

Reproductive

Team *of* Pathology

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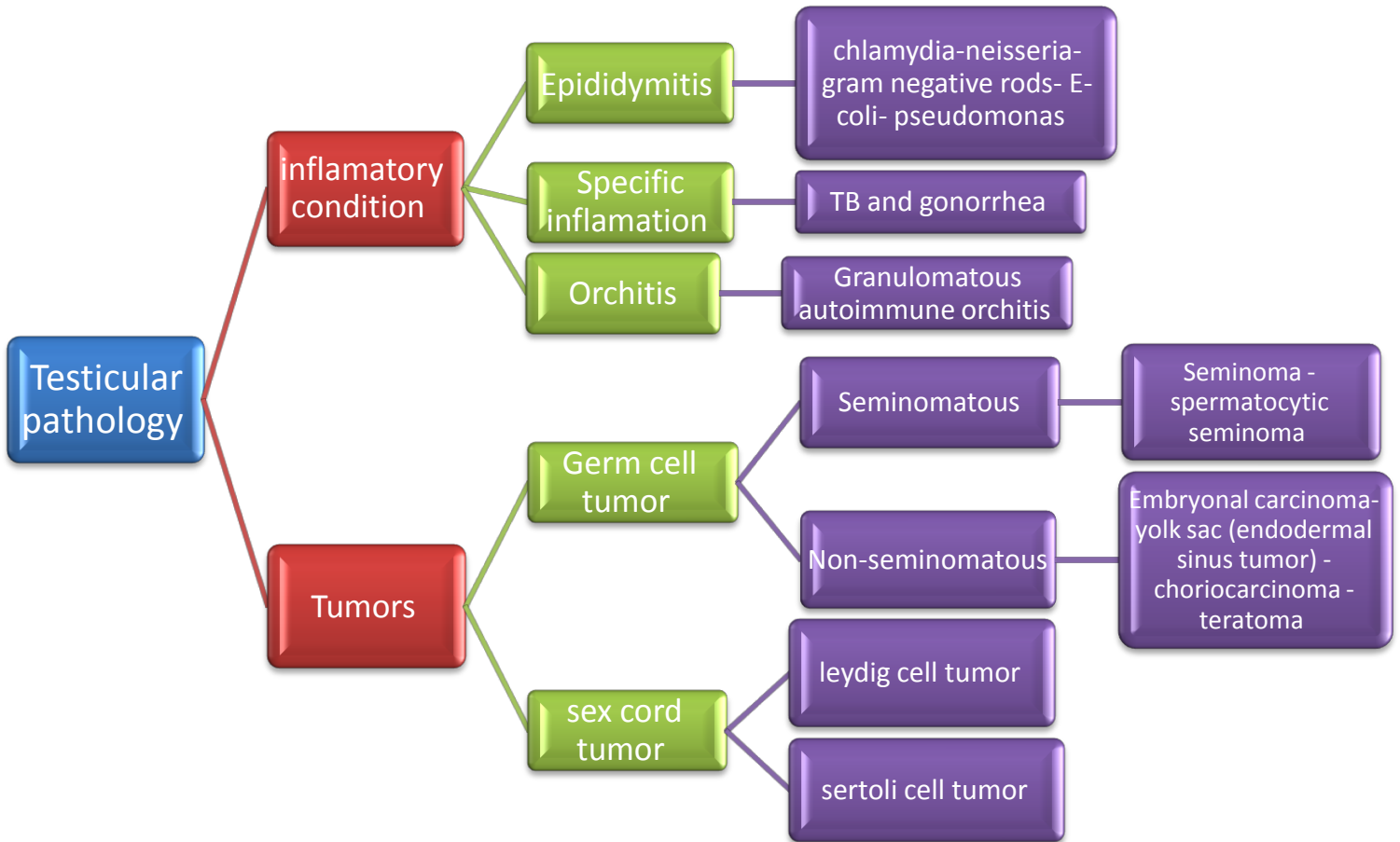
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Disease of the epididymis and testicular tumor

