Objectives:

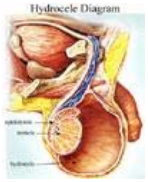
1. Give a differential diagnosis of a painless scrotal mass in an adult. Describe how to differentiate these conditions by physical examination.
2. State the typical age of presentation for germ cell testis tumours. State the most important risk factor for the development of germ cell testis tumours.
3. State three different histologic types of germ cell testis tumours. Describe the site(s) of lymph node metastases from testicular tumours.
4. Describe the urologic evaluation and management of an adult male with a solid, intratesticular mass.

Differential Diagnosis of a Scrotal Mass:

1. hydrocele
2. spermatocele
3. varicocele
4. epididymitis
5. inguinal hernia
6. testicular cancer
7. paratesticular tumour (i.e. adenomatoid tumour)

1. Hydrocele:

a. collection of peritoneal fluid between the parietal and visceral layers of the tunica vaginalis
b. called ‘communicating hydrocele’ if processus vaginalis is patent
c. typically painless
d. may be a small, soft swelling in the morning but gradually enlarges and becomes tense throughout the day
e. transilluminates
f. cannot palpate the testicle
g. no treatment required unless it is for cosmetic reasons



2. Spermatocele:

a. cystic dilatation (aneurysm) of epididymal tubule found superior and posterior to the testicle
b. transilluminates easily and is freely moveable
c. painless
d. can palpate body of testicle separate from the mass
e. no treatment required unless for cosmetic reasons

3. Varicocele:

a. varicosities of pampiniform plexus described as a ‘bag of worms’ superior to the testicle

b. 90% are on the left side
c. seen in 15% of male population
d. typically asymptomatic but may be bothersome for cosmetic reasons if varicocele is large
e. associated with male factor infertility but most men with varicoceles can expect normal fertility
f. surgical or angiographic correction of the varicocele results in improvement in semen parameters (number, motility, morphology) in 70-90% of cases

4. Epididymitis:

a. most common cause of acutely painful scrotum in postpubertal males
b. men < 35 years of age – chlamydia, gonorrhea
c. men > 35 years of age – coliforms (e.g. UTI organisms)
d. history typically consists of gradual development of scrotal pain, with fever, urethral discharge and urinary symptoms
e. diagnosis can usually be made by physical exam as the testicle is not tender but the epididymis is extremely tender (and may be enlarged and indurated)

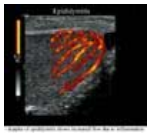
> in advanced cases, pain and swelling make the exam less helpful
- the cremasteric reflex is usually present
- the absence of pyuria make the diagnosis unlikely

f. complications if untreated or incorrectly treated include:

- abscess formation
- testicular infarction
- infertility

g. treatment is 4 weeks of antibiotics with rest, ice and NSAIDs until the pain has started to resolve

h. need to rule out testicular torsion: history, physical exam, and urinalysis may not be conclusive so an ultrasound with Doppler may be required.



5. Inguinal Hernia:

a. commonly presents as a scrotal mass
b. may be able to reduce the hernia back into the abdomen
c. a strangulated hernia presents as a tender mass palpable in the scrotum and requires immediate surgical evaluation
d. for further information on hernias see the General Surgery seminar

Acutely Painful Scrotum:

In adolescents and young men, with no history of trauma, the possibilities include:

1. testicular torsion
2. epididymitis – see above (what about orchitis?)
3. torsion of the appendix testis

> testicular torsion and torsion of the appendix testis are extremely uncommon in older men

History:

- should determine associated voiding symptoms or fever (suggesting infection)

Physical Exam:

- should include a determination of the 'lie' of the testicle – high riding in torsion
- examination of the cremasteric reflex – absent in torsion
- Phren's sign (relief of pain on lifting or supporting the scrotum) – suggests epididymitis
- is not very specific

Urinalysis and Culture:

- should be done in all cases
- pyuria suggests epididymitis

1. Testicular Torsion:

a. an anatomic deformity allows the spermatic cord to twist, resulting in occluded venous flow
b. typically presents with acute onset of severe pain with scrotal swelling not associated with trauma ('acute scrotum'), often associated with nausea and vomiting
c. scrotal edema and erythema are often present
d. age is typically 12-18 years
e. the most common misdiagnoses are torsion of the testicular appendix and epididymitis
f. physical exam should include cremasteric reflex and the physician should differentiate epididymis from the testicle

