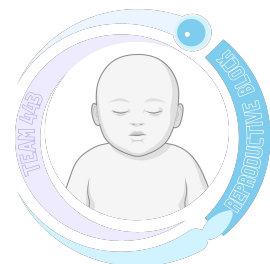
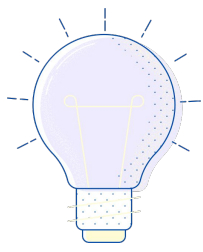
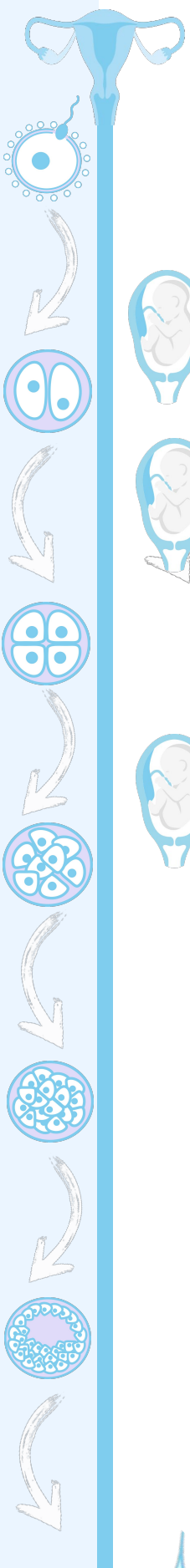




Testicular Pathology





Objectives



Have a working knowledge of the normal histology of the testis and epididymis.



Know the predisposing factors and pathology of epididymitis.

- Non specific epididymitis and orchitis
- Granulomatous/Autoimmune orchitis
- Gonorrhoea
- Tuberculosis



Be familiar with the basic classification and pathology of testicular tumors.

- Seminoma
- Yolk sac tumor
- Embryonal carcinoma
- Teratoma
- Choriocarcinoma

THIS LECTURE WAS PRESENTED BY DR.MARIA ARAFAH & DR.TARIQ ALJOHANI



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Editing File

Color index :

Main text (black)

Female Slides (Pink)

Male Slides (Blue)

Important (Red)

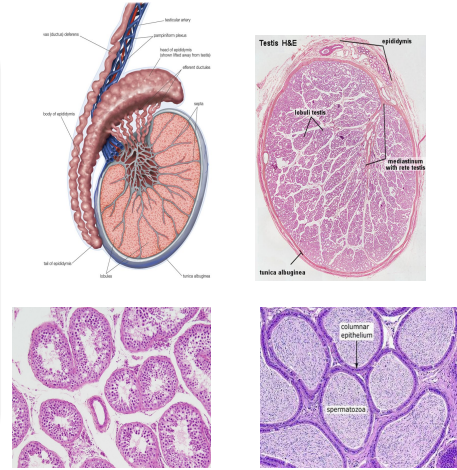
Dr's note (Green)

Extra Info (Grey)

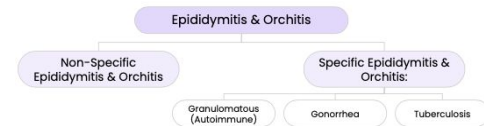
Epididymitis & Orchitis

Introduction

- Epididymitis: Inflammation of epididymis.
- Orchitis: Inflammation of testis.
- Inflammatory conditions are more common in the epididymis than in testis.
- However, some infections, notably Syphilis, may begin in testis with secondary involvement of epididymis.



Non-Specific Epididymitis & Orchitis



Pathology

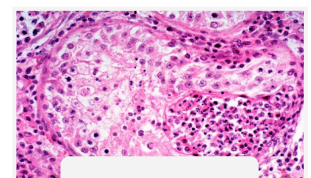
- Are commonly related to infections in the urinary tract (cystitis, urethritis & genito-prostatitis).
- Infections reach the epididymis/testis through:
 - Vas deferens.
 - The lymphatics of spermatic cord.

