Testicular pathology

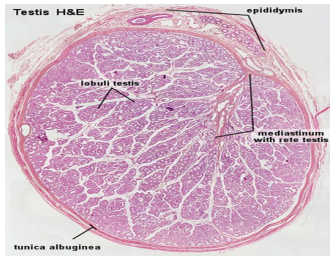
TESTICULARCANCER
AWARENESS

Important note: **Please check out this link before viewing the file to know if there are any additions or changes. The same link will be used for all or our work: Pathology Edit.**

Grey = Extra
Red = Important

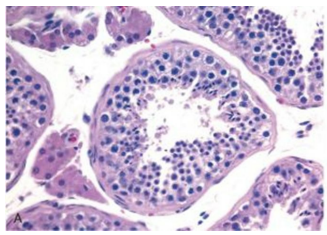
Introduction

Histology of tests:



1- Stroma:

- tunica vagnalis: composed of mesotheilial cells
- Tunica albuginea: dense irregular collagenous C.T
- Tunica vascularis: loose vascular connective tissue
- Septa: divide the tests into 250 lopuls
- Interstitial tissue: composed of interstitial cells of lydic and lose vascular C.T

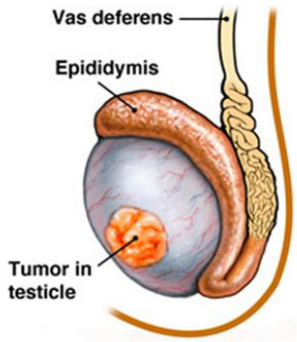


2- parenchyma:

- Interstitial cells of leydig; that secrete testosterone
- Seminiferous tubules; formed of spermatogenic cells and sertoli cells that supports and neutralize the sperms

Testicular diseases:

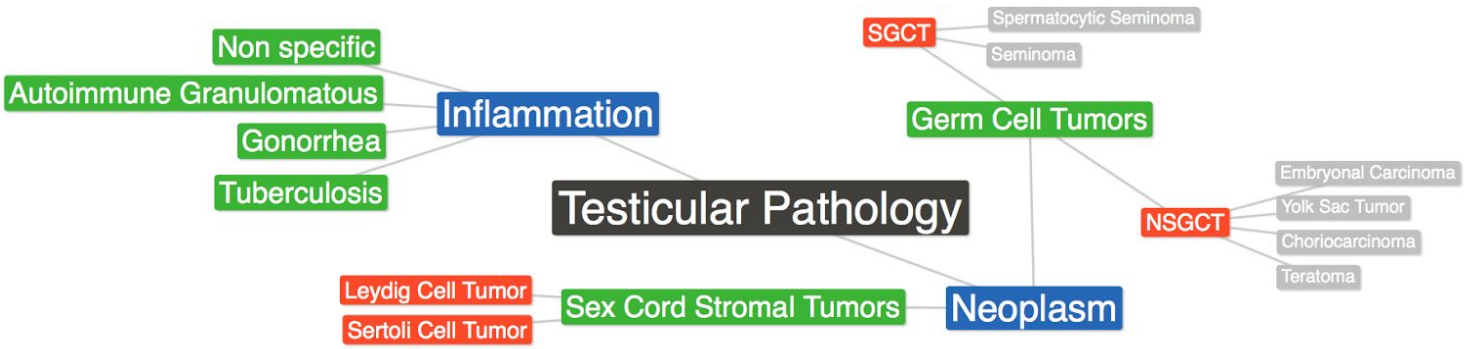
In any diseases there is two basic division. Neoplastic and Nonneoplastic, Nonneoplastic → which commonly involve the inflammatory conditions.



Vascular Disturbance: (only in robbins)

Torsion or twisting of the spermatic cord, typically results in obstruction of testicular venous drainage while leaving the thick walled and more resilient [1] arteries patent, so that intense vascular engorgement and venous infarction follow unless the torsion is relieved.

Mind Map



[1] able to recoil or spring back into shape after bending, stretching, or being compressed.