- reveals a tender, firm, often retracted testis

g. urinalysis should be normal – pyuria suggests epididymitis
h. ultrasound with Doppler is most helpful ancillary test

- see absent Doppler signal in affected testicle

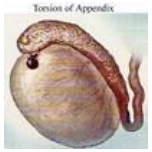
i. management of suspected testicular torsion should start with immediate referral to a urologist

- surgical detorsion will be performed along with bilateral fixation to prevent future torsion
- if blood flow is restored within 6 hours 80-100% of testicles can be saved

2. Torsion of the Testicular Appendix:

a. the appendix testis is a remnant of the Mullerian duct
b. the presentation is similar to testicular torsion with sudden onset of severe pain so it must be distinguished
c. a tiny tender mass may be palpable at the upper pole of the testis and a 'blue dot' sign may be visible on the skin of the scrotum
d. later, inflammation may produce a hydrocele and make diagnosis difficult
e. referral to a urologist is usually recommended but surgical management is not often necessary
f. the time course of this condition is about 2 weeks and management includes:

- scrotal support and NSAIDs



Testis Tumours:

Introduction:

1. testicular cancer is the most common solid malignancy in males aged 15-35 years
2. testicular cancer is more correctly referred to as germ cell tumour (GCT)

a. there are other neoplasms that may arise from the testicular tunics, epididymis, or spermatic cord that may present as a testicular mass but which require different treatments

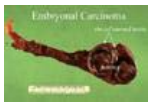
3. there is much interest in testicular cancer for several reasons:

a. metastatic disease is still highly responsive to multimodal chemotherapy
b. there are serum tumour markers that accurately reflect disease activity
c. testicular cancer arises in otherwise healthy young men

Classification of Testis Tumours:

1. Germ Cell Tumours:

a. Seminoma
b. Embryonal carcinoma
c. Teratoma, mature
d. Teratocarcinoma (combination of embryonal carcinoma and teratoma)
e. Choriocarcinoma
f. Yolk sac tumour



2. Non-Germ Cell Tumours:

a. Leydig cell tumour
b. Sertoli cell tumour
c. Gonadoblastoma
d. Adenocarcinoma of the rete testis

3. Secondary Testis Tumours:

a. Lymphoma
b. Leukemia
c. Metastases from solid tumours

4. Paratesticular Tumours:

a. Adenomatoid tumour
b. Rhabdomyosarcoma of spermatic cord
c. Mesothelioma
d. Cystadenoma of epididymis

Germ Cell Tumours:

1. account for over 90% of germ cell neoplasms
2. the lifetime probability of developing a testicular GCT is approximately 1 in 500 for North American, Caucasian males

a. the prevalence among African, African American and Asian males is much less
b. the highest prevalence of GCT is found in Scandinavia

3. there are 3 modal peaks regarding the age at diagnosis

a. infancy: almost exclusively yolk sac tumours
b. 15-35 years
c. 60 years

4. GCT typically arise in the testicle buy may, rarely, arise in other sites (extragonadal GCT) such as the retroperitoneum or mediastinum
5. the only recognized risk factor for the development of GCT is cryptorchidism

a. the relative risk of developing GCT in a male with cryptorchidism is approximately 10-40 times greater than men without cryptorchidism
b. the greater the severity of cryptorchidism, the greater the relative risk of GCT (e.g. abdominal testis is associated with a greater risk than an inguinal testis)
c. surgical correction of cryptorchidism allows for easier examination of the testis but does not change the risk of developing GCT in the future

6. among young men the frequency of histologic subtypes is as follows:

a. seminoma – 40%
b. embryonal carcinoma – 25%
c. teratocarcinoma – 25%
d. teratoma – 5%
e. choriocarcinoma – 1%
f. yolk sac tumours are the most common type of GCT in infants but yolk sac elements may be seen in small amounts with other germ cell tumours in adults

Presentation of GCT:

1. the usual presentation of a testicular GCT is a nodule or painless swelling of a testicle discovered on self-examination

2. pain is usually not a feature but may represent hemorrhage or infarction within the tumour
3. painful testicular swelling is more typical of epididymitis, orchitis or testicular torsion
4. in 10% of cases, the presenting complaint is due to metastases such as:

a. neck swelling (supraclavicular node)
b. cough or hemoptysis (lung metastases)
c. back pain (large retroperitoneal mass)
d. headache (brain metastases)

