Dr. D.Y. PATIL VIDYAPEETH, PUNE
(DEEMED UNIVERSITY)

A RARE TYPE OF ASCITES WITH A UNIQUE CAUSE

Presentation by

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CASE CAPSULE

- **47/ lady**

Patient came to the surgical oncology OPD with complaints of,

- **Abdominal distension since 3 months**
- **Abdominal pain since 8 to 9 months**
- **Admitted previously 8 months ago in medicine for bilateral lower limb swelling and pain**
- **Diagnosed with DVT , managed conservatively**
- **No other comorbidities**

On Examination-

- **Conscious, oriented**

- **Vitally stable, afebrile**

Per Abdomen examination-

- **Abdomen distended, flanks full**

- **Fluid thrill +, no evidence of organomegaly**

P/V-

- **No mass in cervix. Vagina, fornix free.**

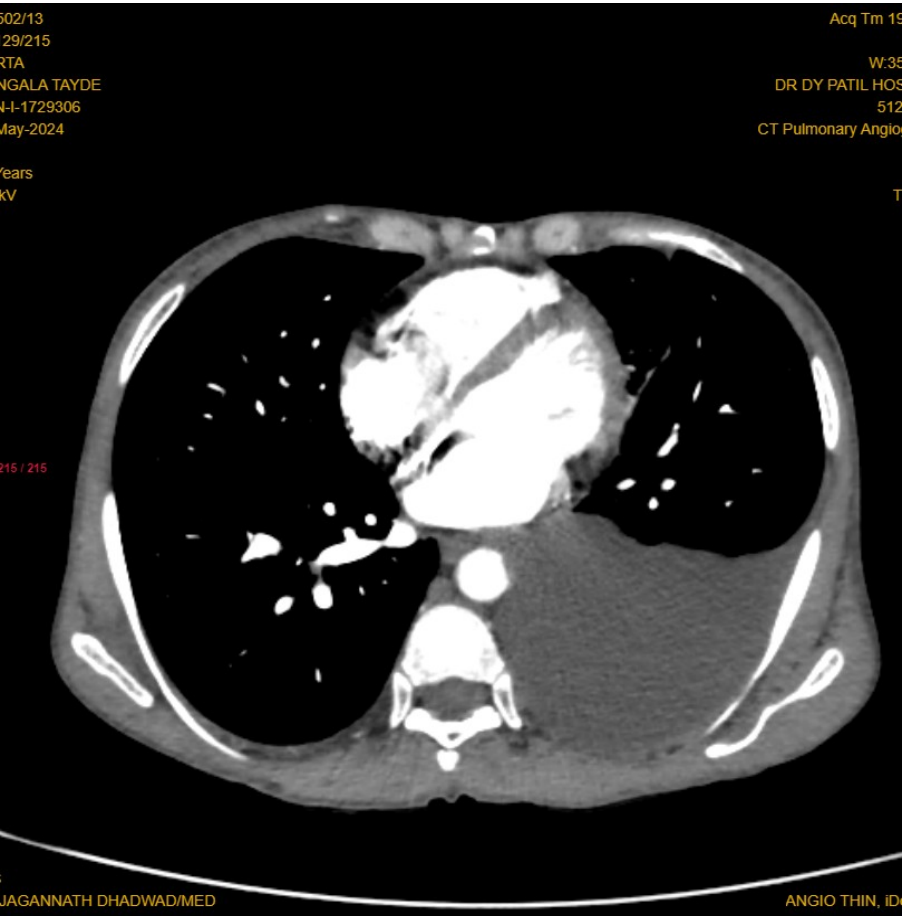
- Ultrasound Examination:

-Multiloculated Cystic lesion involving the right ovary

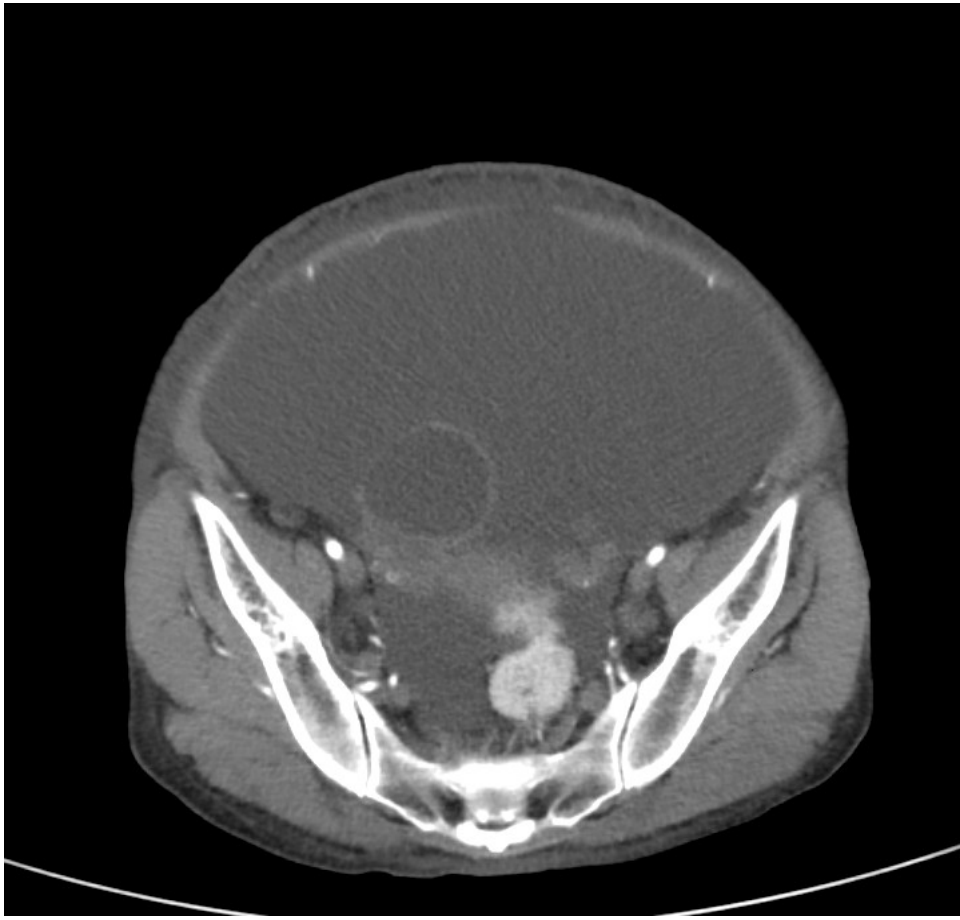
-Gross ascites

- No organomegaly

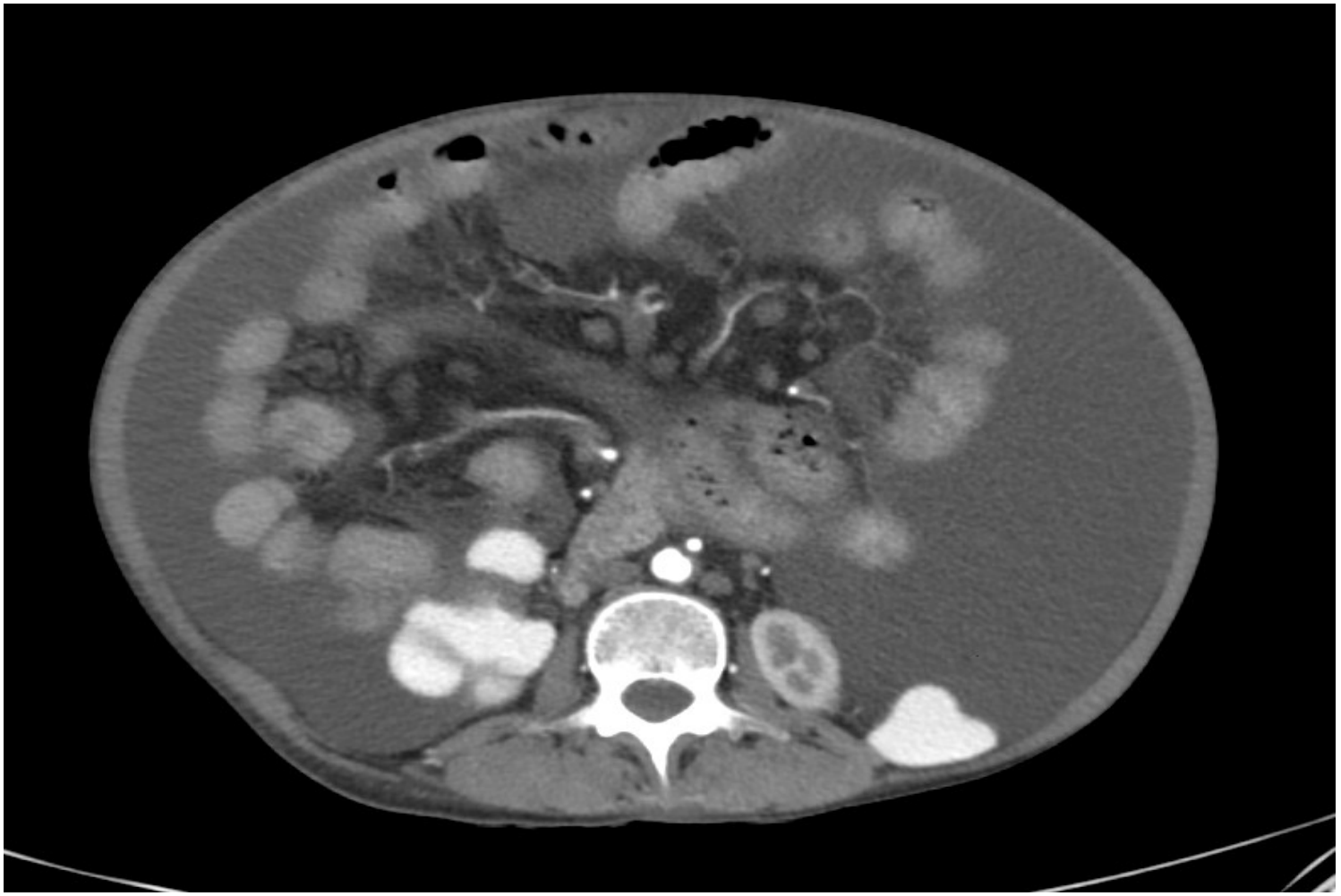
CECT (Abdomen + pelvis)



Moderate Pleural effusion
left hemithorax



Right side enlarged ovary



Gross ascites

Routine Cytology

Characteristics	Ascitic tapping	Pleural tapping
Appearance	**White, Turbid**	**White, Turbid**
Cobweb	Absent	Absent
Deposit	Absent	Absent
Protein	0.7	3.8
Glucose	103	110
TLC	450/cmm	490/cmm
Polymorphs	15%	10%
Lymphocytes	**80%**	**75%**
ADA	3U/L	4U/L
LDH	99U/L	70U/L
Triglycerides	**121mg/dl (N- <110)**	**535mg/dl**
Amylase/Lipase	16/14U/L	12/19U/L
CBNAAT	Negative	Negative

Tumor Markers

- **CA 19.9:- 5.15 U/mL (normal range- <37 U/mL)**
- **CEA:- 1.28 ng/mL (normal range – 0 to 2.5 ng/mL)**
- **CA125- >1000 units/mL (normal range- 0 to 35 units/mL)**

- **Ascitic fluid Malignant cytology- Negative.**
  culture- no growth, no acid fast bacilli seen