Causative Organisms vary with age:

- Children: it is uncommon. Usually associated with a congenital genitourinary abnormality & Gram -ve rods.
- Men younger than 35 y/o: Chlamydia trachomatis & Neisseria are common causative organisms
- Men older than 35 y/o: E.Coli & pseudomonas.

Microscopic Findings:

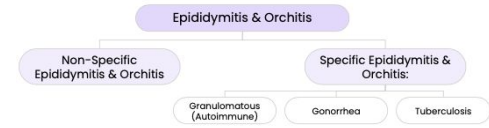
- Congestion, edema & infiltration by neutrophils, macrophages & lymphocytes.
- Initially involves interstitium but later involves the seminiferous tubules.
- Leydig cells are not usually destroyed
- May progress to frank abscess
- The infection heals by fibrous scarring.



Orchitis

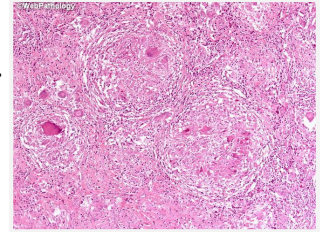
Epididymitis & Orchitis

Specific Epididymitis & Orchitis



Granulomatous (Autoimmune)

- It affects middle-aged men.
- Presents with unilateral testicular mass.
- Mimics testicular tumor
- Autoimmune basis is suspected.
- May be in response to disintegrated sperm, post-infectious, due to trauma or sarcoidosis.
- Microscopy:
 - Granulomatous inflammation with plasma cells & lymphocytes.



Gonorrhoea

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

Tuberculosis

- It begins in epididymis and spreads to the testis.
- There is usually associated tuberculous prostatitis and seminal vesiculitis.
- Microscopy: **Caseating granulomas**

Deep Focus Question



Which of the following is NOT seen with epididymitis?

- Enlarged epididymis
- Decreased blood flow to the epididymis
- May be focal or diffuse
- Orchitis often secondary due to the spread of infection
- Decreased echogenicity of the epididymis

Answer: B

Testicular tumors

01

Testicular tumors are the most important cause of a firm, painless enlargement of testis.

02

Peak incidence is between the age of 15/20 and 34 years.

Testicular tumors are divided into germ cell tumors and sex cord stromal tumors:

GERM CELL TUMORS (95% of testicular tumors)	Tumors with one histologic pattern (pure form) <ul style="list-style-type: none"> ○ Seminomatous germ cell tumors: <ul style="list-style-type: none"> -Seminoma -Spermatocytic tumor (formerly known as spermatocytic seminoma) ○ Non-Seminomatous germ cell tumors (NSGCT): <ul style="list-style-type: none"> -Embryonal carcinoma -Yolk sac (endodermal Sinus) tumor -Choriocarcinoma -Teratoma: they can be mature, immature or with malignant transformation
	Tumors with more than one histologic pattern: mixed germ cell tumor (mixed form)
SEX CORD STROMAL TUMORS.	<ul style="list-style-type: none"> ○ Leydig cell tumor ○ Sertoli cell tumor

- adults, 95% of testicular tumors are germ cell tumors, and all are malignant.
- Sertoli or Leydig cells (sex cord/stromal) tumors are uncommon and are usually benign.



Clinical Note

Tumor markers & stains (in this lecture)

Seminoma	Embryonal	Yolk Sac	Choriocarcinoma
PLAP, OCT4 & c-kit (CD117) stains	Cytokeratin (CK) and CD30 stain.	AFP and alpha1-antitrypsin stain.	human chorionic gonadotropin (HCG)

Germ Cell Tumor

They occur between 15-30\34 years of age, these are the most common tumor in men.

most germ cell tumors are highly aggressive cancers, capable of extensive dissemination.