5. gynecomastia is present in 5% of cases and is often seen in association with elevated B-HCG levels
6. physical examination of the testis is performed by bimanual exam of both testes, beginning with the normal side

a. the epididymis should be differentiated from the body of the testicle and any hard nodule in the testicle should be considered suspicious

7. young men should be taught how to do self-examination and should periodically examine their own testicles until age 36 years
8. ultrasound of the testicles is very useful for characterizing lesions that may be obscured by a hydrocele, lesions that are small or that seem to arise from the epididymis
9. a large, hard, painless testicular lesion that does not transilluminate should be referred immediately to a urologist without waiting for an ultrasound

- a radical orchiectomy will most likely be performed w/o an ultrasound

Staging of Testicular Cancer:

Tis	Carcinoma-in-situ in germinal epithelium
T1	Limited to the body of the testicle
T2	Invasion through tunica albuginea, involving tunica vaginalis
T3	Involvement of the rete testis or epididymis
T4a	Involvement of the spermatic cord
T4b	Involvement of the scrotal skin
N0	No nodal involvement

N1	Retroperitoneal nodal mass < 2 cm in diameter
N2	Retroperitoneal nodal mass >2 cm but <5 cm in diameter
N3	Retroperitoneal nodal mass > 5 cm in diameter, or any mediastinal or supraclavicular adenopathy
M0*	No metastatic disease
M1*	Pulmonary metastases
M2*	Non-pulmonary metastases

*The presence of metastatic disease is often classified as minimal, moderate or advanced:

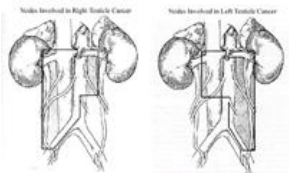
1. minimal refers to elevated serum markers after orchiectomy or less than 5 pulmonary metastases
2. moderate refers to 5-10 pulmonary metastases
3. advanced refers to greater than 10 pulmonary metastases or any bone, liver or CNS involvement

Metastasis of GCT:

1. the majority of testicular GCTs spread through the lymphatics in a predictable manner although hematogenous spread may also take place, especially with choriocarcinoma
2. the primary lymph node drainage (and therefore, the primary location for metastases) from the testicles is to the retroperitoneum

a. the right testicle drains to the inter-aortocaval, pre-caval and para-caval nodes
b. the left testicle drains to the para-aortic nodes
> from the retroperitoneum, the tumour cells spread to the mediastinum

3. inguinal lymph node metastases may occur if the scrotal skin has been invaded or when previous surgery (i.e. orchidopexy) has altered the normal lymphatic flow



General Management of Testicular Cancer:

1. the diagnosis of testicular cancer is clinical and only confirmed on pathological examination after orchiectomy
2. the correct surgical procedure for a suspected testicular cancer is an inguinal orchiectomy with removal of the testicle, tunica vaginalis, and spermatic cord to the level of the internal inguinal ring

3. Scrotal orchiectomy or trans-scrotal biopsies can potentially alter the normal lymphatic flow and make follow-up more complicated due to the potential for inguinal metastases
4. prior to orchiectomy, tumour markers (LDH, ?-HCG, ?-fetoprotein) should be determined
5. if the lesion is a testicular GCT, a CT scan of the chest and abdomen should be done to assess any retroperitoneal, mediastinal and pulmonary metastases
6. Alpha-fetoprotein:

a. produced by yolk sac tumours, embryonal carcinoma or teratocarcinoma (or combined tumours) – elevated in ~80 % of embryonal tumors
b. it can also be elevated in hepatocellular carcinoma, cirrhosis, hepatitis, pregnancy
c. NOT produced by pure seminoma or choriocarcinoma

7. B-HCG:

a. produced by choriocarcinoma and in a limited quantity by seminoma
b. NOT produced by other GCTs

8. LDH:

a. enzyme found in many tissues that is released when cellular damage occurs
b. it is elevated in 50% of testicular cancers
c. LDH is elevated in proportion to tumour volume

9. tumour markers are very useful in documenting success of treatments and recurrence of disease

> failure to normalize levels of ?-HCG or ?-fetoprotein after orchiectomy indicates residual disease even if all imaging studies are negative
> recurrence of disease after surgery or chemotherapy is often detected first by tumour markers