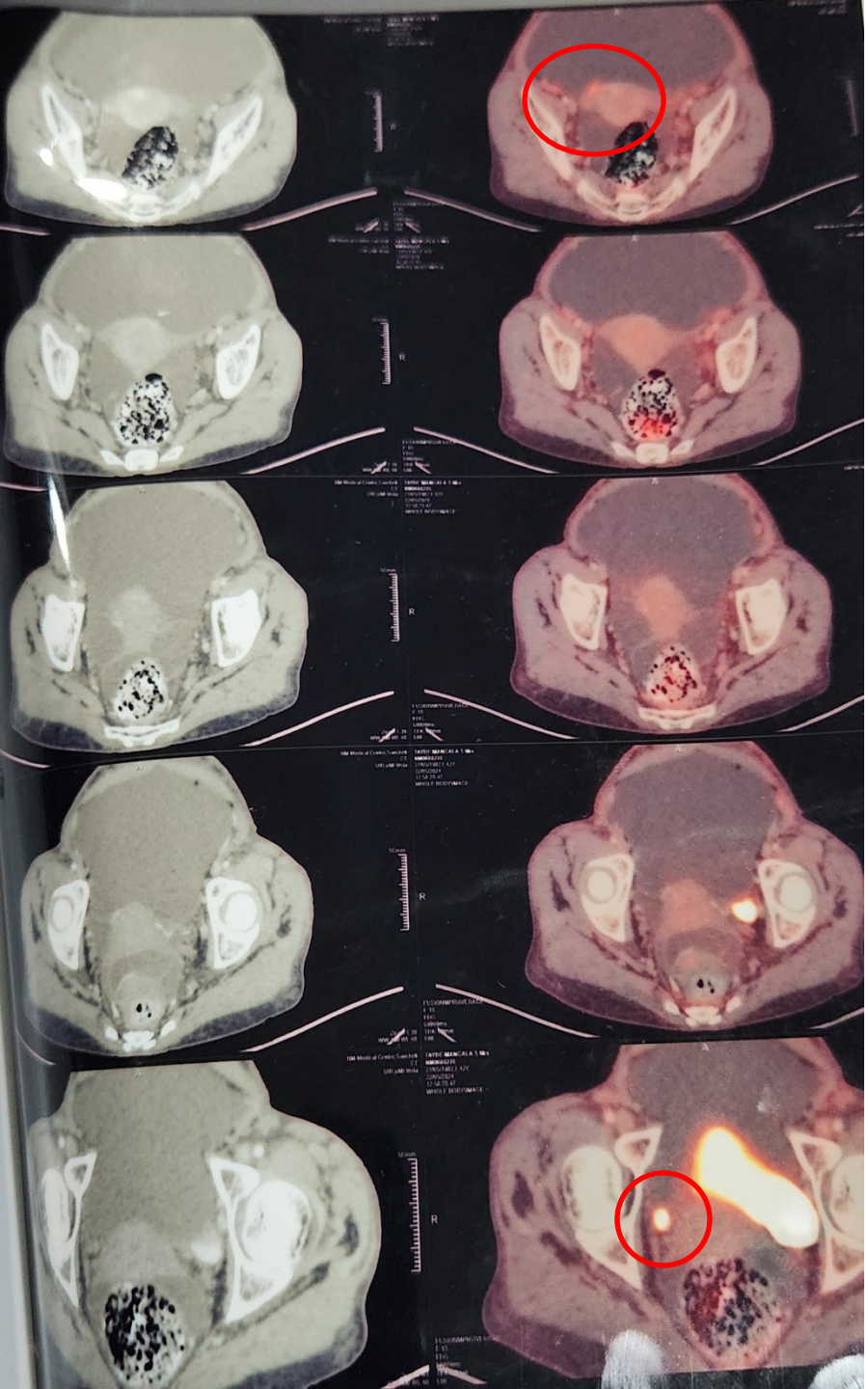
- **Pleural fluid Malignant cytology- Negative**