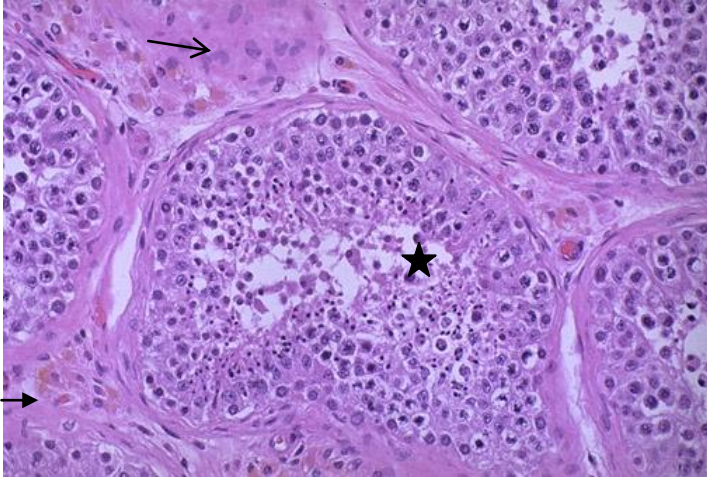


Ist Lecture



Testicular Pathology

Normal testis shows tubules with active spermatogenesis



Normal Anatomy



Pink Leyding cells are seen here in the interstitium(arrow). Note the pale golden brown pigment as well(bold arrow). There is active spermatogenesis ★

Epididymitis And ORCHITIS: it is inflammation of the testis

- Inflammatory conditions are generally **more common in the epididymis than in the testis**
- However, some infections, notably **syphilis, may begin in the testis** with secondary involvement of the epididymis
- Epididymitis and possible subsequent orchitis are commonly related to infections in the urinary tract (cystitis, urethritis, genitoprostatis)
- These infections reach the epididymis/testis through either the vas deference or the lymphatics of the spermatic cord
- Epididymitis present as painful nodule attached to the testis in the scrotum with other features of inflammation like fever (**unlike the testicular tumors which present with painless nodule**).

Epididymitis

-CAUSES: Varies with age

-Children: uncommon, usually associated with a congenital genitourinary abnormality and infection with Gram -ve rods.

-In sexually active men < 35 years → **Chlamydia trachomatis and Neisseria**

-Older than 35 Years → E.Coli and Pseudomonas.

Epididymitis And Orchitis:

Microscopic findings:

-Non specific acute inflammation characterized by congestion, edema and infiltration by lymphocytes, neutrophils and macrophages.

Nonspecific epididymitis and orchitis usually begin as a primary urinary tract infection with secondary ascending infection of the testis through the vas deferens or lymphatics of the spermatic cord

Initially involves the interstitial connective tissue → later involves tubules → may progress to frank abscess.

- Often followed by fibrous scarring.

- Leydig cells are not usually destroyed

Granulomatous (Autoimmune) Orchitis:

-Usually **middle –aged men, unilateral testicular mass.**

-Moderately tender but sometimes may present as **painless testicular mass; mimicking a testicular tumor.**

-Although an autoimmune basis is suspected, the cause of these lesions remain unknown.

-May be a response to acid-fast products of disintegrated sperm, post-infectious, or due to trauma or sarcoidosis

Microscopically: granulomas, restricted within the spermatic tubules.

Specific Inflammations:

Gonorrhea:

Extension of infection from the posterior urethra → prostate → seminal vesicles → epididymis is the usual course of a neglected gonococcal infection.

Can lead to frank abscess may spread to testis and can produce a suppurative orchitis.

Tuberculosis:

Almost invariably begins in the epididymis and may spread to the testis.

In many of these cases ,there is associated tuberculous prostatitis and seminal vesiculitis

Microscopy: Caseating Granulomatous inflammation.