Good news is that with current therapy most of them can be cured.

germ cell tumors may have:

a single tumor type component, or as in 60% / 40% of cases a mixture of components e.g mixtures of seminomatous and non-seminomatous.

most germ cell tumors originate from precursor lesions called intratubular germ cell neoplasia (it is like carcinoma in- situ)

Except spermatocytic tumors (not associated with precursor lesion) and we have to check pediatric patients for this lesion too. Patho441

Risk factors

cryptorchidism: there is a 3 to 5 fold increase in the risk of cancer in the undescended testis and in the contralateral descended testis. About 10% cases of testicular cancer have cryptorchidism.

testicular dysgenesis

genetic factors

strong family predisposition: brothers, fathers and sons of testicular cancer patients are at risk.

race: testicular tumors are more common in whites than in blacks.

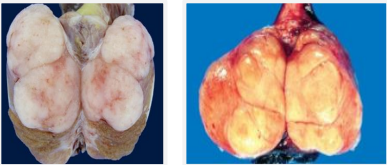
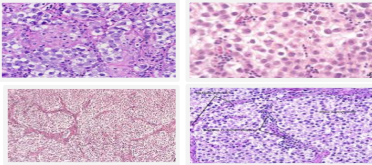
There is a high risk of developing cancer in one testis if the contralateral testis has cancer.

Seminomatous Germ Cell Tumors

Seminoma

Overview

- It is the **most common type of testicular tumors**.
- It is also the most common type of testicular GCT (50%).
- **Identical tumor occurs in the ovary (called dysgerminoma)**.
- Peak incidence is between 40–50 y/o.
- Almost never occur in infants.
- **Secretes lactate dehydrogenase LDH**.

Morphology		Prognosis
Grossly	Microscopically	<ul style="list-style-type: none"> • Classic seminoma is highly sensitive to radiation therapy & the 5-year survival is 90 - 95%.
<ul style="list-style-type: none"> • Bulky masses, sometimes very large. • Homogenous, gray-white, lobulated cut surface. • No necrosis or hemorrhage except in large tumors. • Large tumors may contain foci of coagulative necrosis, usually without hemorrhage. 	<ul style="list-style-type: none"> • Sheets of uniform cells (undifferentiated germ cells). • Divided into lobules by delicate fibrous septa containing lymphocytes. • Cells are large and round with large nucleus and prominent nucleoli. • Cytoplasm of tumor cell has glycogen (appears white and vacuolated). • The tumor cells are positive for: PLAP, OCT4 & c-kit (CD117) stains (Special stains in Seminoma, which help with diagnosis)  <p>Lobules separated by fibrous septa that contain lymphocytes</p>	

Spermatocytic tumor

Overview

- It was called previously **spermatocytic seminoma**.
- Uncommon: 1-2 % of testicular GCTs (Germ cell tumors)
- **Affects men >65 years of age**.
- Slowly growing tumor, does not metastasize.
- **Not associated with intratubular germ cell neoplasia**.
- **Prognosis is excellent**.

Non Seminomatous germ cell tumors

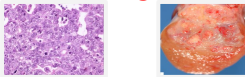
Embryonal Carcinoma

Overview

- Age Group :20 to 30 years.
- It accounts for about 15 to 35% of testicular GCTs
- Can be seen combined with other GCT (in mixed GCTs)
- Tumor cells are positive for **Cytokeratin (CK) and CD30 stain**.

Morphology

- Gross: smaller than seminoma, poorly demarcated
- Microscopic: Variegated with foci of **necrosis and hemorrhage**



Prognosis

- More aggressive than seminomas.
- Metastasizes early via both lymphatic and hematogenous routes.

Treatment

- Not radiosensitive, they are **chemosensitive**
- New chemotherapeutic agents are very effective and greatly improve prognosis.

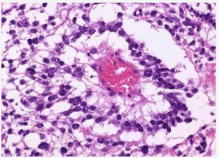
Yolk sac tumor

Overview

- Also called Endodermal sinus tumor.
- Testicular yolk sac tumors occur in two forms:
 - As a pure form seen in young children (pure YST of the adult testis is rare)
 - As in combination with other NSGCTs seen in adults.
- **It is the most common tumor in infant and children up to 3 years of age with a very good prognosis.**
- **In adults it occurs as a part or component of mixed GCT (commonly mixed with embryonal carcinoma).**

