CASE OF THE FORTNIGHT

Dr Aditi Dixit (Senior Resident) ; Dr Sherin Daniel (Assistant Professor)

Department of General Pathology

Christian Medical College and Hospital, Vellore

CLINICAL HISTORY

- 3-year-old girl diagnosed with Peutz Jeghers Syndrome was brought to paediatric oncology OPD with

History of left ovarian mass detected elsewhere at the age of 1.5 years

PAST HISTORY

1) Post multiple intestinal polyp excision

- At birth,
- Sigmoid colectomy in 2018(one month of age),
- Subtotal colectomy in 2019 (1.5 years of age)

} Hamartomatous polyps.

At 1.5 years,

2) Diagnosed with isoechoeic lesion in segment 4 of liver ?hemangioma on imaging.

3) Enucleation of left ovarian cyst – Sex cord stromal tumour with annular tubules(SCTAT).

CLINICAL EXAMINATION IN CMC

- Blue pigmented lesions in the cheeks since the beginning of 2021.
- Perianal area- fecal discharge.
- P/A – soft. No mass palpable.

INVESTIGATIONS

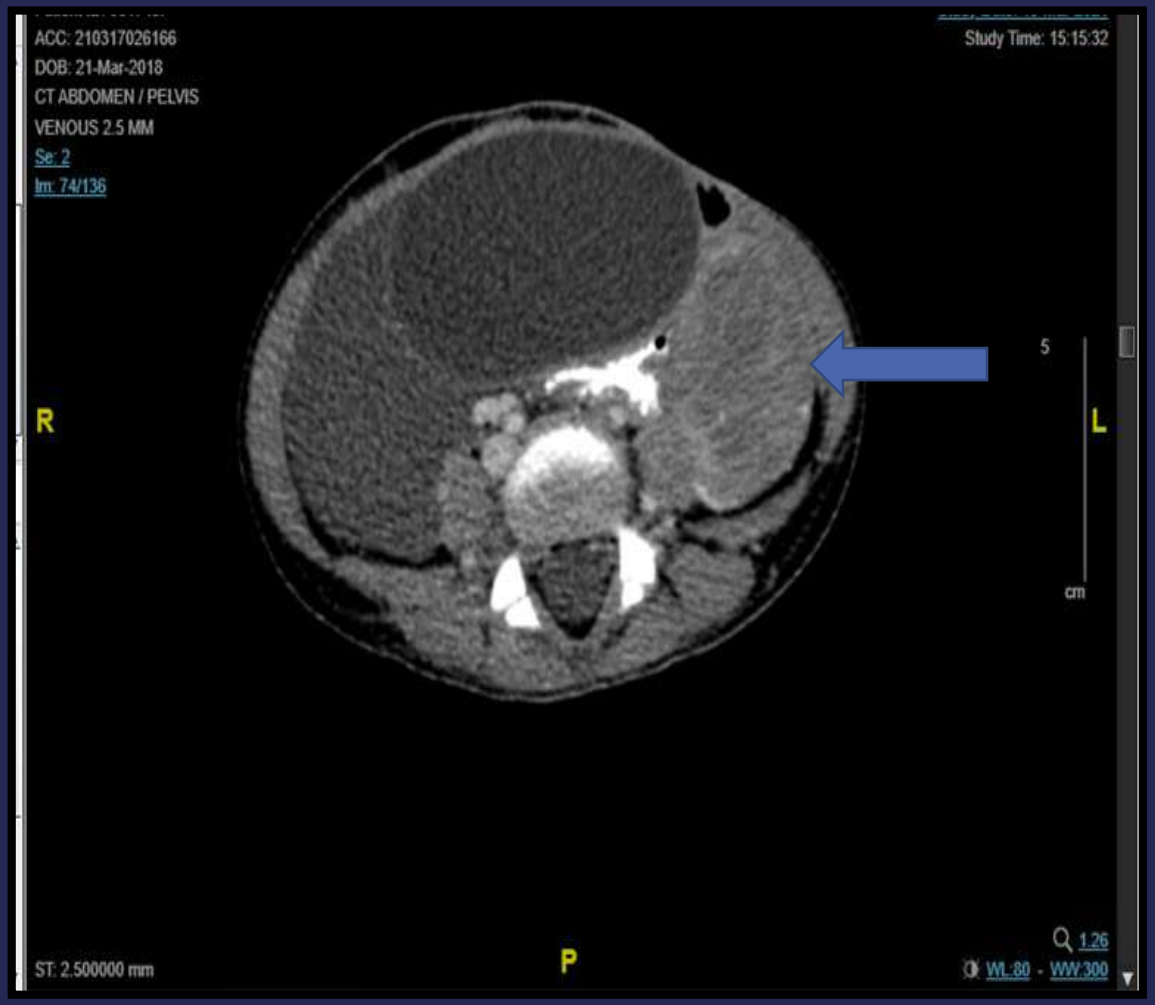
SERUM TUMOUR MARKERS

- AFP: 2.0 IU/ml; Beta HCG <0.100mIU/ml; CA125: 10.6U/L.

ULTRASOUND

- Solid cystic lesion in the left ovary of ~34x27mm.

CT FINDINGS



- Well-defined solid mass with small cystic component arising from the left adnexa s/o left ovarian mass (arrow).

Other findings:

- Multiple polyps in the rectum.
- Well- defined cystic lesion in right lower abdomen- peritoneal inclusion cyst or lymphangioma.
- Hemangioma of liver.

INTRA-OPERATIVE FINDINGS

LEFT SALPINGO-OOPHORECTOMY

-Ascites noted.

-Well defined left ovarian tumour with no adhesions.

-Right streak ovary.

MACROSCOPY

- Left ovarian solid mass of 6x4.5x3.5cm.