Testicular Tumors

-Complex mixture of anatomic types

-95% of them originate from germ cells,

-**Age group**→15-30 years(young age group), whites> blacks (unlike prostate cancer in blacks more)

-Most of gem cell tumors are highly aggressive cancers

-Capable of wide ,extensive dissemination

-Current therapy ,**most of them can be cured**

-Non germinal tumors are generally benign

It is all low grade malignancy

Classification:

Germ cell tumors :

Seminomatous:

Seminoma

Spermatocytic seminoma

Non Seminomatous:

Embryonal carcinoma

Yolk sac (endodermal Sinus) tumor

Choriocarcinoma

Teratoma

Sex Cord Tumors:

Leydig cell tumor

Sertoli cell tumor

Testicular Tumors Pathogenesis:

Predisposing factors:

-Cryptorchidism :10% of testicular tumors

-Testicular dysgenesis

-Genetic factors

Seminoma

The most common type of germ cell tumors (50%)

Peak incidence in thirties (Almost never occur in infants)

Identical one occurs in the ovary (Dysgerminoma)

-Best prognosis among all tumors because it is **radiosensitive**.

-Always present as **painless** testicular mass

Bulky masses:

-Homogenous

- Gray-white, -Solid

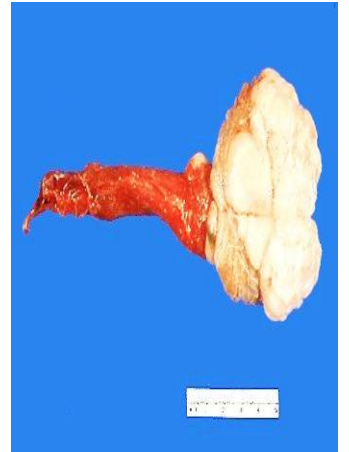
-Lobulated cut surface

Usually no necrosis or hemorrhage (that means it's less aggressive, unlike the non-seminoma)

Tumors which shows areas of hemorrhage and necrosis (more aggressive)

-In 50%, the entire testis is involved

Occasionally extends to the epididymis, spermatic cord, or scrotal sac



Seminoma of the testis appears as a fairly well-circumscribed, pale, fleshy, homogeneous mass

Seminoma , Morphology:

-Microscopically ,sheets of uniform atypical spermatogonia cells

-Lobules separated by delicate **fibrous septa with many lymphocytes** (or granulomas)

-Cells are large ,round ,has distinct cell membrane

-Large nucleus with prominent nucleolei

-Tumor cells are **positive for PLAP** (placental alkaline phosphatase)

-Normal spermatogenesis on left, seminoma on right

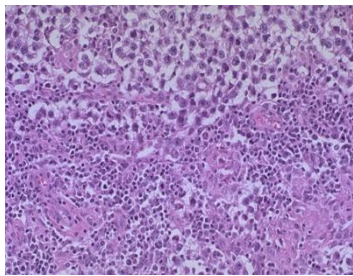
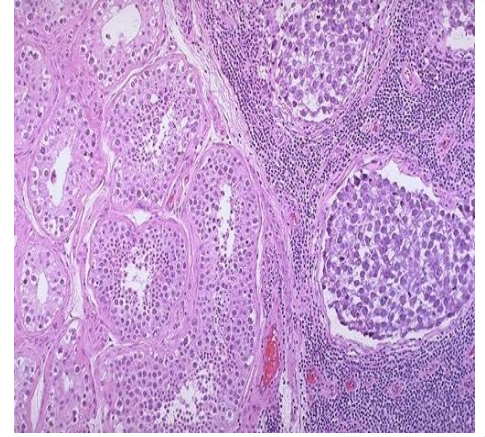
- Sheets of uniform cells

-Lobules separated by delicate **fibrous septa with many lymphocytes**

-Cells are large ,round ,has distinct cell membrane

-Large nucleus with prominent nucleolei

-Positive for PLAP



Large cells with distinct cell borders, pale nuclei, prominent nucleoli, and a sparse lymphocytic infiltrate