Non Seminomatous germ cell tumors

Yolk sac tumor

Morphology	Gross	Non encapsulated, homogenous, yellow white, mucinous.
	Microscopic	Tumor shows structure resembling endodermal sinuses called as Schiller - Duval bodies are characteristic. Hyaline-pink globules 
Diagnosis		<p>Patients have elevated serum alpha fetoprotein (AFP). AFP may be used to confirm the (aid in) diagnosis and as a marker of disease progression in the patient's Serum or recurrence.</p> <p>Tumor cell are positive for alpha fetoprotein and alpha-1-antitrypsin stain</p>
Treatment		<ul style="list-style-type: none"> The biologic behavior of YST is similar to that of embryonal carcinoma. <p>(But responds well to chemotherapy)</p>

CHORIOCARCINOMA

Overview

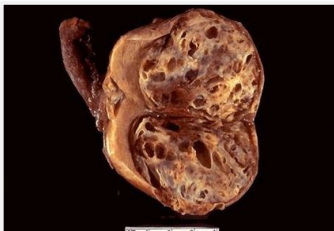


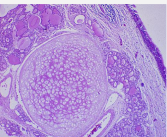
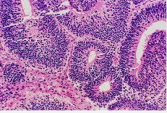
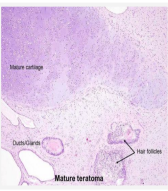
- it is a highly malignant tumor.
- Patients have elevated serum human chorionic gonadotropin (HCG).
- They are small sized lesions
- They are made up of malignant trophoblastic (placental) tissue (cytotrophoblastic and syncytiotrophoblastic cells) with prominent hemorrhage and necrosis.
- Tumor cells are positive for HCG stain.
- Pure choriocarcinoma of the testis is extremely rare, and the tumor is much more common as a component of mixed GCT.

Non Seminomatous germ cell tumors

Teratoma

Overview

- It is a tumor of various types of cells or organ components.
- They can occur at any age (from infancy to adult life).
- In its pure form, it is common in infants and children second to yolk sac tumors.
- In adults, the pure form is rare, it occurs usually as a part of a mixed GCT.

Morphology		Prognosis
Grossly	Microscopically	
<p>Large (5 -10 cm).</p> <ul style="list-style-type: none"> ◦ Solid and cystic areas ◦ Heterogeneous: bizarrely distributed collection of different type of cells or organ structures (e.g: bone, cartilage and teeth). ◦ Heterogeneous appearance with solid and cystic areas. Can show bone, cartilage and teeth grossly.   	<p>Any cell type of various organs can be present: neural, cartilage, bone, squamous epithelium, hair, glandular cells, smooth muscle, thyroid tissue, bronchial epithelium of lung , pancreatic tissue etc.</p> <p>A. Mature: if the cells/tissue are mature looking B. Immature: if some cells/tissue are immature C. Teratoma with malignant transformation: if any of the cells/tissues undergo a non germ cell type of malignant transformation e.g. squamous cells developing into squamous cell carcinoma or glandular cell developing into Adenocarcinoma</p>   	<ul style="list-style-type: none"> • Prepubertal males → benign. (mature only, immature is always malignant) • Postpubertal males → malignant (Majority) (regardless of maturity, unlike females) • Mature & immature teratomas are both capable of metastasis. • Behavior of teratoma: <ul style="list-style-type: none"> ◦ In infants and children, mature teratomas are benign and immature teratoma is considered malignant. ◦ In post pubertal male, all teratomas are regarded as malignant, and capable of metastasis, regardless of whether the elements are mature or not.

Germ Cells Tumors (GCTs)

Mixed Germ Cell Tumors (GCTs)

Overview

- Common.** Half of testicular tumors are composed of a mixture of GCTs.
- The common combinations or mixtures are:
 - Seminoma + embryonal carcinoma.
 - Teratoma + embryonal carcinoma +/- yolk sac tumor.

Metastasis

- Can spread by Direct extension to the epididymis, spermatic cord, or scrotal sac.
- Lymphatic spread: Retroperitoneal and para-aortic nodes are first to be involved.
- Hematogenous spread to Lung, liver, Brain, and bones.