- C/s-

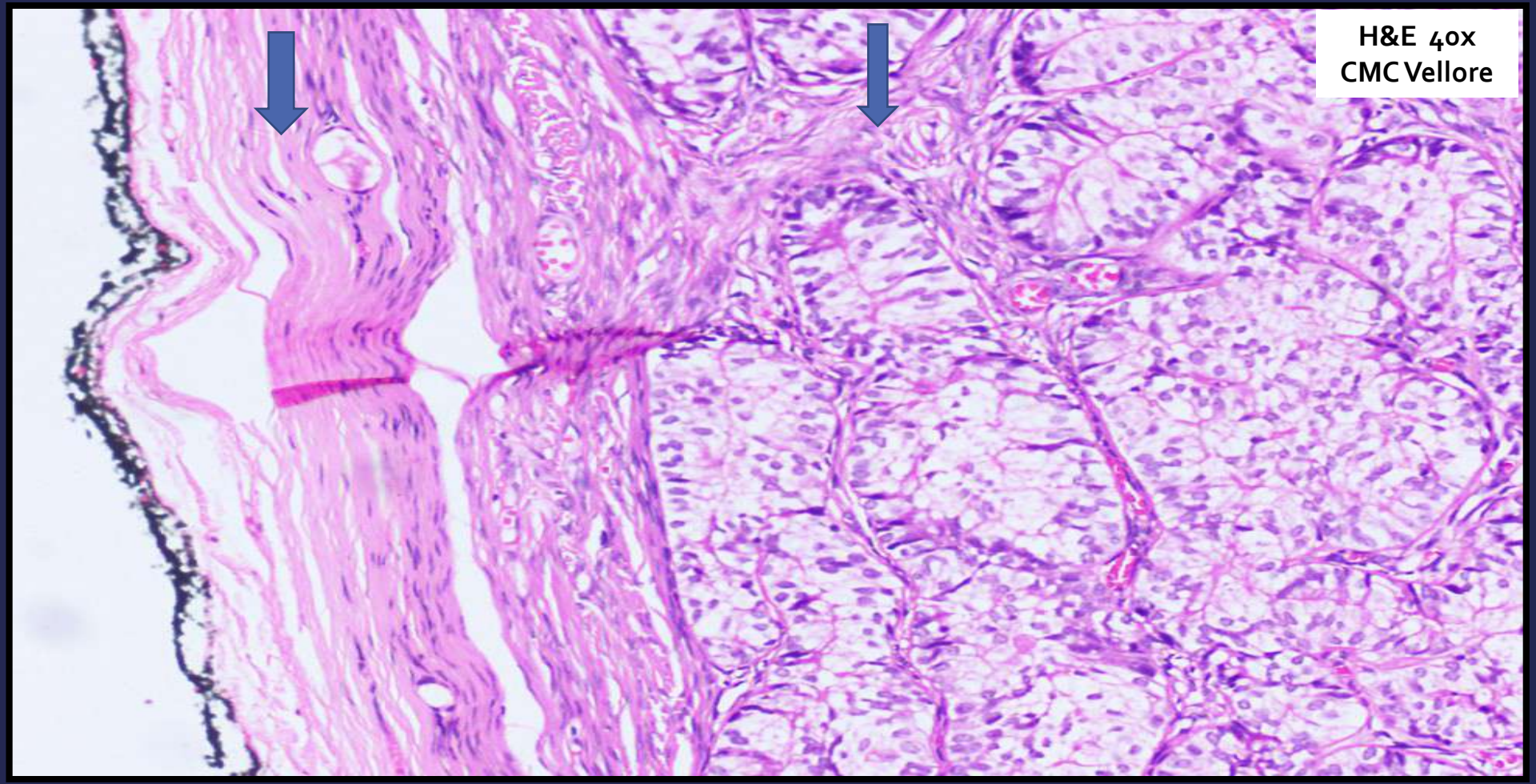
Well circumscribed solid- cystic tumour.

Solid area: Lobulated, tan yellow and firm.

Cystic area: Thin uniloculated cyst with septation, filled with clear fluid.