Management of Testicular Seminoma:

A. for seminoma confined to the testicle or with small volume retroperitoneal nodes:

1. the treatment is external beam radiotherapy (2500-3500 cGy) to the retroperitoneum and ipsilateral pelvic nodes
a. the contralateral testis is shielded to try and preserve fertility
2. radiotherapy is recommended even if the CT scan shows no evidence of disease in the retroperitoneum as approximately 25% of cases will be understaged
3. 5 year disease free rates (roughly equivalent to a cure) are over 90%
4. any relapse is treated with chemotherapy

B. for seminoma with large volume retroperitoneal nodes or other metastatic disease:

1. cis-platinum based chemotherapy is used with a typical regimen consisting of cis-platinum, vinblastine and bleomycin (PVB)
2. seminoma is extremely responsive to cis-platinum and complete response rates of 90% are expected, even with extensive retroperitoneal, mediastinal or pulmonary metastases
3. the response is usually durable with 90% of the CR (?) patients maintaining their NED (?) status beyond 5 years

Cis-platinum – alkylating agent causing inter and intrastrand DNA cross linking

1. nausea, vomiting and bone marrow suppression can be severe and may limit the amount of drug that can be given
2. nephrotoxicity is common and can lead to chronic renal failure

a. risk of this is minimized by adequate IV hydration before administration

3. renal wasting of potassium and magnesium are very common during and immediately after treatment
4. other important side effects are high frequency hearing loss and peripheral neuropathy

Vinblastine – vinca alkaloid which inhibits microtubule formation (disrupts mitotic spindle)

1. important side effects include myelosuppression and neurotoxicity
2. inadvertent intrathecal administration can cause death

Bleomycin – glycopeptide antibiotic (DNA intercalator) which causes single and double stranded breaks in DNA

1. acute 'anaphylactoid' reaction may occur on initial administration
2. chronic pulmonary fibrosis is a major toxicity seen in 10% of cases

Management of Testicular Non-Seminomatous GCTs:

1. generally non-seminomatous GCTs follow a less favourable course than pure seminomas
2. 50-70% of non-seminomatous tumours have retroperitoneal or distant metastases at the time of presentation (versus 20-30% for seminoma)
3. non-seminomatous GCTs are often a mixture of different elements e.g. seminoma, teratoma, and embryonal carcinoma may be seen within the same tumour
> this would be called a teratocarcinoma and the seminoma component would be ignored as it is less aggressive

A. For non-seminomas with no evidence of disease after radical orchiectomy:
1. a period of 'surveillance' is usually recommended

a. a typical surveillance regimen would be a history, physical exam, chest x-ray and tumour markers every month for 1 year, every 2 months for the second year and then every 3-6 months for a total of 10 years
b. CT scan of the abdomen is also done every 2-3 months for the first 2 years, then every 6 months for a total of 10 years

2. for patients unwilling or unable to undergo this extensive regimen, a retroperitoneal lymph node dissection may be performed to determine the correct stage of disease and guide decisions about chemotherapy
3. routine radiation to the peritoneum is not done as theses tumours are not very radiosensitive
4. approximately 30% of patients with no evidence of disease after orchiectomy will relapse during surveillance and require chemotherapy
5. overall survival for these patients is 90-92%

B. For patients with evidence of retroperitoneal or distant metastases at presentation, or relapse during a surveillance program, chemotherapy is indicated

1. frequently used regimens include BEP (bleomycin, etoposide

(VP-16) and cis-platinum) or VIP (VP-16 (etoposide), ifosfamide, and cis-platinum)
2. following chemotherapy it is not unusual to have a persistent mass due to the persistence of mature teratoma elements

a. these are histologically benign but may continue to grow and cause symptoms due to compression of local structures

3. a persistent retroperitoneal mass following chemotherapy is usually managed with surgical excision

a. if the mass is pure teratoma then the surgery is curative
b. if there is any persistent embryonal carcinoma, seminoma or choriocarcinoma then further chemotherapy is given

4. survival statistics depend on the volume of metastatic disease at presentation and involvement of non-pulmonary sites

a. CNS is a relative sanctuary from chemotherapeutic agents

5. patients with minimal metastatic disease have durable complete response rates of 90%
6. advanced metastatic disease is associated with a long-term survival of 30%