Clinical features

- Painless solid enlarging mass in the testis. Generally any solid testicular mass should be considered neoplastic.
- They can secrete hormones and enzymes that can be detected in blood: HCG (in choriocarcinoma), AFP (yolk sac tumor), and lactate dehydrogenase, LDH (seminoma)

Prognosis

- A biopsy of a testicular tumor is not recommended because it is associated with a risk of tumor spillage. The standard management: radical orchiectomy.
- Seminomatous tumors → **radiosensitive**: respond well to radiotherapy. > **95%** of patients can be cured.
- Non-seminomatous tumors → **chemosensitive**: respond very well to chemotherapy > **90%** of patients achieve complete remission with aggressive chemotherapy.
- The rare pure choriocarcinoma is the most aggressive non-seminomatous tumor. Pure choriocarcinoma has a poor prognosis (more common in females)

Seminomas	Nonseminomatous Germ Cell Tumors
Seminoma	Embryonal, yolk sac, choriocarcinoma, teratoma
Radiosensitive	Not radiosensitive
Chemosensitive	Chemosensitive
Late metastasis	Early metastases to retroperitoneal lymph nodes
Excellent prognosis	More aggressive

Keywords

Germ Cell Tumors	<ul style="list-style-type: none"> all are malignant highly aggressive cancers, capable of extensive dissemination originate from precursor lesion called intratubular germ cell neoplasia Risk factors : Cryptorchidism , Testicular dysgenesis , family predisposition 		
	Seminomatous Germ Cell Tumors	Seminoma <ul style="list-style-type: none"> most common type Identical to ovarian dysgerminoma Bulky masses Homogenous, gray-white, lobulated cut surface. Sheets of uniform cells & glycogen rich fibrous septa containing lymphocytes. positive for: PLAP, OCT4 & c-kit (CD117) stains highly sensitive to radiation therapy 	
		Spermatocytic tumor <ul style="list-style-type: none"> Slowly growing tumor does not metastasize. previously spermatocytic seminoma. Prognosis is excellent. 	
	Non Seminomatous germ cell tumors	Embryonal Carcinoma <ul style="list-style-type: none"> positive for Cytokeratin (CK) and CD30 stain. poorly demarcated Microscopic: Variegated with foci of necrosis and hemorrhage chemosensitive Metastasizes early via both lymphatic and hematogenous routes. 	
		Yolk Sac Tumor <ul style="list-style-type: none"> As a pure form seen in young children As in combination with other NSGCTs seen in adults. most common tumor in infant and children elevated serum alpha fetoprotein (AFP) positive for AFP and alpha-1-antitrypsin stain. Non encapsulated, homogenous Schiller-Duval bodies Hyaline-pink globules 	
		Choriocarcinoma <ul style="list-style-type: none"> more common as a component of mixed GCT. positive for human chorionic gonadotropin HCG stain Malignant trophoblastic (placental) tissue hemorrhage and necrosis. 	
		Teratoma <ul style="list-style-type: none"> Heterogeneous: bizarrely distributed collection of different type of cells or organ structures (e.g: bone, cartilage and teeth). Prepubertal males → benign. Postpubertal males → malignant 	
	Mixed Germ Cell Tumors	<ul style="list-style-type: none"> Direct extension to the epididymis, spermatic cord, or scrotal sac. Lymphatic spread: Retroperitoneal and para-aortic nodes are first to be involved. Hematogenous spread to Lung, liver, Brain, and bones. They can secrete hormones and enzymes that can be detected in blood: HCG (in choriocarcinoma), AFP (yolk sac tumor), and lactate dehydrogenase LDH (seminoma) 	
	Epididymitis & Orchitis	Granulomatous (Autoimmune)	<ul style="list-style-type: none"> in response to disintegrated sperm, post-infectious, due to trauma or sarcoidosis. Granulomatous inflammation with plasma cells & lymphocytes.
		Gonorrhoea	<ul style="list-style-type: none"> Gonococcal infection with suppurative orchitis and even abscess
Tuberculosis		<ul style="list-style-type: none"> Caseating granulomas 	

YOU VS MCQs



Question 1

Patient with testicular cancer with lymphocytes, homogenous cells with pale cytoplasm and dark nucleus, identify the tumor?