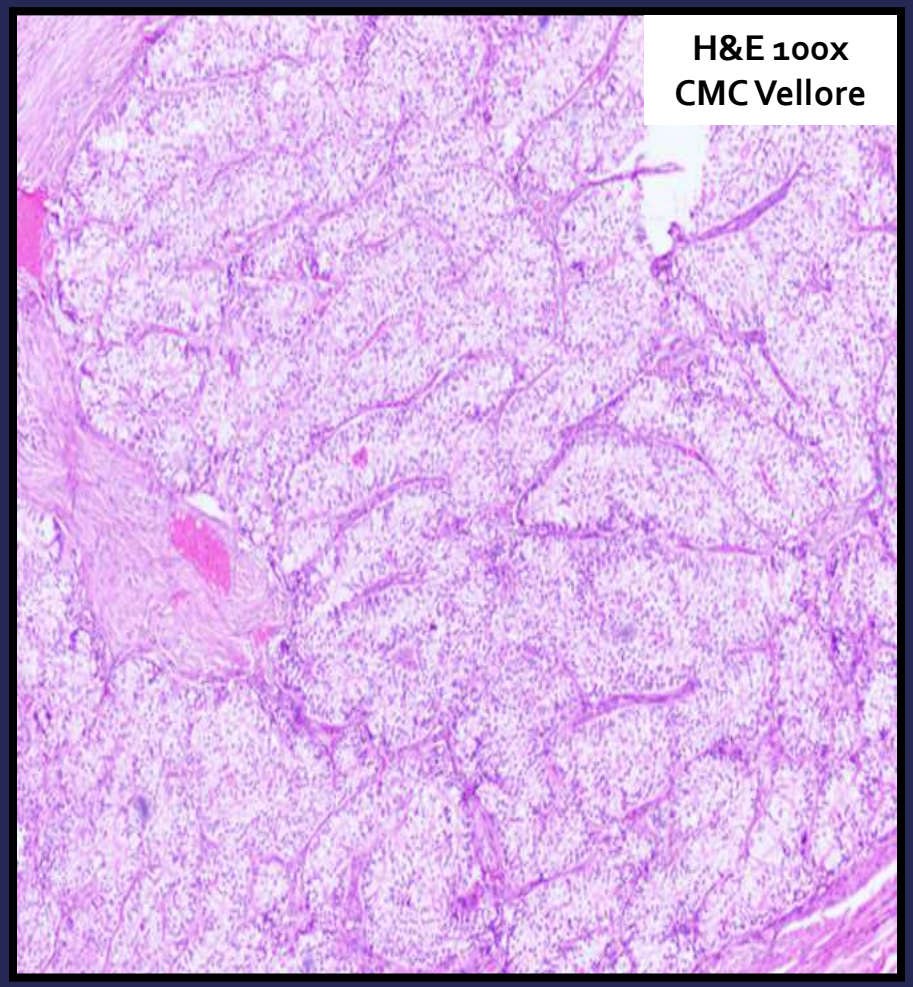
MICROSCOPY – SOLID COMPONENT

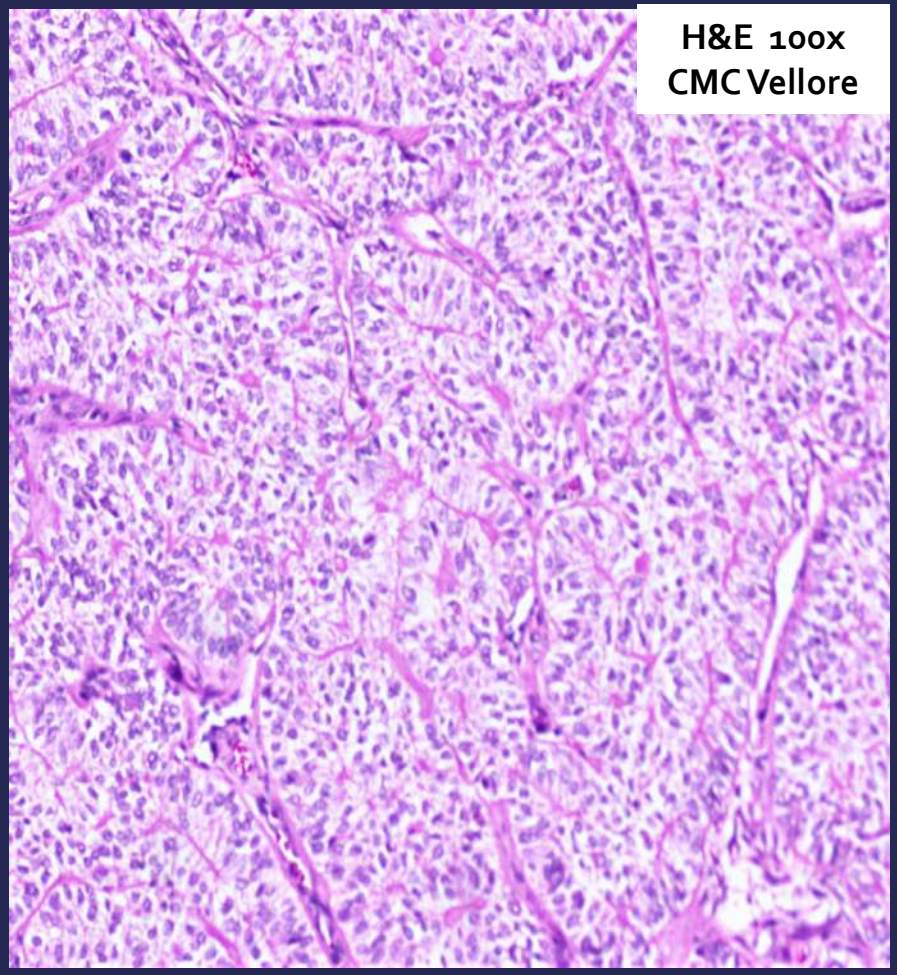
Ovarian tissue infiltrated by a tumor.



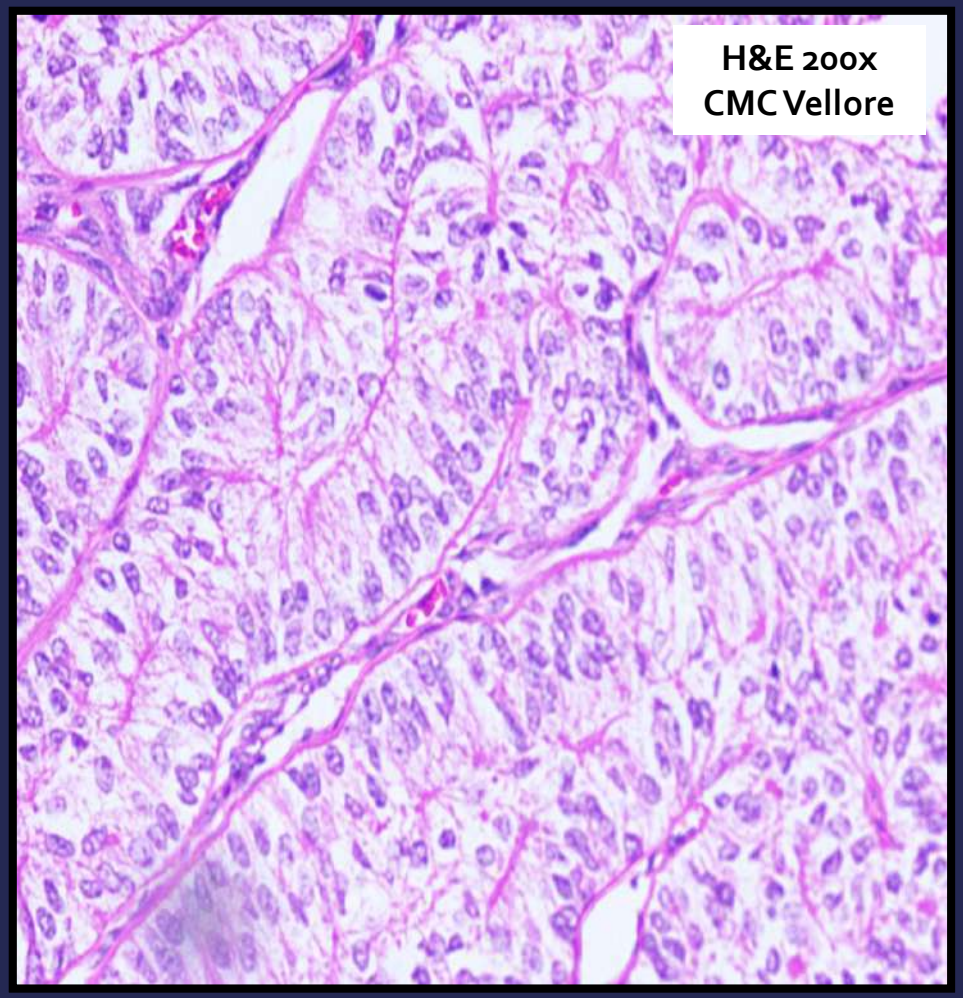
MICROSCOPY – SOLID COMPONENT

Nodular architecture with elongated solid tubules and cords separated by fibrous septa