Epididymitis and orchitis:

Epididymitis: Inflammation of epididymis.
Orchitis: Inflammation of testis.

- Inflammatory conditions are generally **more common in the epididymis** than in the testis.
- However, some infections, notably syphilis[2], may begin in the testis with secondary involvement of the epididymis.

1. Non specific epididymitis and orchitis:

Begin as a primary urinary tract infection (cystitis, urethritis and genitoprostatitis) then spreads to the testis through the vas deferens or the lymphatics of the spermatic cord.

❖ **Causative organisms vary with age:**

➢ **Children:** it is uncommon. Usually associated with a **congenital** genitourinary abnormality and infection with Gram –ve rods.

➢ **In men younger than age 35 years**: ***Chlamydia trachomatis*** and ***Neisseria gonorrhoea*** are common causative organisms(sexually transmitted organisms).

➢ **In men older than 35 years: *E.Coli*** and ***Pseudomonas***. urinary tract infection pathogens spread into the reproductive tract.

❖ **Microscopic findings:**

1-Congestion, edema and **infiltration by neutrophils**, macrophages and lymphocytes.
2-May progress to frank **abscess**.
3-Heals by **fibrous scarring**.

- Initially involves the interstitium but later involves seminiferous tubules.
- Leydig cells are not usually destroyed.

2. Granulomatous (autoimmune) epididymitis & orchitis:

- Middle–aged men present with unilateral testicular mass.
- Mimic testicular tumor. (Because it present as solid mass)
- Autoimmune basis is suspected.
- May be in response to disintegrated[3] sperm, postinfectious, due to trauma or sarcoidosis.[4]
- **Microscopy:** granulomatous inflammation with plasma cells and lymphocytes involving the seminiferous tubules.

3. Gonorrhea:

Gonococcal infection can spread from urethra to prostate, seminal vesicles and then to epididymis and testis leading to suppurative orchitis and even abscess.

4. Tuberculosis:

- Begins in the epididymis and spreads to the testis.
- There is associated tuberculous prostatitis and seminal vesiculitis.
- **Microscopy:** Granulomatous inflammation and Caseous necrosis.

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[2] Syphilis is a chronic sexually transmitted infection caused by *Treponema pallidum*.
[3] break up into small parts
[4] is an inflammatory disease that affects multiple organs in the body.

Testicular Tumors

- Testicular tumors are the most important cause of firm, painless, solid enlargement of testis.
- Peak incidence between the ages of 20 and 34 years. (Young adults)
- They are more common than inflammation.
- It's important to know their classification in order to treat them because each tumor has a different method of treatment.

Classification of testicular tumors:

Testicular tumors are a heterogeneous group of tumors divided into germ cell tumors and sex cord stromal tumors:

- Pure tumor = testicular tumor is composed of one type of cells.
- Mixed tumor = testicular tumor is composed of multiple types of cells.

<table>
<tr><th colspan="2">1) GERM CELL TUMORS (95% of testicular tumors) (Arise from cells in seminiferous tubules)</th></tr>
<tr><th colspan="2">A. Tumors with One Histologic Pattern (pure form)</th></tr>
<tr><th>Seminomatous germ cell tumors</th><th>Non-Seminomatous germ cell tumors (NSGCT)</th></tr>
<tr><td>1. Seminoma
2. Spermatocytic seminoma</td><td>1. Embryonal carcinoma
2. Yolk sac (endodermal Sinus) tumor
3. Choriocarcinoma
4. Teratoma: they can be mature, immature or with malignant transformation</td></tr>
<tr><th colspan="2">B. Tumors with more than one Histologic Pattern: mixed germ cell tumor (mixed form)</th></tr>
<tr><th colspan="2">2) SEX CORD STROMAL TUMORS (Arise from cells in interstitium)</th></tr>
<tr><td colspan="2">1. Leydig cell tumor
2. Sertoli cell tumor</td></tr>
</table>

- In adults, 95% of testicular tumors are **germ cell tumors, and all are malignant.**
- Sertoli and Leydig cells (sex cord/stromal tumors) are **uncommon and are usually benign.**
- Pure tumor = testicular tumor is composed of one type of cells.
- Mixed tumor = testicular tumor is composed of multiple types of cells.