Spermatocytic Seminoma:

-Distinctive tumor ,clinically and histologically

-1-2 % of testicular tumors

-Over age 65(old age)

-Slow growing tumor ,rarely metastasise

-Prognosis is excellent(rarely metastasize)

-Embryonal Carcinoma:

-20 to 30 year age group (young age group)

-More aggressive than seminomas

-Smaller than seminoma

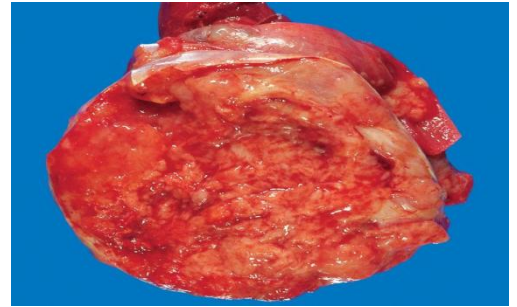
-Grossly, shows foci of necrosis and hemorrhage

-Microscopically,shows sheets of undifferentiated cells as well as primitive glandular differentiation. Cells grow in alveolar or tubular pattern ,sometimes with papillary convolutions.

-Could be present with other neoplasm in 45%

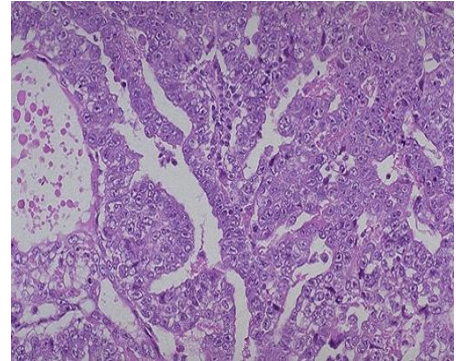
In gross picture we see:

- Embryonal carcinoma.
- Hemorrhagic mass.



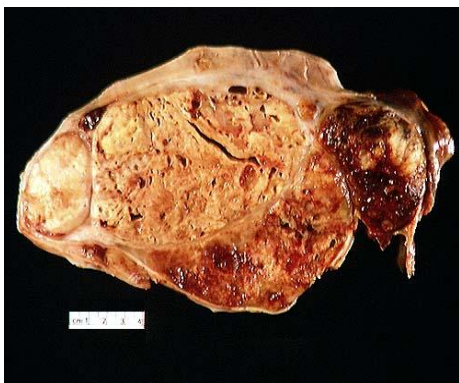
Microscopically:

- Embryonal carcinoma shows sheets of undifferentiated cells as well as with primitive glandular differentiation.
- The nuclei are large and hyperchromatic.



Yolk Sac Tumor

- Also known as Endodermal sinus tumor
- The most common tumor in infant and children up to 3 years of age**
- Has a very good prognosis.
- Grossly: Non encapsulated, homogenous ,mucinous appearance.

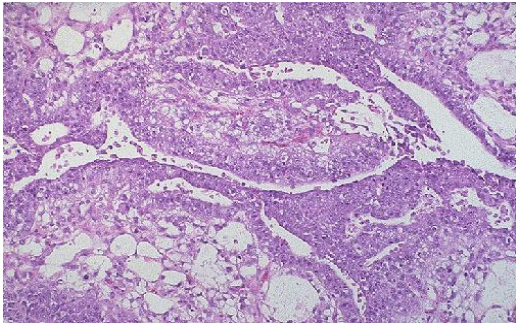


Mixed germ cell tumor of testes, with embryonal carcinoma, yolk sac tumor

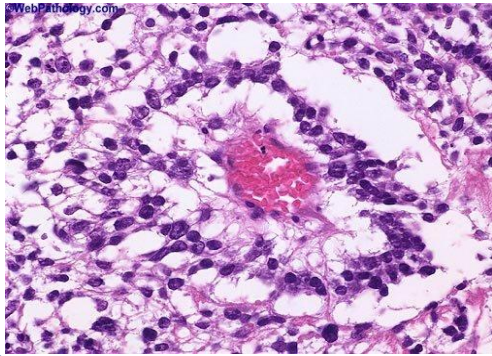
Mixed germ cell = (embryonal , yolk sac or teratoma
it is not pure it is mixed) most of the time it is mixed

