Germ Cell Tumors

MCQs - Questions - TT

- 35y male presents - painless enlargement & heaviness of right testis since 2 months.
  USG - hypoechoic & homogenous mass in right testis.
  a) What are the Tx markers that will help you diagnose PLAP OCT 3/4 NANOG
  b) classify testicular tumours + +.
  c) Clinical feature, gross, m/c of any one TT.
  (▷ painless testicular enlargement, Heaviness).

(2) describe etiopathogenesis, Gross, mc of m/c malignant Tx of testis.

(3) 50y male - painless, firm testicular swelling, loss of testicular sensation.
- diagnosis ?
- classification, etiopathogenesis

(4) 40y male CP → testicular mass.
- what is your DD? → TT, hydrocele, spermatocele, varicocele, Epididymal cyst.
- draw m/c in the condition. (KU 18).

a) Seminoma - Gross, mc, Histomorphology of classical seminoma
a) Spermatocytic seminoma.
a) classification of Germ cell Tx of testis.
a) diff btw classical & spermatocytic seminoma.

! *95% germ cell Tx ✓ write this ✓.
0 *~5% - Sex cord stromal
(▷ HINT: Hormonal therapy - gynaecomastia etc

a) 45y m presented as cauliflower growth in penis (not testis). he also had multiple Inguinal nodes
- diagnosis ?
- m/c appearance ?
- what are the premalignant conditions.

SCC - penis

a) premalignant lesion of penis
-) Bowens disease.
-) Bowenoid papulosis.

-) Cryptorchidism, its complication
-) Benign prostatic hyperplasia
-) morphology of nodular hyperplasia of prostate.
-) grading & staging of prostatic adenocarcinoma.
-) obstructive uropathy (KU) Learn in Kidney
-) Ca prostate - Tx marker.
  (▷ PSA, PAP, AMACR.

* Schiller duval body
* Reinke's crystals.

- 1.5 - 4.5 lakh/mm³
- 7-10 days.

WHO - classification of Testicular Tx (2022 latest)

Photo

I. Germ cell tumours

(A) Germ cell Tx derived from (GCNIS) germ cell neoplasia insitu.

1. Non-invasive germ cell Neoplasia.
   - → Germ cell Neoplasia insitu
   - → Specific forms of intratubular germ cell Neoplasia.
   - → Gonadoblastoma
2. The germinoma family of tumours.
   - → Seminoma
3. Non seminomatous germ cell Tx.
   - → Embryonal carcinoma.
   - → yolk sac Tx, postpubertal type.
   - → Choriocarcinoma
   - → Placental site trophoblastic Tx.
   - → Trophoblastic Tx: Choriocarcinoma.
   - → Teratoma post pubertal type
4. Mixed germ cell Tx.

   Mixed germ cell Tx
   - polyembryoma
   - diffuse embryoma.

(B) Germ cell Tx unrelated to (GCNIS)

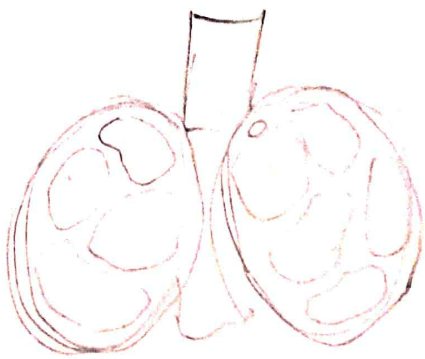
① → Spermatocytic Tx.
② → Teratoma - prepubertal.
③ → Yolk sac - prepubertal.
④ → Mixed - teratoma & yolk sac Tx prepubertal type.

II. Sexcord-stromal tumours.

- Leydig cell Tx
  - leydig cell Tx
  - Malignant leydig cell Tx.
- Sertoli cell Tx
  - sertoli cell Tx
  - Malignant sertoli cell Tx.
- Granulosa cell Tx.