GERM CELL TUMORS (GCT)

- Between 15-30 years of age, these are the most common tumor in men.
- Most of germ cell tumors are highly aggressive cancers, capable of extensive dissemination. (metastasize very fast to mediastinum)
- Excellent prognosis.
- Germ cell tumors may have:
  - A Single (Pure) tumor type component.
  - A mixture of tumor types 60% of cases e.g. mixtures of seminomatous and nonseminomatous components.
- Most GCTs originate from precursor lesions called **intratubular germ cell neoplasia** (it is like carcinoma-in-situ).[5]

Predisposing factors:

1. **Cryptorchidism**[6] associated with a 3 to 5 fold increase in the risk of cancer. About 10% cases of testicular cancer have cryptorchidism.
2. **Testicular dysgenesis**.
3. **Genetic factors**
4. **Strong family predisposition.**
5. **Contralateral testis has cancer**.(other testis might develop cancer)
6. **Testicular tumors** are more common in whites than in blacks.

Clinical features:

- Present as a painless enlarging mass in the testis. Generally **any solid testicular mass should be considered neoplastic.**
- Germ cell tumors secrete hormones and enzymes that can be detected in blood such as (HCG, AFP, and lactate dehydrogenase).
- The standard management of solid testicular tumors is **radical orchiectomy**[7]**,** Biopsy of a testicular tumor is **not recommended** because it is associated with a risk of tumor spillage.
- GCTs can spread by direct extension to the epididymis, spermatic cord, or scrotal sac.
- Lymphatic spread is common by retroperitoneal and para-aortic nodes are first to be involved, and Hematogenous spread to Lung, liver, Brain, and bones.
  - **Seminomatous tumors are radiosensitive.**
  - **Non-seminomatous tumors are chemosensitive** and respond very well to chemotherapy.

Prognosis:

- More than 95% of patients with seminoma can be **cured.**
- 90% of patients with nonseminomatous tumors can achieve complete remission with aggressive chemotherapy, and most can be cured.
- The rare pure choriocarcinoma is the most aggressive non-seminomatous tumor and has a poor prognosis.

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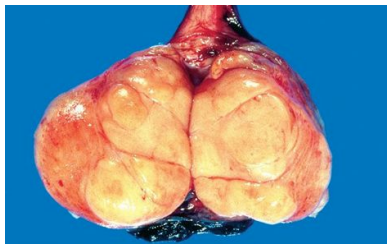
[5] Pre-cancer type of cells.
[6] undescended testis. Usually just one testicle is affected, but about 10 percent of the time, both testicles are undescended.
[7] surgical procedure in which one or both testicles are removed.

Seminoma (classic seminoma).

- Is the most common type of testicular tumors in adults.
- It is also the most common type of testicular GCT (50%).
- Almost never occur in infants,Peak incidence in the 30ies.
- An identical tumor occurs in the ovary (called dysgerminoma) and in brain called germinoma, they have the same histological findings.
- Classic seminoma is highly sensitive to radiation therapy, and the overall 5-year survival is 90 to 95%.(excellent prognosis).
- Positive for PLAP, OCT4 stain and c-kit (CD117).