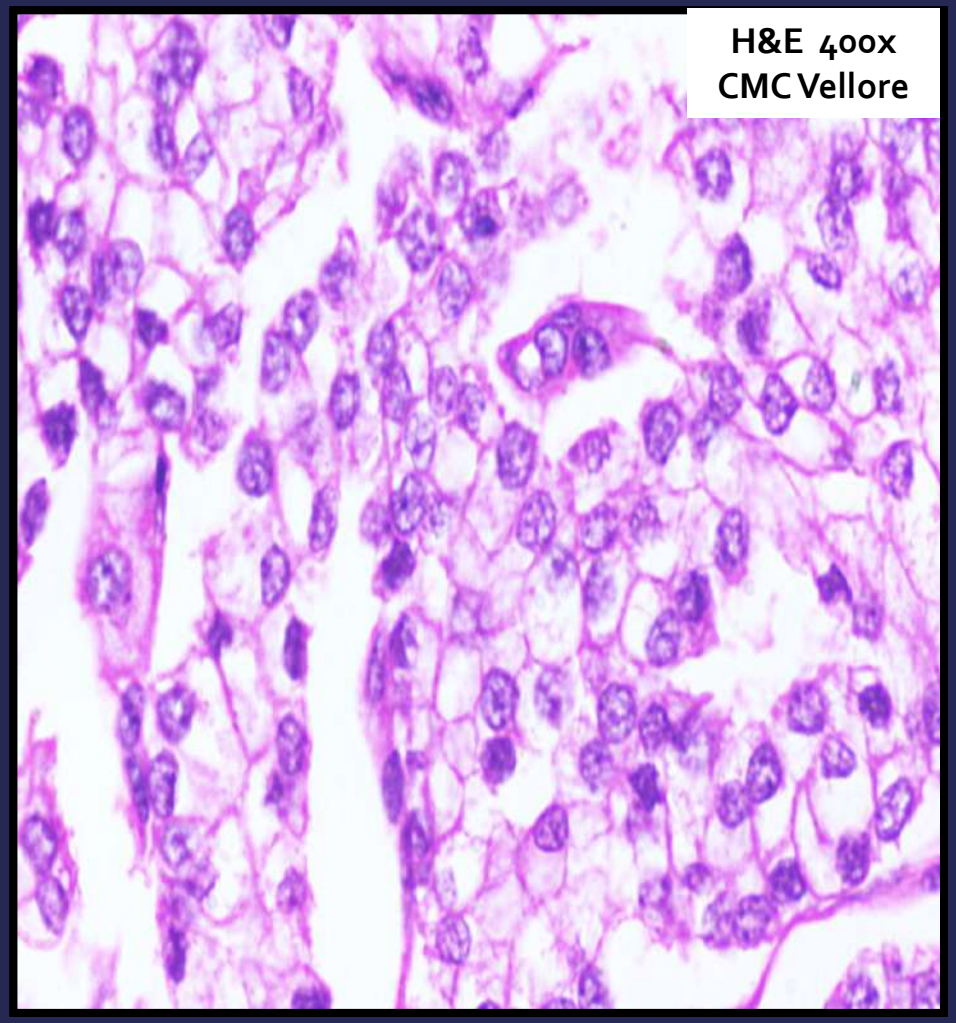
MICROSCOPY – SOLID COMPONENT

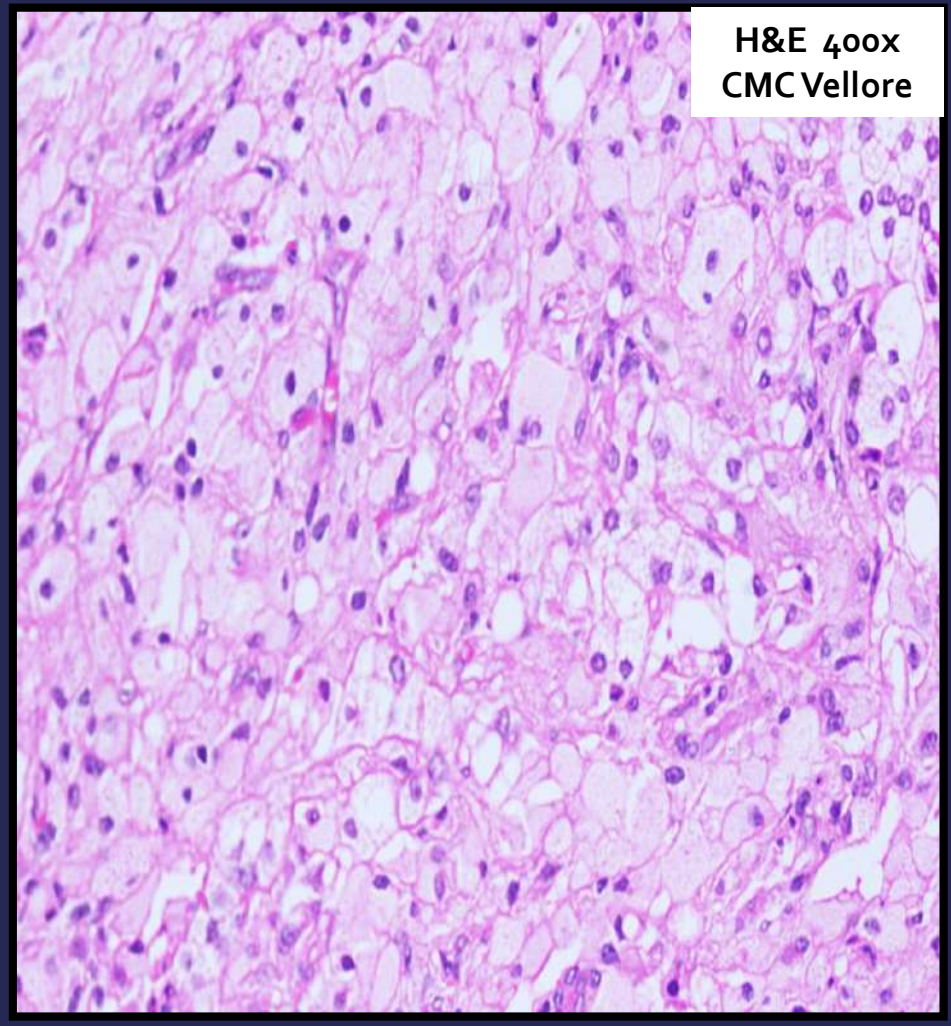


- Tubules lined by bland columnar cells with clear to pale eosinophilic cytoplasm & mild nuclear pleomorphism.
- Rare mitotic figures.
- No evidence of Leydig cell component.

MICROSCOPY – SOLID COMPONENT

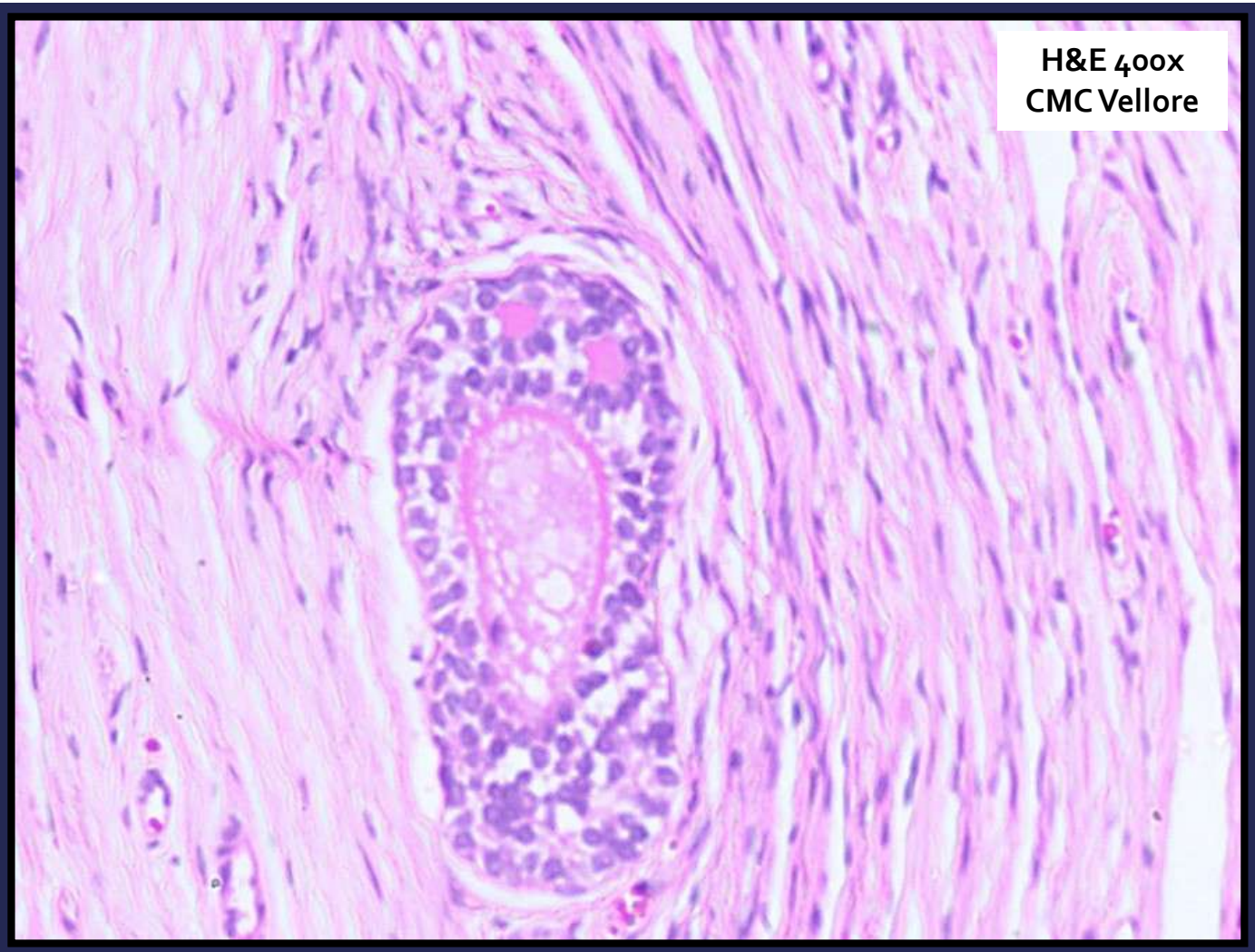
Areas with clear to vacuolated cytoplasm. Areas with abundant foamy cytoplasm.





