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
"Any hypoechoic area within tunica albuginea is markedly suspicious for testicular Ca"

**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
- Fibrom, angioma, neurofibroma, leiomyoma
- Granuloma (TB, shisto, malakoplakia)
- Infection or infarct (mumps, syphiilis, W. bancrofti)
- Hematoma

**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**

**Epidermoid cyst:**
- Onion ring
- -ve tumor markers
- No blood flow

**Tunica albuginea cyst**
- Pain, swelling and firm pinhead sized mass
- Meet criteria for simple cyst
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 = azoosperma
  - Volume: 3.8 ml
  - Concentration: 0
  - Motility: 0
  - Normal forms: 0

Azoosperma = absence of sperm in ejaculate (2)
- Pre-testicular
- Testicular
- Post-testicular

Aspermia = complete absence of seminal fluid
- Retrograde ejaculation
- Failure of emission

Ddx for Azoosperma

- 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 Azoosperma

Pre-testicular
- Testes – small soft
  - ↓ FSH, ↓ T
  - LH, prolactin
  - Head CT/MRI
- Karyotype, Y-microdeletions
- Varicocele, toxins, orchitis

Testicular failure
- Testes – small firm
  - ↑ FSH, ↓ T
  - Karyotype, Y-microdeletion
- Vasectomy, orchitis, orchiditis

Post-testicular (obstruction)
- Testes – normal
  - N FSH, T
  - Vas
  - CFTR genetic testing

Azoospermia: treatment options

- NOA: 0-6 sperm / tubule
- OA: 17-35 sperm / tubule
- Varicocele repair
- TESE (40-60%)
- TESE micro-dissection
- Sperm or spermatid for ICSI
- Scrotal exploration
- Vasovasostomy
- Vasoepididymostomy
- TESE / ICSI
  - 33% pregnancy rate / embryo

Clinical course

- Right testis
- Vas
- Serum testosterone
- Serum FSH
- Serum LH
- 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

<table>
<thead>
<tr>
<th>TESE (30 pts vs 77 pts) - Human Reproduction, 2003</th>
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<tr>
<td>Testicular Cancer</td>
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<tr>
<td>- 60% have low sperm counts (with high FSH)</td>
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<tr>
<td>- After orchiectomy, 65% achieved insemination while on surveillance - Herr et al, 1998</td>
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| - Complete spermatogenesis                    |
| - No LVIN                                     |

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                          |
| - TESE + IVF with ICSI                       |

- Obstructive azoospermia in testes Ca?

| - Clinical course                            |
| - Obstructive Azoospermia: Bilateral Cryptorchidism |
| - Obstructive Azoospermia: CFTR Genetic Testing? |
| - 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

Infertility

- Testicular 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
    - Dose dependent
    - 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