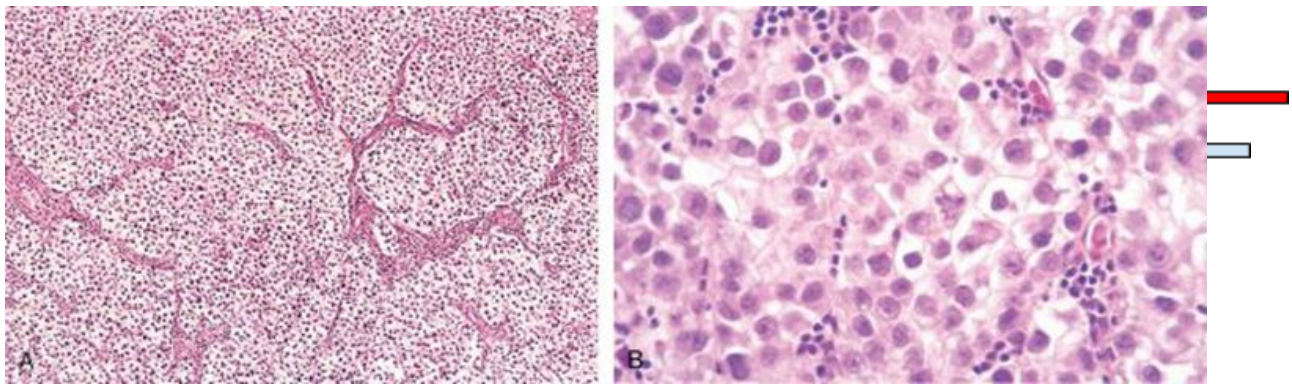


Gross morphology:

- Bulky masses, sometimes very large.
- Soft, homogenous, gray-white, lobulated cut surface.
- No necrosis or No hemorrhage.

Microscopic morphology:

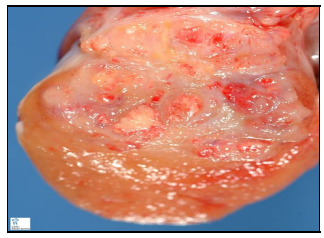
1. Sheets of uniform cells divided into lobules by delicate fibrous septa containing lymphocytes(look to red arrow)
2. Cells are large (look to blue arrow) and round with large nucleus and prominent nucleoli, with clear cytoplasm.
3. Cytoplasm of tumor cell has glycogen



Spermatocytic Seminoma

- Uncommon: 1-2 % of testicular GCTs
- Over age 65
- Slow growing tumor, does not metastasize
- Prognosis is excellent
- **Exactly same with classic seminomas In contrast with:**
  - Age group
  - Lack lymphocytic infiltrates, granulomas, and syncytiotrophoblasts
  - Not admixed with other germ cell tumor.

Embryonal Carcinoma



Characteristics:

- 15 to 35% of testicular GCTs.
- occur in 20 to 30 year age group.
- More **aggressive** than seminomas.
- Metastasizes early via both **lymphatic and hematogenous routes.**
- **Radiation is not as effective** as with seminoma, but newer chemotherapeutic agents are very effective with greatly improved prognosis. But Chemotherapy may result in differentiation into another type of germ cell tumor (e.g., teratoma).
- Can be seen combined with other GCTs **(in mixed GCTs).** Commonly
- Tumor cells are positive for **cytokeratin (CK)** and **CD30 stain.**

Gross:

- Variegated with foci of necrosis and hemorrhage.
- Smaller than seminoma, poorly demarcated.

Yolk Sac Tumor. (Endodermal sinus tumor)

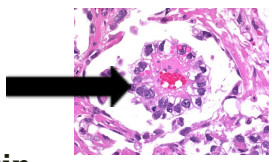
Testicular yolk sac tumors occur in two forms:

1. **Pure form** in young children (pure YST of the adult testis is rare), **most common** form in infants and young children up to 3 years and have a **very good prognosis.** (rare in adults)
2. **Mixed form** in combination with other NSGCTs, mainly embryonal carcinoma, in adults.

- Patients have elevated serum alpha fetoprotein (AFP). AFP may be used as a marker of disease progression in the patient's serum and also aid in diagnosis. (tumor markers are used for prognosis & follow up after treatment only, they aren't used for diagnosis)
- The biologic behavior of YST is similar to that of embryonal carcinoma.