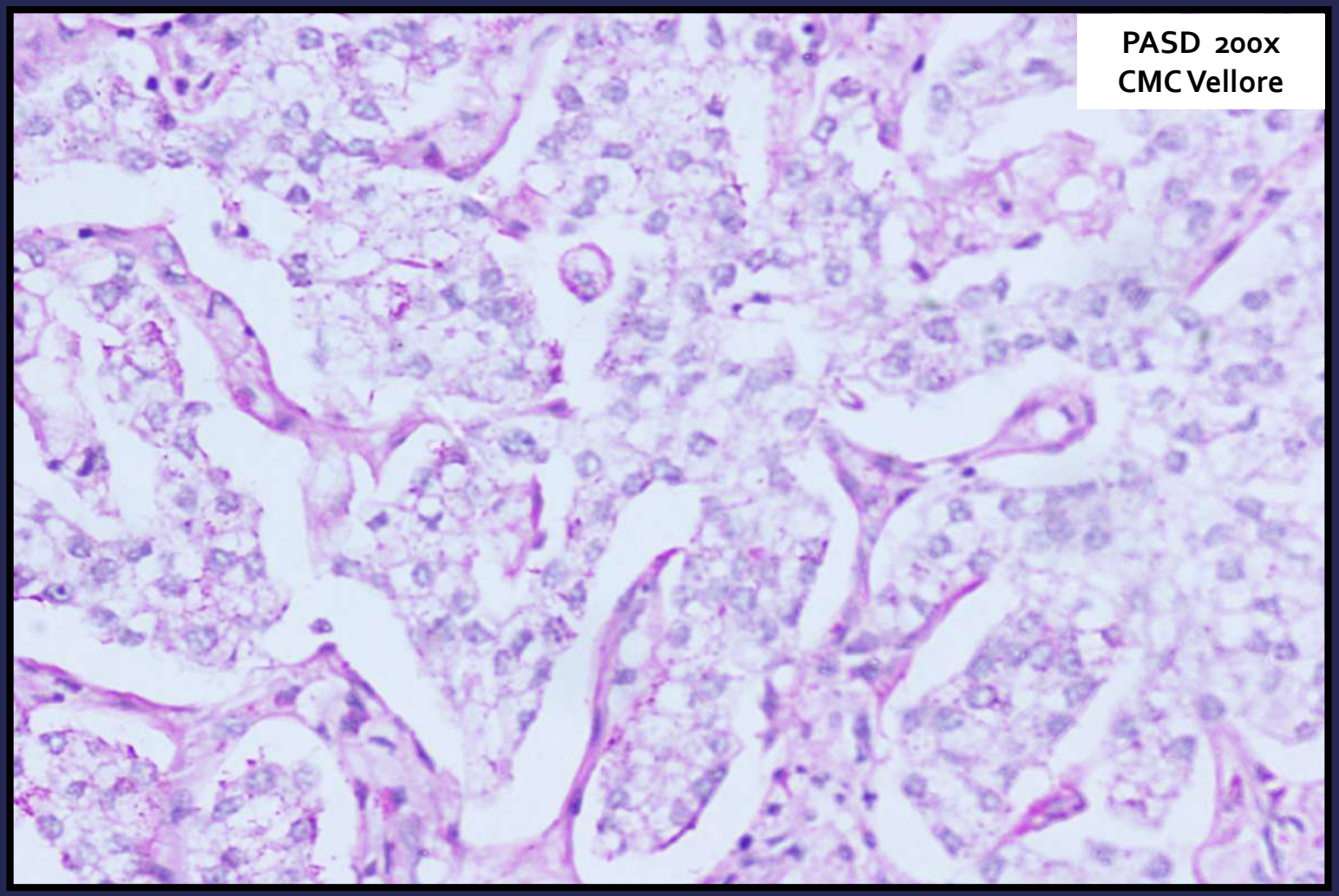
MICROSCOPY – SOLID COMPONENT

Microscopic focus of sex cord stromal tumorlet with annular tubules.