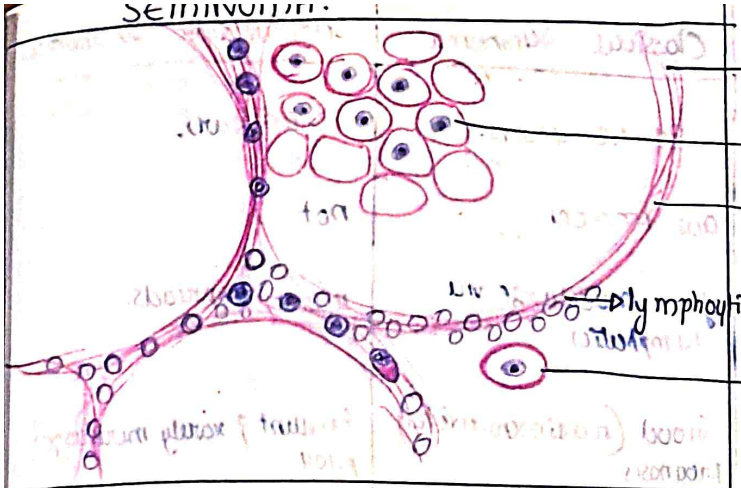
  Adult,
  Juvenile granulosa cell Tx.
- Mixed & other sex cord stromal Tx

  myoid gonadal stromal Tumour, NOS



GROSS

Seminoma:



→ delicate fibrous septa - with lymphocytic & plasma cells infiltrate.

→ nests of uniform cells - seminoma cells.

→ Tumour cells in poorly formed lobules.

→ lymphocytic & plasma cell infiltration in stroma.

→ clear cytoplasm
central nucleus
prominent nucleoli

Etiopathogenesis - of seminoma & Germ cell Tx in general.

Etiology

1. Testicular dysgenesis syndrome.

Germ cell Tx are linked to (TDS) which includes:

1) cryptorchidism {most strongly linked ~10%}.
2) hypospadias.
3) poor sperm quality.

2. Genetic / family predisposition

- Strong familial predisposition.
- mutations in KIT ligand gene.
- presence of isochromosome 12p.

3. Environmental factors.

- in utero exposure to pesticides, nonsteroidal estrogens.

4. Others

- Klinefelter syndrome.
  - ↑ risk of mediastinal GCT
  - ✗ not testicular seminoma

✗ Don't write in seminoma
✓ write in GCT. ✓

pathogenesis. → FIGURE in mobile

abnormal primordial germ cells (in utero)

↓

Precursor lesion

- Intratubular germ cell Neoplasia (ITGCN) - remain dormant till puberty.

↓ Puberty activation.

i(12p) gain + KIT mutations.
overexpression of OCT 3/4, NANOG.
or hormonal ⊕

↓

Invasive Germ cell Tx

↓ Seminoma.

↓ Non-seminomatous GCT.

- Exceptions: pediatric yolk sac Tx. // teratoma // spermatocytic seminoma — not from ITGCN.

- pubertal hormonal surge → ⊕ dormant ITGCN.

Germ cell tumours unrelated to Germ cell neoplasia insitu

- Spermatocytic Tumour AKA spermatocytic seminoma.

Definition: a rare, slow growing germ cell tumour of testis that is clinically & histologically distinct from classical seminoma.

Clinical feature.

- older men – > 65 years {usually}.
- painless testicular mass.
- very slow growing.
- No metastasis {rarely}.

Morphology

GRoss: soft, pale- gray mass.

cut surface: may show mucoid cyst.

m/c

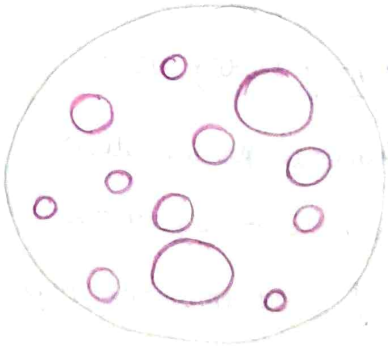
hallmark – tripartite – polymorphous population of Tx cells.