Gross morphology: Non encapsulated, homogenous, yellow white, mucinous

Microscopic morphology:



- Tumor shows structure resembling endodermal sinuses called as **Schiller-Duval bodies** (glomerulus-like structures) **are characteristic.**
- Hyaline–pink globules
- Tumor cell are positive for **alpha fetoprotein (AFP) and alpha-1-antitrypsin stain.**

Choriocarcinoma. (in this tumor keep in mind "placenta")

- **Highly malignant** tumor. (the worst tumor)
- Patients have elevated serum **human chorionic gonadotropin (HCG[8])**. (produced by the placenta).
- Made up of malignant trophoblastic (placental) tissue (cyto-trophoblastic and syncytio-troblastic cells).
- Tumor cells positive for human chorionic gonadotropin **(HCG) stain.**
- Pure choriocarcinoma of the testis is **extremely rare**, and the tumor is much more **common as a component of mixed GCT.**

Gross appearance :

- **Small sized** lesions.(some time not even detected)
- Prominent hemorrhage and necrosis.(As placenta)

Teratoma

What's the story behind this tumor?

In embryogenesis there will be many precursor cells that will turn to different type of cells → tissue → organ e.g heart, lung, brain, bone, hair.

- **Teratoma is a mass full of these precursor cells.**
- Usually they are benign and found at birth.

- **It is a tumor composed of various different types of cells or organ components.**
- It can affect any age group (infants to adult)

It can be present as:

1. **Pure form** is most common in infants and children after yolk sac tumor. (rare in adult)
2. **Mixed GCTs** which is common in adult.

Features:

- Usually large 5 -10 cm
- Heterogenous appearance with solid and cystic areas.

Teratoma components:

- Composed of bizarrely distributed collection of different type of cells or organ structures.
- It can show **bone**, **cartilage** and **teeth** grossly or any of the following cell types of various organs can be present: neural/brain, cartilage, bone, squamous epithelium, hair, glandular cells, smooth muscle, thyroid tissue, bronchial epithelium of lung, pancreatic tissue etc.

[8] Is a hormone produced by the emberyo following implantation from the placenta.

Types of Teratomas:

Mature Teratoma	If the cells/tissue is mature looking.
Immature Teratoma	If some of the cells/tissue component is immature. (has a malignant potential must follow up)
Teratoma with malignant transformation (rare)	If any of the cells/tissue undergoes non-germ cell type of malignant transformation e.g squamous cells develop squamous cell carcinoma or the glandular cells develop adenocarcinoma.

Behavior of teratomas:

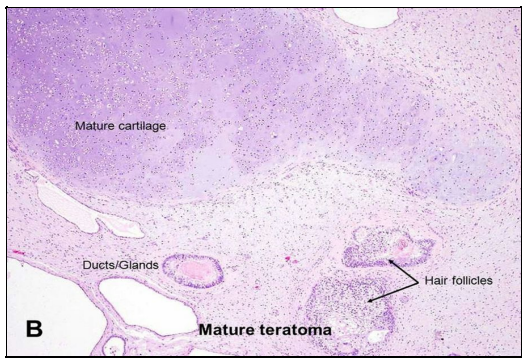
- In infants and children, **mature teratomas** are benign and **immature teratoma** is considered malignant.
- In post pubertal (Adult) male, all teratomas are regarded as **malignant**, and capable of metastasis, regardless of whether the elements are mature or not.

Mixed GCTs.

- Mixed Germ Cell Tumors are quite **common.**
- About half of testicular tumors are composed of a mixture of GCTs.

The common combinations/mixtures are:

1. Teratoma + embryonal carcinoma +/- yolk sac tumor
2. Seminoma + embryonal carcinoma



Summary.

Difference between seminoma and nonseminomatous germ cell tumors:

Seminomas	Nonseminomatous Germ Cell tumors
Seminoma	Embryonal, yolk sac, choriocarcinoma, teratoma
Radiosensitivity	chemosensitive
Late metastasis	Easy metastases to retroperitoneal lymph nodes
Excellent prognosis	More aggressive