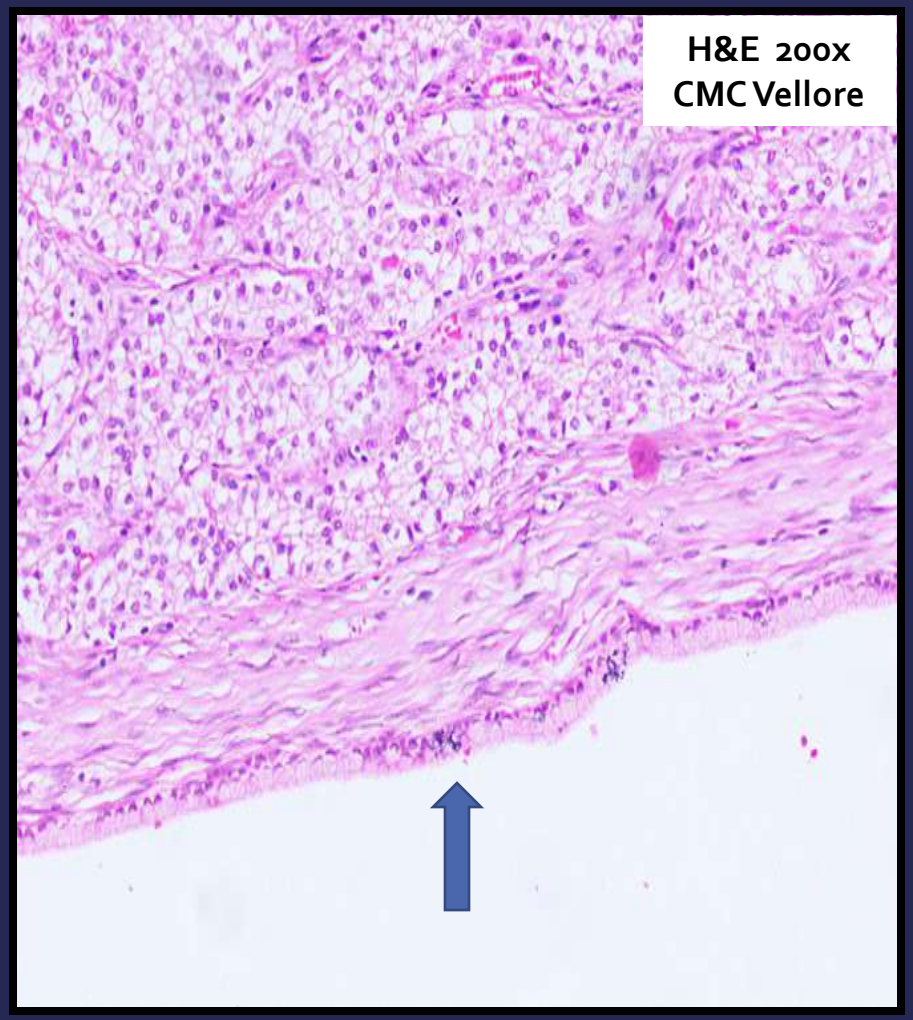
SPECIAL STAIN - PASD

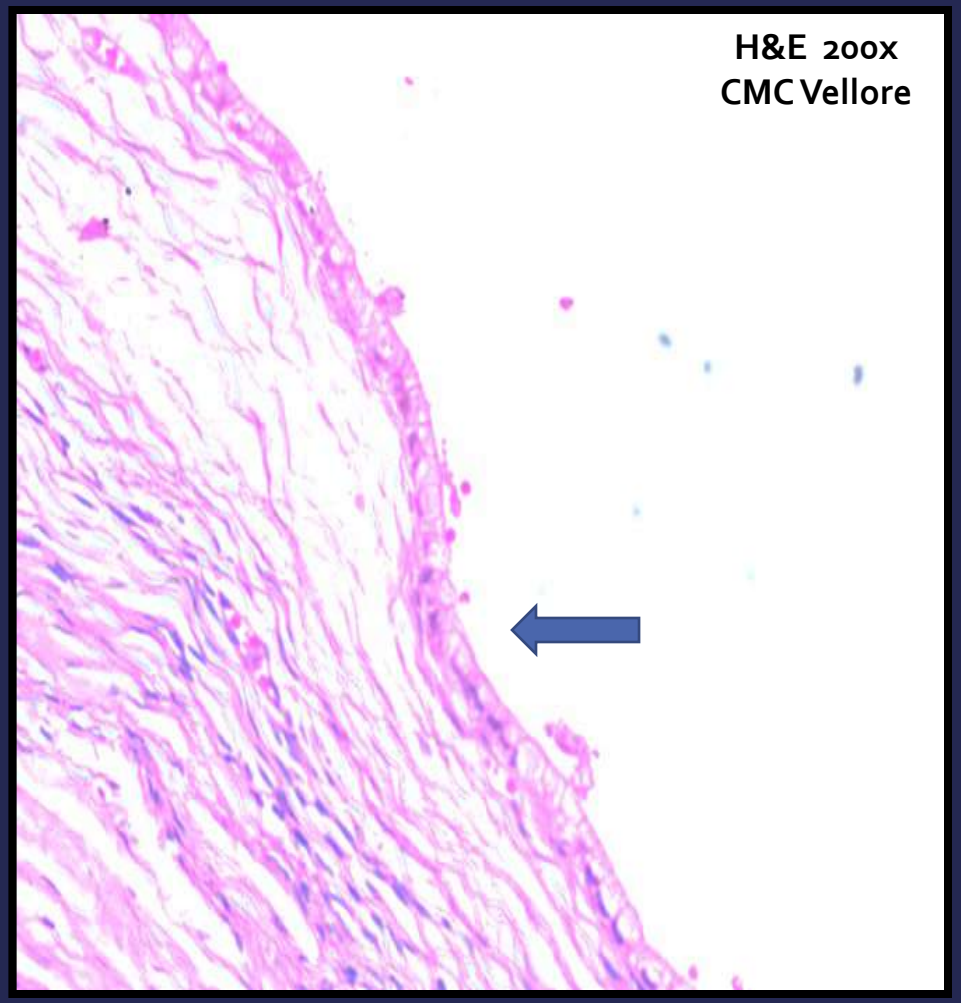
PASD stain indicates absence of intracytoplasmic mucin in the clear cells.



MICROSCOPY- CYSTIC COMPONENT

The adjacent cystic component is lined by single layered of benign tall mucin secreting columnar epithelium.





DIFFERENTIAL DIAGNOSES ?????

