorio)
- Leydig cell tumor
- Sertoli cell tumor
- Gonadoblastoma
- Granulosa cell tumor
- Lymphoma (NH), leukemia, plasmacytoma
- Secondary (prostate, lung, colon, melanoma, kidney)
- Adenocarcinoma of rete testis



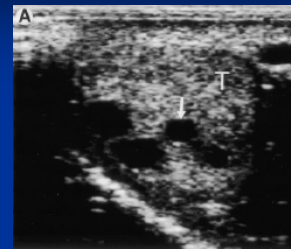
In comparison



Tubular ectasia of rete testis

A/w spermatoceles, obstruction, prior scrotal surgery

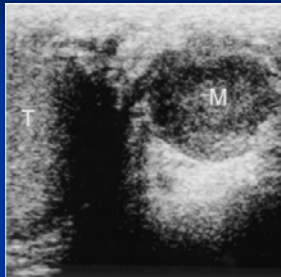
In comparison



Intratesticular varicocele

↑ flow during Valsalva
Pain from to passive congestion of testis

In comparison



Adenomatoid tumor

Most common paratesticular tumor

A little more history by urologist

- History of bilateral UDT
- Bilateral orchiopexy at age 4 yo
- Normal puberty
- No STDs, orchitis, UTIs
- N ROS
- No GU or abdominal surgeries


On exam

- Normal secondary sexual characteristics
- No gynecomastia, SC nodes, abdo masses
- Inguinal scars, no inguinal adenopathy
- Normal right testis
- Left testes – 1 x 2 cm nodule in upper pole
- Palpable vasa

Work-up

■ LDH	338	300-600 U/L
■ AFP	2.0	< 11 ug/L
■ HCG	0	< 5.0 IU/L

Sperm freezing



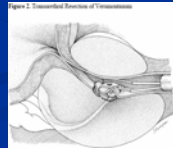
- Genesis Fertility Centre (\$295, 2 yrs of storage)
- Seminal fluid analysis = **azoospermia**
 - Volume: 3.8 ml
 - Concentration: 0
 - Motility: 0
 - Normal forms: 0

Azoospermia = absence of sperm in ejaculate (2)

- Pre-testicular
- Testicular
- Post-testicular


Aspermia = complete absence of seminal fluid

- Retrograde ejaculation
- Failure of emission



Ddx for Azoospermia

- Pre-testicular = hypogonadotropic hypogonadism**
 - Kallmann's syndrome
 - Pituitary failure
- Testicular = spermatogenic failure**
 - Klinefelter's, Y microdeletions
 - Toxins – heat, radiation, chemo, orchitis, varicocele, UDT
- Post-testicular = ductal obstruction**
 - CBAVD, Young's syndrome
 - Epididymal / vasa obstruction



Work-up for Azoospermia

Pre-testicular

- Testes – small soft
- ↓ FSH, ↓ T
- LH, prolactin
- Head CT/MRI

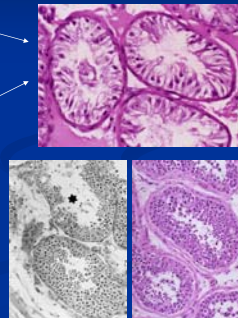
Testicular failure

- Testes – small firm
- ↑ FSH, ↑ T
- Karyotype, Y-micro deletion
- Varicocele, toxins, orchitis

Post-testicular (obstruction)

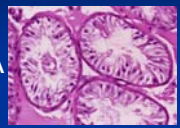
- Testes - normal
- N FSH, T
- Vas
- CFTR genetic testing

• Karyotype and genetic tests
• Genetic counseling
• Testis biopsy +/- freezing



Azoospermia: treatment options

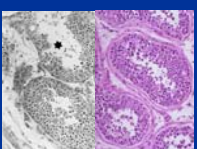
NOA (Non-obstructive azoospermia)



→ 0-6 sperm / tubule


Varicocele repair
TESE (40-60%)
TESE micro-dissection
Sperm or spermatid for ICSI

OA (Obstructive azoospermia)



33% pregnancy rate / embryo

Spermatid: 15% pregnancy rate / embryo



Clinical course

- Right testis: N
- Vas: N
- Serum testosterone: N
- Serum FSH: N
- Serum LH: N
- Left radical orchiectomy:
 - Pathology

Clinical course

- Staging
 - CT abdo/pelvis No mets
 - CXR No mets
- Stage 1 (T1N0M0) seminoma
 - 3 cm
 - No LVI
- Complete spermatogenesis

Obstructive Azoospermia

- Contributing factors in our patient?
 - Bilateral UDT
 - Bilateral orchiopexy
 - Testicular cancer
 - CFTR gene status?