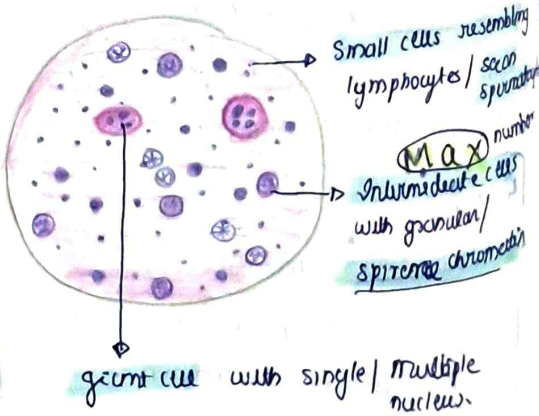
3 cell types

1. Smaller cells – resemble secondary spermatocyte.
   - narrow rim of eosinophilic cytoplasm.
2. Medium sized cells – round nucleus, eosinophilic cytoplasm.
   - some show Spireme chromatin
3. Scattered giant cells:

- No lymphocytes, no granuloma, no syncytiotrophoblast.
- No ITGCN association.

Classical Seminoma	Spermatocytic Seminoma
30–45 years.	> 65 years.
aw GTGCN	not
often metastasize via lymphatic	rarely spreads.
Good (radiosensitivity) prognosis	Excellent; rarely metastasis; prog
• uniform cells + lymphocytes	• 3 cell type. No lymphocytes.
• PLAP, OCT 3/4, NANOG +	• No typical markers
syncytiotrophoblast present ~15% βHCG⊕	absent.





thread like.

Spireme chromatin: Chromatin in meiotic phase of non-neoplastic spermatocyte.

Testicular tumors.

[Learn classification basic]

Germ cell tumors (95%)

Etiology

① Environmental factors

- Germ cell tumors are linked to Testicular dysgenesis syndrome., which includes:

① Cryptorchidism

② Hypospadias

③ poor sperm quality.

→ cryptorchedism is the strongest risk factor. ~10% of testicular GCT cases.

② Genetic factors.

- Isochromosome 12p ★

- Klinefelter → ↑ risk of mediastinal GCT ✓ not testicular GCT.

- Mutations in

→ KIT ligand ✓ ★ BAK genes.

→ Genes related to Sex hormone metabolism.

pathogenesis

Origin: arises from primordial germ cells with an acquired defect in differentiation

Early transformation: activation of Growth factor receptor signaling, often via KIT receptor Tyrosine kinase mutations, lead to uncontrolled proliferation

precursor lesion: Germ cell Neoplasia insitu. develops, present in ~90% of testes with germ cell tumors {except spermatocytic tumors & infantile type}

Key markers: OCT 3/4
NANOG

chromosomal alterations: progression to invasive GCT is linked to (i 12p.)

high risk of progression: ~ 70% of Individuals with GCNIS develop invasive GCTs within 7 years.

SEMINOMA

etiology?

Seminoma is a malignant germ cell tumor of the testis that arises from Germ cell Neoplasia insitu. It is the most common pure germ cell tumor. and is Composed of large, uniform cells with clear cytoplasm, central nuclei & prominent nucleoli - resembling primordial germ cell.

- Excellent prognosis
- Radiosensitive.

Treatment

* seminomas contain isochrom 12p.
* KIT mutations.

- Seminomas are the most common type of germ cell tumor. (~50% of germ cell tumors)
- age group & peak incidence: 3rd decade. (30 - 40 years).

origin: Classical seminoma. arises from undifferentiated Germ cells.

MORPHOLOGY

FIGURE!!

GROSS

- bulky, solid masses, rubbery firm sometimes 10X size of testis. bosselated.

Cut surface: homogenous, gray-white lobulated.
- devoid of hemorrhage, necrosis
- tunica albuginea is not penetrated.

MICROSCOPY

pattern: sheets or nests of uniform cells

- cells are - large, round-polyhedral, distinct cell membr.

Cytoplasm: clear / watery appearing. ↓ glycogen + lipid. (PAS +).

nucleus: large central nuclei with 1-2 prominent nucleoli.

Stroma: seminoma cells are divided into poorly demarcated lobules by delicate fibrous septa.
- Septa are infiltrated with moderate amount of lymphocytes and plasma cells.