Microscopically:

- The tumor is composed of lace like (reticular) network of medium sized cuboidal or elongated cells. It also shows
- Schiller-Duval bodies
- Hyaline –pink globules
- AFP positive (alpha feta protein)



-An endodermal sinus tumor (yolk sac tumor) of the testis is shown composed of primitive germ cells. These tumors are most frequent in children, but overall they are rare



-Schiller-Duval body is a structure seen in yolk sac tumor.

-It consists of a **central vessel surrounded by tumor cells** – the whole structure being contained in a cystic space often lined by flattened tumor cells

Choriocarcinoma: (common in female)

-Highly malignant tumor

-Cytotrophoblastic and syncytiotrophoblastic cells

-Small lesions

-beta hCG positive (beta human chorionic gonadotropin hormone)

It is present in urine in pregnant lady so we use it to test pregnancy.

Teratoma

Complex tumor having various cellular or organoid components, reminiscent of normal derivatives from more than one germ cell layer.

Any age, infancy to adult life

Mature forms are common in infants and children

Adult forms are rare

As a component with other histological type in 45% cases.

Usually large 5 -10 cm

Heterogeneous appearance

Hemorrhage and necrosis indicate embryonal component

Composed of heterogeneous collection of cells or organoid structures

Neural tissue ,cartilage ,squamous epithelium ,glandular components....

In children ,mature teratomas behave benign

In post pubertal male ,all teratomas regarded malignant ,and capable of metastasis ,regardless of whether the elements are mature or not.

Types of teratoma:

1-mature: we can make out what it is (skin-cartilage and adipose tissue)

2-immature: we can't make out what it is (primitive cells) – if there is immature element in mature we call it immature.

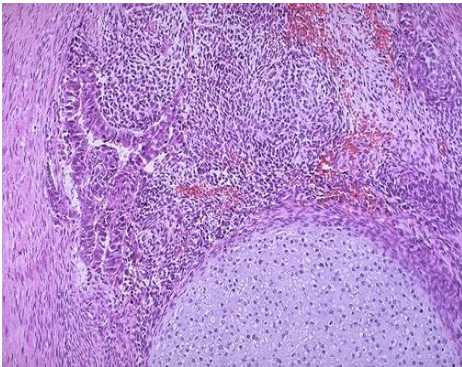
3- malignant behavior



A small testicular carcinoma is shown here.

There is a mixture of bluish cartilage with red and white tumor tissue.

This neoplasm microscopically contained mainly teratoma, but areas of embryonal carcinoma were also present



At the bottom is a focus of cartilage. Above this is a primitive mesenchymal stroma and to the left a focus of primitive cells most characteristic for embryonal carcinoma. This is embryonal carcinoma mixed with teratoma.

Testicular tumors Clinical Features:

-Biopsy of a testicular tumor is associated with a risk of tumor spillage

-The standard management of solid tumors is **radical orchiectomy (remove a testicle and the full spermatic cord)**

-Lymphatic spread is common

-Retroperitoneal and para-aortic nodes are first to be involved

-Hematogenous spread to Lung, liver, Brain, and bones.