Germ cell Tumor	Incidence	Morphology		Tests	Treatment	Notes
		gross	**Microscopic**			
Seminoma	30's	- Bulky - No necrosis - No hemorrhage	- Sheets of uniform cells with cleared cytoplasm - Cells are large	-PLAP -OCT4 stain -c-kit (CD117)	Radiation therapy	Best prognosis of all GCT
Spermatocytic Seminoma	Older than 65 yrs	Same as seminoma But with less lymphocytic infiltration and metastasis		-	Radiation therapy	-
Embryonal Carcinoma	20-30 yrs	-Foci of hemorrhage & necrosis -Smaller than seminoma	-	-Cytokeratin (CK) - CD30 stain	Chemotherapy Radioresistant	-Can be mixed -More aggressive than seminomas
Yolk Sac Tumor (Endodermal sinus tumor)	**Pure** < 3 yrs **Mixed**: adults	Non-encapsulated, homogenous, yellow white, mucinous	-Endodermal sinuses called Schiller-Duval bodies -Hyaline–pink globules	-Alpha fetoprotein (AFP) -Alpha-1-antitrypsin stain	Very good prognosis Chemotherapy	Most common in children and infants
Chorio-carcinoma	-	-Small sized lesions -Prominent hemorrhage and necrosis	Made up of malignant (placental) trophoblastic tissue.	Human chorionic gonadotropin (HCG)	Chemotherapy	-Highly malignant -Extremely rare as pure **usually mixed**
Teratoma	All ages	Heterogenous appearance with solid and cystic areas	Composed of bizarrely distributed collection of different type of cells (neuronal tissue, muscles bundle, cartilage, etc)	-	Chemotherapy	2nd most common GCT in children and infants

MCQ's.

1) A 4 year old boy was admitted to the hospital, he was diagnosed with Epididymitis. The lab test shows that he had an infection with Gram –ve rods. Which one of the following could be the associated reason?

A) Chlamydia trachomatis
B) Urinary tract infection
C) Congenital genitourinary abnormality
D) none of the above

2) A 32 year old male present with testicular enlargement, microscopy findings shows granulomatous inflammation with plasma cells and lymphocytes, what's the most likely diagnosis?

A) Orchitis
B) seminoma
C) embryonal carcinoma
D) yolk sac tumor

P.S Granulomatous (autoimmune) orchitis Mimic testicular tumor.

3) A 20-year-old man presents with dysuria, urgency, and urethral discharge. Physical examination shows suppurative urethritis, with redness and swelling at the urethral meatus. Which of the following is the most likely etiology of urethritis in this patient?

A) Borrelia recurrentis
B) E. Coli
C) Haemophilus ducreyi
D) Neisseria gonorrhoeae

Note: the key point is "suppurative urethritis"

4) A 2-year-old boy is brought to the physician because his parents noticed a mass on his right testicle. Physical examination confirms the parents' observation. An orchiectomy is performed. Microscopic examination of the surgical specimen shows neoplastic cells forming glomeruloid Schiller-Duval bodies. Which of the following serum markers is most useful for monitoring the recurrence of tumor in this patient?

(A) CA-125
(B) Estrogen
(C) α-Fetoprotein
(D) Human chorionic gonadotropin

Note: 1st the diagnosis was made which was yolk sac tumor (due to Schiller-Duval bodies), then the marker for the tumor was chosen

5) Which of the following is the most common type of tumor originating from the testicles?

A) seminoma
B) embryonal carcinoma
C) teratoma
D) choriocarcinoma

6) A 26 year old man. He was diagnosed with testicular cancer. The patient was treated with radiotherapy. However, treatment was not effective. Later investigations showed Cytokeratin and CD30 positive tumor cells. Which of the following types is most likely in this case?
A)seminoma
B)Embryonal carcinoma
C)choriocarcinoma
D)Teratoma

7) Which of the following is the most aggressive type of tumor?
A)seminoma
B)Embryonal carcinoma
C)choriocarcinoma
D)Teratoma

Answers: 1) C, 2) A, 3) D, 4) C, 5) A, 6) B, 7) C

For any suggestions or questions please don't hesitate to contact us on: Pathology434@gmail.com
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GOOD LUCK !!

ريم لبني
هديل السلمي
منى القحطاني
مها الربيعة

حسين الكاف
نواف الفوزان
فيصل ابو نهية
آحمد الصالح
محمد المحمود
فهد السحيباني
خالد الدريبي