Immunohistochemistry

amplification.
- KIT ✓ * NANOG
- * OCT 3/4
- podoplanin.
- Placental alkaline phosphatase (PLAP) ✓
- 15% cases - HCG (+) {containing syncytio trophoblast}
- SALL4 Never AFP
- cytokeratin (-)

Spread

local → - testicular parenchyma
- rete testis
- epididymis

lymphatic → para-abdominal L.N.

prognosis

- radiosensitive. - extremely (R.S) - melts ✓.
- remain localized to testis for a long time
- maintain mainly involve {L.N.}
- BEST prognosis.

Non-Seminomatous Germ cell Tumors.

① Embryonal Carcinoma

- more aggressive than Seminoma.
- age - 20-30 years.

Locally aggressive

Morphology

GROSS

Cut surface:

- variegated appearance.
- areas of hemorrhage or necrosis.
- poorly demarcated at margins.
- ~~[illegible]~~

MICROSCOPY

pattern: alveolar / tubular / papillary patterns.

- more undifferentiated tumors shows sheets of cells.

Tumor cells: Large epithelioid cells.
pleomorphic nuclei
macronucleoli
dense amphophilic cytoplasm.

- mitotic figures and tumour giant cells.

IHC

cytokeratin (+)
CD30 (+)
KIT (-)

Teratoma → post pubertal Type.

definition

- a malignant germ cell tumor in post pubertal males derived from germ cell neoplasia in-situ.
- Composed of multiple tissue types from one or more germ layers. (Ecto, meso, endoderm)
- can contain - well differentiated mature tissue, or
- immature embryonic-type tissues

Types

- post-pubertal.
- pre pubertal

Morphology

GROSS

- large, nodular, firm.
- Cut surface: heterogenous. with solid cartilaginous cystic areas.

MICROSCOPY — Helter-skelter pattern

- contains differentiated or immature structures from multiple germ layers including → neural tissue, muscle, cartilage, squamous epithelium, bone, blood vessel, bronchial epithelium

post pubertal → malignant.

prepubertal - benign,
good prog.

YOLK SAC TUMOR

- most Common Testicular tumor in infants. (< 3 y old).
- ~~good prognosis in pre pubertal~~

Morphology

~~(illegible)~~

m/c : lace like pattern of cuboid, flattened or spindle cells

- Schiller - Duval bodies (50% cases).

↓

mesodermal core + central capillary, surrounded by visceral & parietal layers.

- resembles primitive glomeruli

IHC

- AFP - alpha fetoprotein
- α-1 antitrypsin.
- glypican

CHORIOCARCINOMA

- highly malignant GCT.
- Serum HCG ↑

Morphology

- hemorrhage & necrosis.

Q (ell type)

① Syncitiotrophoblast - multinucleated. contain hCG

② cytotrophoblast - single nucleus cords, sheets.

IHC

① hCG ★, hPL
GATA 3
GDF3

CF

- most aggressive
- early hematogenous spread.
- lung, liver, GI, brain, spleen, adrenals.

Non- Seminomatous tumors of more than one histological Type.

MIXED GERM CELL TUMORS

- malignant tumors with more than one GCT component
- Common mixture:
  - Teratoma + Emb Ca + Yolk ST.
  - Seminoma + E.Ca.
  - Teratoma + E.Ca.

GERM CELL TUMORS UNRELATED TO GERM CELL NEOPLASIA IN SITU

Spermatocytic Tumors

- uncommon.
- older people > 64 years.
- slow-growing, does not metastasize
- i12p X
- Gain of ch 9
- Origin: germ cells undergoing spermatogenesis.

Morphology

GROSS

- lobular to multinodular.
- soft & pale gray.

MICROSCOPY

Arrangement: diffuse to multinodular pattern.

3 cell types

① Smaller lymphocyte like cells
- dense chromatin with narrow rim of eosinophilic cytoplasm.

② medium-sized cells.
- → spireme type chromatin.

③ giant cells
Scattered.

- Never mixed with other GCT.

SEX CORD - STROMAL TUMORS

- Leydig cell tumor,
Sertoli cell tumor etc...

↳ Notes are not in Ramdeo
if u want u can write from
Robbins later

* premalignant lesions of penis
→ from Ramadeo.

- BPH
- Ca prostate markers.
- Schiller duval body
- Reinke crystals.