- Yolk sac
- Choriocarcinoma
- Seminoma
- Dysgerminoma



Question 2

A testicular tumor obtained from a 3 year old boy showed glomeruloid Schiller-Duval bodies on histopathologic examination. Which one of the following tumor markers is useful for monitoring the recurrence of this malignant testicular neoplasm in this patient?

- Alpha fetoprotein
- Ca 125
- Human chorionic gonadotropin
- Carcinoma embryonic antigen



Question 3

Which of the following is a predisposing factor to testicular tumors?

- Cigarette smoking
- Cryptorchidism
- Trisomy 21
- Testicular torsion



Question 4

A 31-year-old male presented with painless testicular mass after removal of the mass they sent it to the pathologist. Under microscope there were uniform large cell with prominent large nucleoli and serum CD117 was elevated. What is the diagnosis?

- Embryonal cell carcinoma
- Seminoma
- Choriocarcinoma
- Yolk sac tumor

YOU VS MCQs



Question 5

Which of the following is not a testicular tumor?

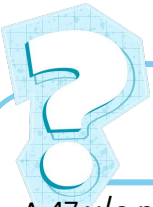
- Seminoma
- Dysgerminoma
- yolk sac
- Orchitis



Question 6

38 y/o male was suspected to have non-specific epididymitis, what could be the causative organism?

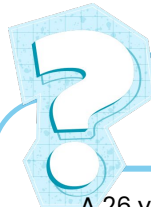
- Chlamydia Trachomatis
- Candida Albicans
- Escherichia Coli
- Staphylococcus Aureus



Question 7

A 47 y/o male presented with a large bulky mass, the microscopic biopsy showed sheath of large round cells with prominent nucleoli and detected glycogen in the cytoplasm. The result is expected to be positive for which of the following stains?

- NSE
- Prostate-specific antigen
- CD117
- HCG



Question 8

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?

- Yolk sac tumors
- Embryonal carcinoma
- Seminoma
- Teratoma

Cases

1. 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. *Chlamydia trachomatis*

C. *Haemophilus ducreyi*

D. *Neisseria gonorrhoeae*

2. A 60-year-old man with a history of nodular prostatic hyperplasia and recurrent cystitis presents with pain in the scrotum. His temperature is 38°C (101°F). Physical examination reveals a small, tender nodule attached to the testis. Which of the following is the most likely diagnosis?

A. Epididymitis

B. Orchitis

C. Spermatocele

D. Urethritis

3. An 8-year-old boy is brought to the physician because his parents noticed a mass on his left testicle. Physical examination reveals a solid mass that cannot be transilluminated, and biopsy shows a haphazard arrangement of benign differentiated tissues, including squamous epithelium, glandular epithelium, cartilage, and neural tissue. The left testicle was removed surgically, and the patient is symptom free 5 years later. Which of the following is the most likely diagnosis?

A. Embryonal carcinoma

B. Mature teratoma

C. Mixed germ cell tumor

D. Seminoma

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?

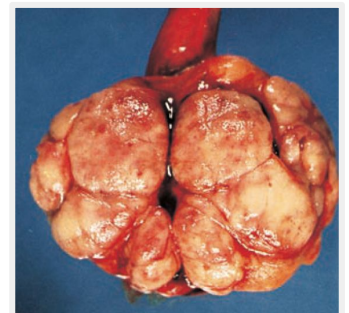
A. CA-125

B. Carcinoembryonic antigen

C. α -Fetoprotein

D. Human chorionic gonadotropin

5. A 32-year-old man presents with a testicular mass that he first noticed 2 weeks ago. The mass cannot be transilluminated and appears solid and homogeneous on ultrasound examination. No tumor markers are detected on serologic testing. An orchiectomy is performed, and the surgical specimen is shown in the image. Which of the following is the most likely diagnosis?