Summary

Table 18-2. Summary of Testicular Tumors

| Tumor | Peak Age (yr) | Morphology | Tumor Markers |
|------------------------|---------------|---|--------------------------------------|
| Seminoma | 40-50 | Sheets of uniform polygonal cells with cleared cytoplasm; lymphocytes in the stroma | 10% have elevated hCG |
| Embryonal carcinoma | 20-30 | Poorly differentiated, pleomorphic cells in cords, sheets, or papillary formation; most contain some yolk sac and choriocarcinoma cells | 90% have elevated hCG or AFP or both |
| Yolk sac tumor | 3 | Poorly differentiated endothelium-like, cuboidal, or columnar cells | 90% have elevated AFP |
| Choriocarcinoma (pure) | 20-30 | Cytotrophoblast and syncytiotrophoblast without villus formation | 100% have elevated hCG |
| Teratoma | All ages | Tissues from all three germ-cell layers with varying degrees of differentiation | 50% have elevated hCG or AFP or both |
| Mixed tumor | 15-30 | Variable, depending on mixture; commonly teratoma and embryonal carcinoma | 90% have elevated hCG and AFP |

AFP, α -fetoprotein; hCG, human chorionic gonadotropin.

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SUMMARY Testicular Tumors

Testicular tumors are the most common cause of painless testicular enlargement. They occur with increased frequency in undescended testis and in males with gonadal dysgenesis. Germ cells are the source of 95% of testicular tumors, and the remainder arise from Sertoli or Leydig cells. Germ cell tumors may be composed of one histologic pattern (60% of cases) or mixed patterns (40%). They are often preceded by in situ lesions. The most common single histologic patterns of testicular tumors are seminoma, embryonal carcinoma, yolk sac tumors, choriocarcinoma, and teratoma. Mixed tumors contain more than one element, most commonly embryonal carcinoma, teratoma, and yolk sac tumors. Clinically testicular tumors can be divided into two groups: seminomas and nonseminomatous tumors. Seminomas remain confined to the testis for a long time and spread mainly to para-aortic nodes—rarely to distant sites. Nonseminomatous tumors tend to spread earlier both by lymphatics and blood vessels. hCG is produced by syncytiotrophoblasts and is always elevated in choriocarcinomas and in those seminomas that have syncytiotrophoblasts. AFP is made by yolk sac cells and is elevated in yolk sac tumors. Most nonseminomatous tumors have mixed patterns and hence elevation of both hCG and AFP.

Questions

1- A 27-year-old man presents with a testicular mass, which is resected and diagnosed as being a yolk sac tumor. Which of the following substances is most likely to be increased in this patient's serum as a result of being secreted from the cells of this tumor?

- Acid phosphatase
- AFP
- β -hCG
- PLAP

2- A 44-year-old man presents with painless enlargement of one testicle. Physical examination reveals a single testicular mass that does not trans-illuminate. The mass is resected, examined histologically, and radiation therapy is subsequently given based on the pathologist's diagnosis. Which of the following best describes the expected microscopic appearance of this tumor

- a. A mixture of malignant cytotrophoblasts and syncytiotrophoblasts
- b. Abnormal tissue derived from all three germ levels with scattered immature neural elements
- c. Large tumor cells with abundant eosinophilic, granular cytoplasm, and rare intracytoplasmic rhomboid crystals
- d. Numerous lymphocytes in the fibrous stroma between groups of tumor cells having distinct cell membranes and clear cytoplasm Sheets of undifferentiated tumor cells having focal glandular differentiation

3- A 3-year-old boy is brought to the pediatrician because his mother noticed an abnormal mass in his scrotum while changing his diapers. Further workup demonstrates elevated levels of serum a-fetoprotein. Which of the following is the most likely diagnosis?

- a. Choriocarcinoma
- b. Endodermal sinus (yolk sac) tumor
- c. Leydig cell (interstitial) tumor
- d. Teratoma

4- Which of the following is the most common tumor originating from the testicles ?

- a. seminoma
- b. embryonal carcinoma
- c. teratoma
- d. choriocarcinoma

5- what is the most common organism causing epididymitis in sexually active men ?

- a. e.coli
- b. niesseria spp
- c. pseudomonas
- d. klebsella

answer:

b,d,b,a,b