1) Sex cord stromal tumour

   ??? Sertoli Leydig cell tumour

   ??? Sertoli cell tumour

2) Yolk sac tumour

3) Endometrioid carcinoma with sertoliform variant

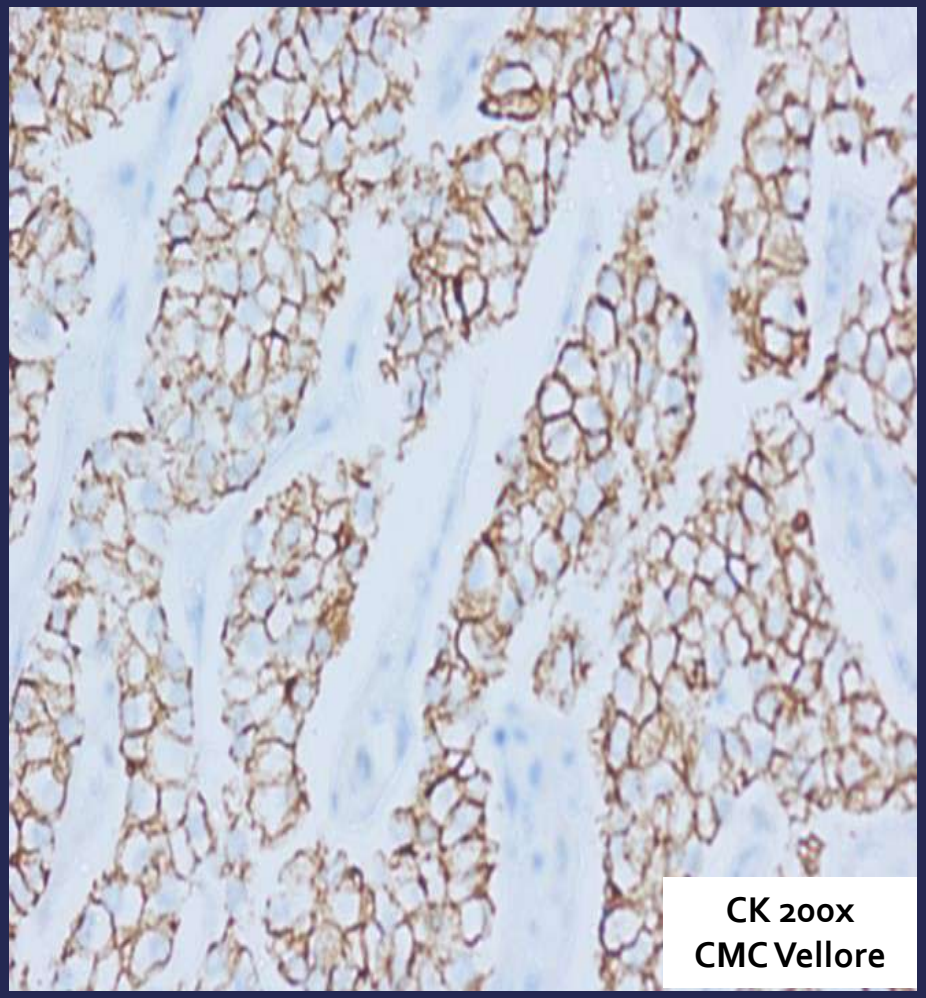
4) Primary/metastatic carcinoid tumour

5) Struma ovarii with tubular pattern

6) Sertoli cell adenoma in a phenotypic female with androgen insensitivity syndrome.