A. Choriocarcinoma

B. Embryonal carcinoma

C. Seminoma

D. Yolk sac carcinoma



1-D / 2-A / 3-B / 4-C / 5-C

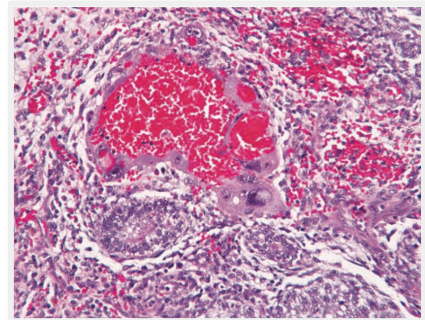


NEED EXPLANATION ? [CLICK HERE](#)

Cases

EXTRA CASES MAY REQUIRE EXTRA INFO

6. A 38-year-old man presents with a 10-month history of a painless testicular mass. Physical examination reveals a small nodule of the left testis. The mass cannot be transilluminated and appears to be solid on ultrasound examination. A testicular biopsy is shown in the image. The multinucleated giant cells in this neoplasm are derived from which of the following cell types?

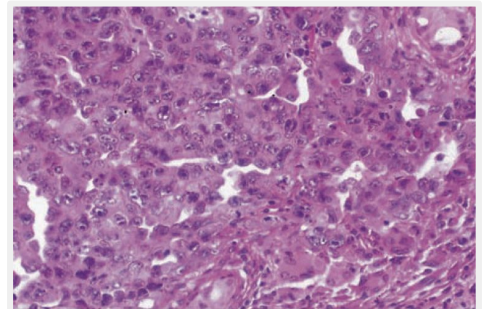


- | | | | |
|-----------------|---------------------|------------------------|------------------------|
| A. Leydig cells | B. Oligodendrocytes | C. Smooth muscle cells | D. Trophoblastic cells |
|-----------------|---------------------|------------------------|------------------------|

7. A left orchiectomy is performed in the patient described in Question 6. Which of the following serum markers would be most useful for monitoring tumor recurrence of this neoplasm following surgery?

- | | | | |
|-----------|-----------------------------|--------------------------|---------------------------------|
| A. CA-125 | B. Carcinoembryonic antigen | C. α -Fetoprotein | D. Human chorionic gonadotropin |
|-----------|-----------------------------|--------------------------|---------------------------------|

8. A 25-year-old man presents with a 4-week history of a painless mass in the scrotum. Physical examination reveals a testicular mass that cannot be transilluminated. Serum levels of AFP and hCG are normal. A hemi orchiectomy is performed. On gross examination, the testicular tumor shows foci of hemorrhage and necrosis. Microscopic examination of the tumor is shown in the image. The patient was cured by orchiectomy followed by chemotherapy. Which of the following is the most likely diagnosis?



- | | | | |
|--------------------|------------------------|--------------------|-----------------------|
| A. Choriocarcinoma | B. Embryonal carcinoma | C. Mature teratoma | D. Yolk sac carcinoma |
|--------------------|------------------------|--------------------|-----------------------|



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6-D / 7-D / 8-B



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Pathology Team

Leader

لمى العتيبي



سديم اليحيى



الجوهرة الوهبي



عائشة إبراهيم



ريناد صالح الشهري



شادن الهزاني



دانه المحيسن



ساره الدوسري



الدانه عبدالله



هدى الجدعان



ساره الشهراني



ليان الرويلي



أفنان الأحمري



ساره العجايي



هيا الزير



رغد الحامد



محمد معشي



مشعل الدخيل



يزيد المطيري



سلمى السعدون



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Leader

زياد العتيبي



رغد المطلح



ألين الكلية



مريم الغنام



محمد العرفج



رند ابا الخيل



وجد المطيري



ربوف الأحمري



سلطان البقمي



شوق الخليفة



عروب المحمود



هياء العجمي



ريماس المحمود



لؤي الحديثي



فيصل الشويعر



محمد السلامة



عبدالمحسن الدايل



أريج القريني



عبدالله الزامل



رزان السطيحي