## Granulosa Cell Tumour

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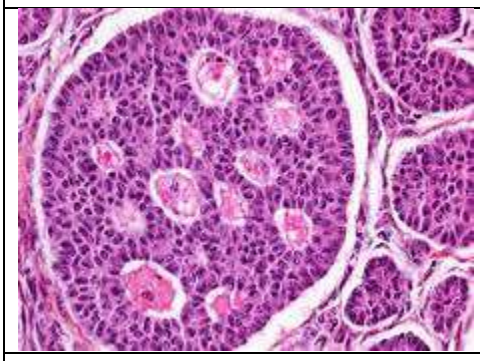
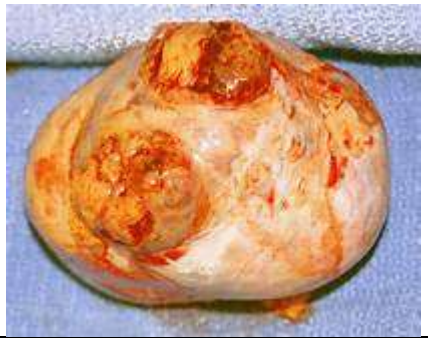
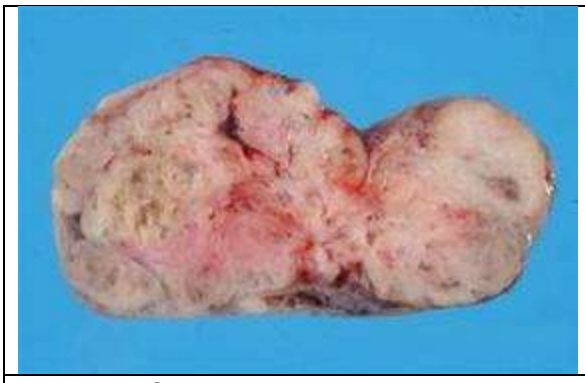
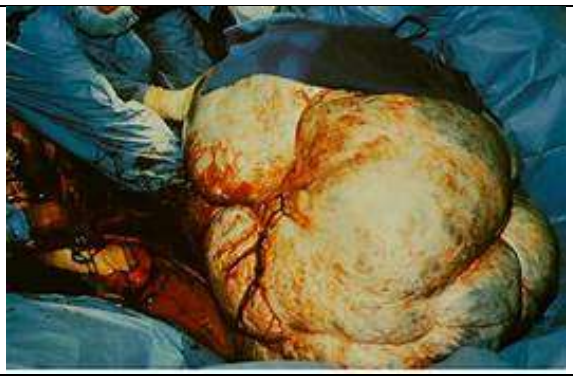
|---|---|---|
| ***Ovary:*** | • Is enlarged<br>• Shows a tumour | |
| | ***The tumour:*** | • Is moderately large (less than 8 cm.)<br>• Somewhat ovoid |
| | ***External surface:*** | • Smooth (in general)<br>• Lobulated (in few areas) |
| | ***Cut surface:*** | • Circumscribed<br>• Smooth (or slightly lobulated)<br>• Slightly nodular (in parts)<br>• Cystic (in other parts)<br>• Fleshy<br>• Solid and granular (in parts)<br>• Greyish-pink with pale yellowish patches<br>• Some necrotic foci<br>• Few reddish haemorrhagic patchs |
| | ***Consistence:*** | • Firm |



***NB:***

- Granulosa cell tumour is considered rather benign (or in some cases is of very low-grade malignancy, or still in few other cases malignant with formation of metastases)
- It is a **feminizing tumour** (due to excessive production of oestrogenic hormone); it varies in size rfom 1-8 cm. and is usually unilateral.
- It is sharply defined, with smooth external surface and yellowish grey cut surface.
- It is solid (but possibly with cystic degeneration).
- *The clinical effects and manifestations depend upon the period of life (age of patient).*

**Essential features**

- **Low grade indolent sex cord stromal tumor** of the ovary with 20 - 30% chance of local recurrence, 5 - 20 years after diagnosis
- Should be considered in the differential diagnosis of solid / cystic and hemorrhagic ovarian mass in postmenopausal patients
- *FOXL2* mutation by immunohistochemistry or sequencing identified in > 95%
- Immunohistochemical panel could include inhibin, Carletinin, FOXL2, SF1, EMA and reticulin special stain

- Accounts for **2% of all ovarian tumors** and is the second most common ovarian sex cord stromal tumors after fibroma / Thecomas
- Most granulosa cell tumors are **adult type (95%) and 5% are juvenile type**
- Wide age range; most common in postmenopausal women with peak age 50 - 55
- Rarely reported in male testes