IMMUNOHISTOCHEMISTRY

Diffuse strong positivity for cytokeratin

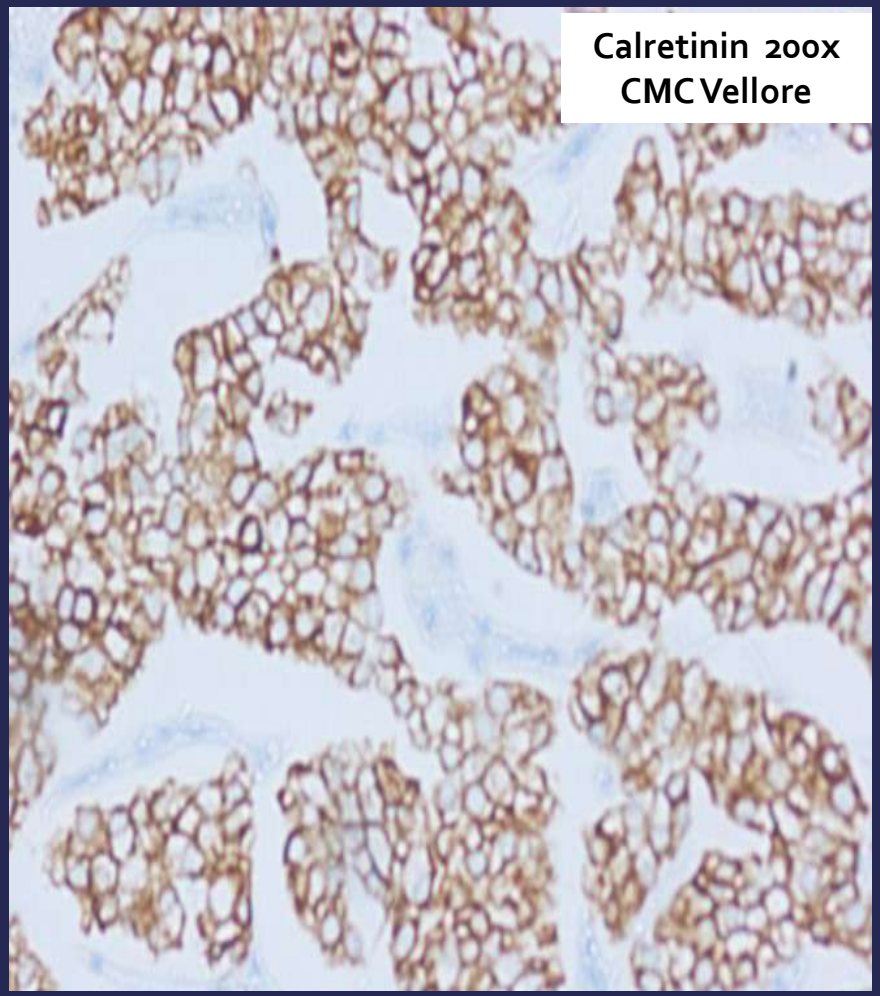


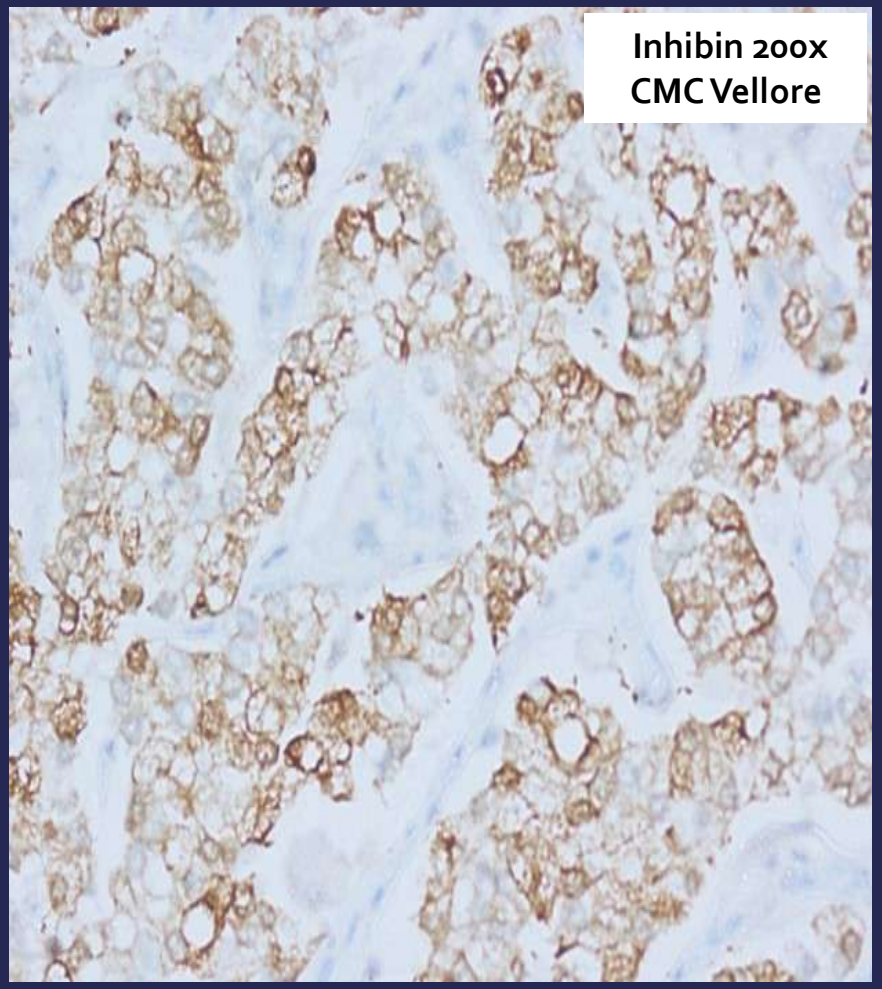
NEGATIVE IHC MARKERS

- EMA
- Glypican 3
- Melan A
- Synaptophysin

IMMUNOHISTOCHEMISTRY

Diffuse strong positivity for calretinin and inhibin





FINAL DIAGNOSIS

Left salpingo-oophorectomy specimen:

Sertoli cell tumour with concomitant mucinous cystadenoma in a patient with Peutz Jeghers syndrome

- Pathological TNM staging : pT1aNxMx.

SERTOLI CELL TUMOUR - DISCUSSION

- Rare sex cord neoplasm that usually occurs in less than 30 years of age.
- A subset of patients have Peutz Jeghers Syndrome.
- Unilateral solid neoplasm with tan to yellow cut surface and have a broad range of architectural patterns on microscopy with most common being the characteristic hollow or solid tubules.
- Lipid rich & oxyphilic tumours may be associated with Peutz Jeghers Syndrome.
- Minor area with sex cord stromal tumour with annular tubules may be seen, especially in patients with Peutz Jeghers Syndrome.

* *Robert J. Kurman, Lora Hedrick Ellenson ,Brigitte M. Ronnett. Blaustein's pathology of the female genital tract. 7th edition. Chapter on Sex Cord-Stromal, Steroid Cell, and Other Ovarian Tumors with Endocrine, Paraendocrine, and Paraneoplastic Manifestations.; pg 991.*

* *Kommoss F and Liu AJ. Sertoli cell tumour. WHO classification of female genital tumours 2020. 5th edition.*

SERTOLI CELL TUMOUR - IHC

POSITIVE

- Inhibin
- Calretinin
- SF1
- CD99
- WT1
- Broad spectrum cytokeratins

NEGATIVE

- EMA
- CK7
- GATA3
- PAX8
- Chromogranin
- Glypican 3

SERTOLI CELL TUMOUR – DIFFERENTIAL DIAGNOSES

1) Well differentiated sertoli leydig cell tumour

- 50% have endocrine manifestations, usually virilization related to testosterone production.
- Adequate sampling reveals absence of Leydig cell component.

2) Yolk Sac Tumour

- Have varied morphology.
- Distinguished based on IHC studies with glypican-3.

3) Struma ovarii with tubular pattern

- Identification of more typical patterns of struma.
- Distinguished based on IHC studies with positivity for thyroglobulin.

SERTOLI CELL TUMOUR – DIFFERENTIAL DIAGNOSES

4) Endometrioid carcinoma with sertoliform variant

- Clinical profile.
- Adequate sampling reveals foci with characteristic features of endometrioid carcinoma.
- EMA positive.

5) Primary/metastatic carcinoid tumours

- Rarely have solid tubular pattern
- Distinguished with IHC for neuroendocrine markers (chromogranin, synaptophysin)

6) Sertoli cell adenoma in a phenotypic female with androgen insensitivity syndrome.

SERTOLI CELL TUMOUR - DISCUSSION

- Prognosis is generally excellent.
- Usually unilateral and Stage I tumours.

- Features predictive of malignant behaviour:

1) Size >5cm,
2) Mitosis > 2/mm^2(>5/10HPF of 0.55mm in diameter & 0.24mm^2 in area)
3) Nuclear atypia
4) Necrosis

Oliva EA, Alvarez T, Young RH. Sertoli cell tumors of the ovary. A clinicopathological and immunohistochemical study of 54 cases. Am J Surg Pathol 2005;29:143–56.

PEUTZ JEGHERS SYNDROME & SERTOLI CELL TUMOUR

- It is an autosomal dominant disease with germline mutations in gene *STK11* on chromosome 19p13.3 & characterized by gastrointestinal polyposis, mucocutaneous pigmentation and cancer predisposition.
- They have increased risk of malignancy for gastrointestinal and breast cancer.
- There are several gynaecologic tumours that associated with PJS

OVARIAN TUMOURS

1) Sex cord tumour with annular tubules (SCTAT) – MOST COMMON
2) Sertoli Leydig cell tumour(SLCT)
3) Sertoli cell tumour(SCT)
4) Granulosa cell tumour
5) Unclassified sex cord tumours.

Rarely surface epithelial tumours and germ cell tumours like dysgerminoma & dermoid cyst.

* There is weak evidence that mucinous cytsic tumours of the ovary may occur with increased frequency in patients with PJS.

ENDOCERVICAL TUMOUR

Gastric type endocervical adenocarcinoma (adenoma malignum)

* *Ferry JA, Young RH, Engel G, et al. Oxyphilic Sertoli cell tumor of the ovary: a report of three cases, two in patients with the Peutz-Jeghers syndrome. Int J Gynecol Pathol. 1994;13:259–266.*

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2) Young RH, Scully RE. Ovarian Sertoli cell tumors. A report of ten cases. Int J Gynecol Pathol 1984;2:349–63.

3) Tavassoli FA, Norris HJ. Sertoli tumors of the ovary. A clinicopathologic study of 28 cases with ultrastructural observations. Cancer 1980;46:2281–97.

4) Ferry JA, Young RH, Engel G, et al. Oxyphilic Sertoli cell tumor of the ovary: a report of three cases, two in patients with the Peutz-Jeghers syndrome. Int J Gynecol Pathol. 1994;13:259–266.

5) Phadke DM, Weisenberg E, Engel G, Rhone DP (1999). Malignant Sertoli cell tumor of the ovary metastatic of the lung mimicking neuroendocrine carcinoma: report of a case. Ann Diagn Pathol 3:213–219

6) Ravishankar S, Mangray S, Kurkchubasche A, Yakirevich E, Young RH (2016) Unusual Sertoli cell tumor associated with sex cord tumor with annular tubules in Peutz-Jeghers syndrome: report of a case and review of the literature on ovarian tumors in Peutz-Jeghers syndrome. Int J Surg Pathol 24:269–273

7) Solh HM, Azoury RS, Najjar SS (1983) Peutz–Jeghers syndrome associated with precocious puberty. J Pediatr 103:593–595