Obstructive Azoospermia: Bilateral Cryptorchidism

TESE (30 pts vs 77 pts) - *Human Reproduction, 2003*

	Bilateral orchiopexy	Presumed NOA
N spermatogenesis	40%	9%
Maturation arrest / Sertoli only	33%	62%
Sperm retrieval	77%	40%

- Vas or epididymal obstruction is associated with bilateral orchiopexy and cryptorchidism

Obstructive Azoospermia: CFTR Genetic Testing?

- Cystic fibrosis > 95% have CBAVD
- CFTR gene mutations
 - 2-6% of obstructive azoospermia
 - A/w CBAVD, absent vas, epididymal obstruction
- If CFTR mutation found:
 1. Renal US
 2. Partner genetic screening for CFTR
 3. Genetic counseling

Obstructive Azoospermia in Testes Ca?

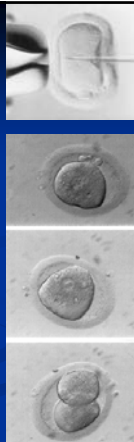
- Testicular Cancer
 - 60% have low sperm counts (with high FSH)
 - After orchiectomy, 65% achieved insemination while on surveillance - *Herr et al, 1998*
- Obstructive azoospermia in testes Ca?

Next step? Surgical reconstruction?

- Testis Bx
 - Demonstrate OA and rule out CIS
- Scrotal exploration
 - Vasovasostomy
 - Vasoepididymostomy
 - Vasography if suspect inguinal obstruction
- TESE + IVF with ICSI

Infertility in Testis Ca

- Options for sperm banking:
 - Pre-op sperm banking and cryopreservation
 - Intra-op sperm retrieval and cryopreservation from testis containing seminoma
 - Post-treatment contralateral testis biopsy (TESE)
 - In pts after chemo with permanent non-obstructive azoospermia
- Hum Reprod 2003



Investigational:

Germ cell transplantation: ICSI from spermatozoa generated in xenogeneic testes

- Human Reproduction Update 2003

- Transplantation of donor male germ cells into seminiferous tubules of a xenogeneic recipient
- Donor spermatogonia are capable of differentiating to form spermatozoa morphologically characteristic of donor species
- Alternative approach for gonadal protection and fertility preservation in patients with cancer, management of non-obstructive azoospermia

Human Reproduction vol.12 no.2 pp.286-291, 1997

Fertilization with human testicular spermatids: four successful pregnancies

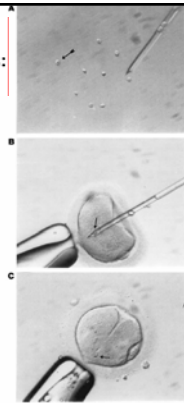


Figure 1. Injection procedure. (A) a small spermatid is aspirated into the injection needle. (B) the small spermatid is then injected into the cytoplasm of a metaphase II oocyte. (C) Following injection into the oocyte cytoplasm, the small spermatid is

Infertility

- Testicular Ca
 - Testis Ca
 - Men with testicular cancer had significantly higher frequency of severe sperm pathology – *Ceska Gynekologie 2002*
 - Tumor-induced azoospermia
 - Anti-sperm antibodies
 - Reversible?
 - Chemotherapy
 - Inactivates Sertoli cells
 - Permanent azoospermia
 - All chemotherapeutics can cause infertility
 - EXRT
 - Dose dependant
 - Reversibility?
 - RPLND
 - Sympathetic nerve damage, retrograde ejaculation
 - Nerve-sparing techniques
 - Electro-ejaculation?
- Worst effect on sperm is alkylating agents and testicular Ca

Testis-sparing surgery

Options

- Options for management of stage I seminoma
 - Surveillance
 - Retroperitoneal EXRT
 - Dog-leg
 - Para-aortic
 - +/- Ipsilateral groin and scrotum (may ↑ risk of azoospermia)
- High risk features for stage I seminoma

Surveillance

- Long term
- Follow-up
- Treatment of recurrence
- Contraindications

Retroperitoneal EXRT

- Dog-leg
 - Long-term
 - Complications
- Para-aortic
 - Long-term
 - Complications