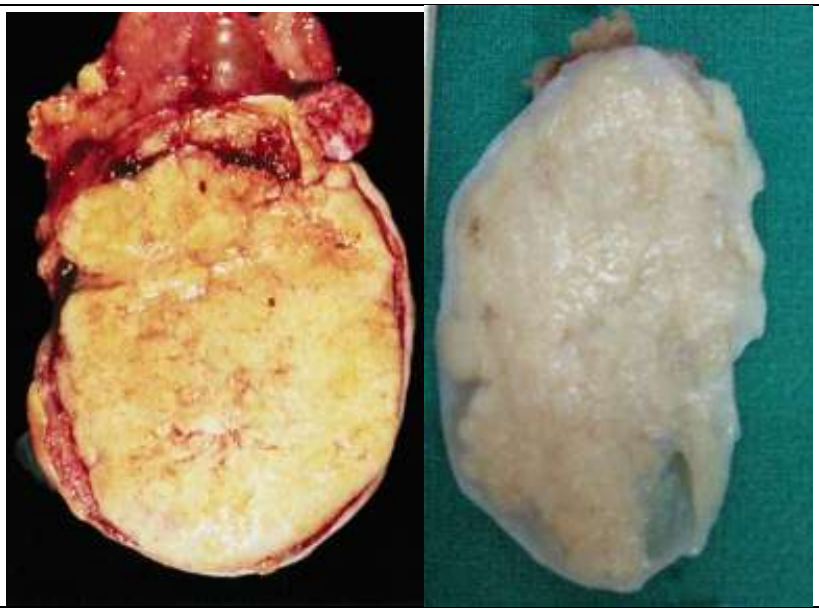
**Clinical features**

- Mostly present with symptoms due to **adnexal mass or endocrine manifestations**
- 10% present with **ovarian torsion**, tumor rupture and hemoperitoneum
- Most associated with **hyperestrogenism**, causing:
    - Metrorrhagia, (hemorrhage between periods)
    - Postmenopausal bleeding,
    - **Endometrial hyperplasia / carcinoma** (5%, usually Figo grade 1 and superficial) in adults and
    - If in children, associated with **precocious puberty**
- Rarely associated with **hyperandrogenism** presenting with virilization or hirsutism
- 10 year survival > 90%; tends to recur locally in the abdomen / pelvis in 20 - 30% of cases, usually 5 years after diagnosis and up to 20 years later
- Most are confined to the ovary (stage I); rarely distant metastasis to lung and liver
    - Lymph node metastasis uncommon

**Gross description**

- **> 95% unilateral** and confined to the ovary
- Variable size, average 10 - 12 cm
- **Encapsulated with smooth lobulated surface**,
    - Tan or yellow (depending on the degree of luteinization and lipid content),
    - Soft to firm (depending on the amount of fibromatous component),
    - usually solid and cystic with straw colored or mucoid fluid,

- can have areas of necrosis and hemorrhage
- The more luteinized tumors are more yellow / orange
- May resemble serous cystadenoma
- Rare androgenic tumors tend to be large with thin walled cysts



**Microscopic (histologic) description**

- Small, bland, cuboidal to polygonal cells with **scant cytoplasm** and pale, uniform **angulated and usually grooved nuclei (coffee bean)**
- Various patterns, including
  - **Diffuse (the most common),**
  - **Trabecular and corded,**
  - **Insular,**
  - **Watered silk (moiré silk) pattern**
  - **Gyriform pattern**
  - **Microfollicular (resembling Call-Exner bodies of the Graafian follicles: small follicle-like structures filled with eosinophilic material) and**
  - **Macrofollicular (the least common)**
  - **Usually a mixed growth pattern is seen**
- Rarely can be seen **with juvenile type**; classification should be based on the predominant histology
- **Luteinized adult type** (such as during pregnancy): rare (1%) if extensive (> 50%), plump cells with moderate to abundant eosinophilic cytoplasm, conspicuous nucleoli, no nuclear grooves, myxoid or edematous stroma; may resemble steroid cell tumor
- **Mitotic activity** is usually not brisk (< 3/10 high power fields)
- **Stroma is usually hypervascular** with variable amounts of fibroblasts and theca cells
- **Theca cell proliferation** is considered a stromal response rather than a second population of tumor **cells (granulosa - theca cell tumor)**
- Can have a **prominent fibrothecomatous stroma**; need 10% granulosa cells to be classified as adult granulosa cell tumor, otherwise best classified as ***Thecomas or fibroma with minor sex cord elements***

- ***Predominantly cystic granulosa cell tumor or macrofollicular pattern may mimic ovarian follicle***
- Small aggregates of non-neoplastic granulosa cells can be seen within vascular spaces adjacent to the follicles: probably a surgery related artifact

**Positive stains**

- **FOXL2: > 95%,** less common in other sex cord stromal tumors so is considered sensitive and specific
- SF1: most sensitive marker for this as well as most common sex cord stromal tumors
- Inhibin A: more specific marker
- Calretinin
- Reticulin: shows lack of pericellular staining and highlights nests or large groups of granulosa cells and vessels, helps differentiate diffuse pattern from Fibrothecomas
- **Low molecular weight cytokeratin** (CAM5.2, AE1 / AE3): 30 - 60%, usually dot-like or globoid perinuclear pattern
- S100: 50%, CD99: 70%, EGFR: 65% of primary and 85% of recurrent
- Vimentin, WT1, CD56 and SMA

**Negative stains**

- EMA (in contrast to juvenile type) & CK7