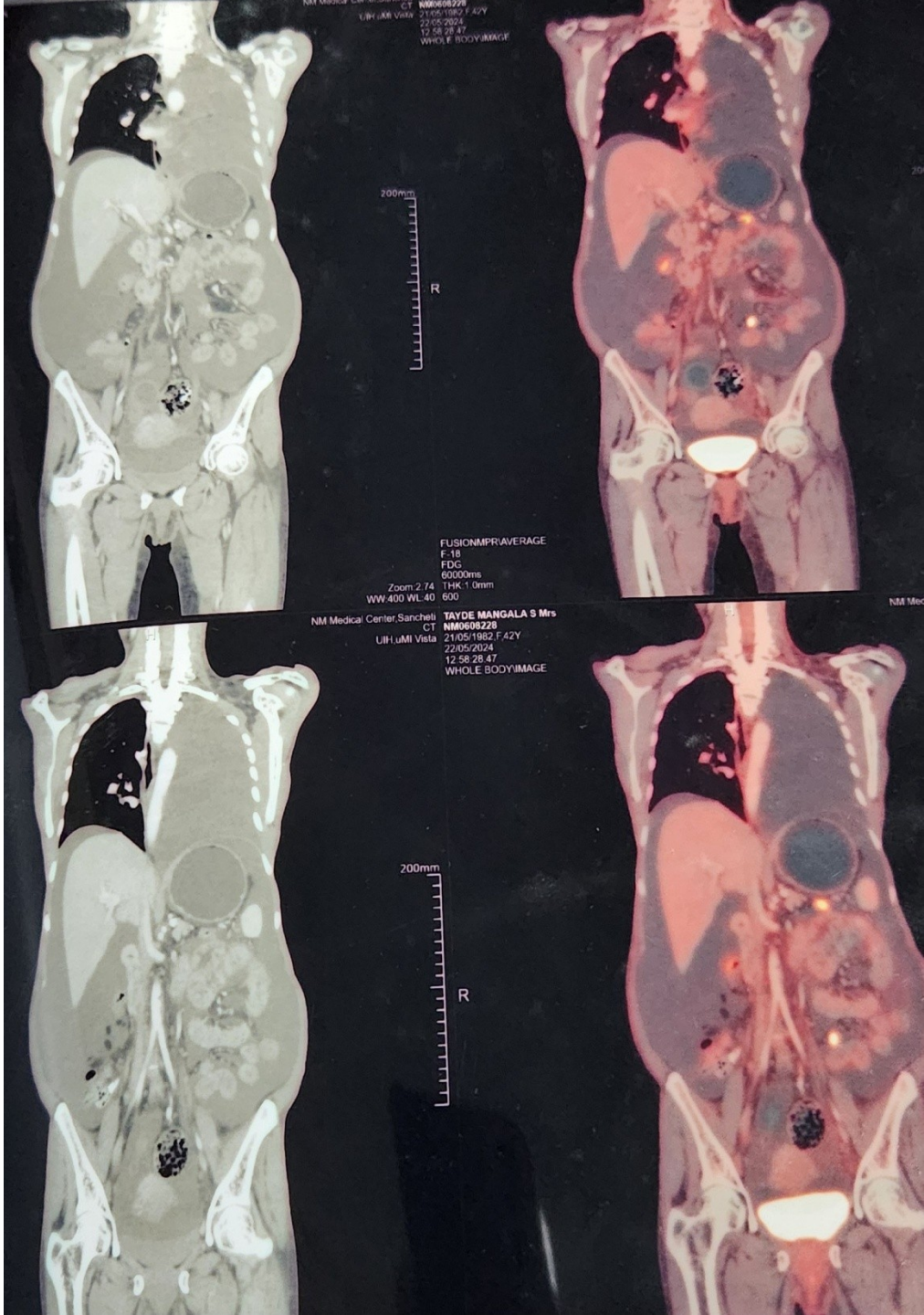
- **PET-CT SCAN:**

- Moderate **left sided pleural effusion** is seen with resultant passive atelectasis

- Septate **cystic density lesion** with **enhancing solid components** seen in the right adnexa(4.5 x 4.7 cm) -SUVmax (8.8).
- **Similar solid cystic density lesion** is seen in the left adnexa with SUVmax (4.2).

- There is gross ascites. Few mildly **enlarged bilateral external iliac lymph nodes** are present, SUVmax (3.1)

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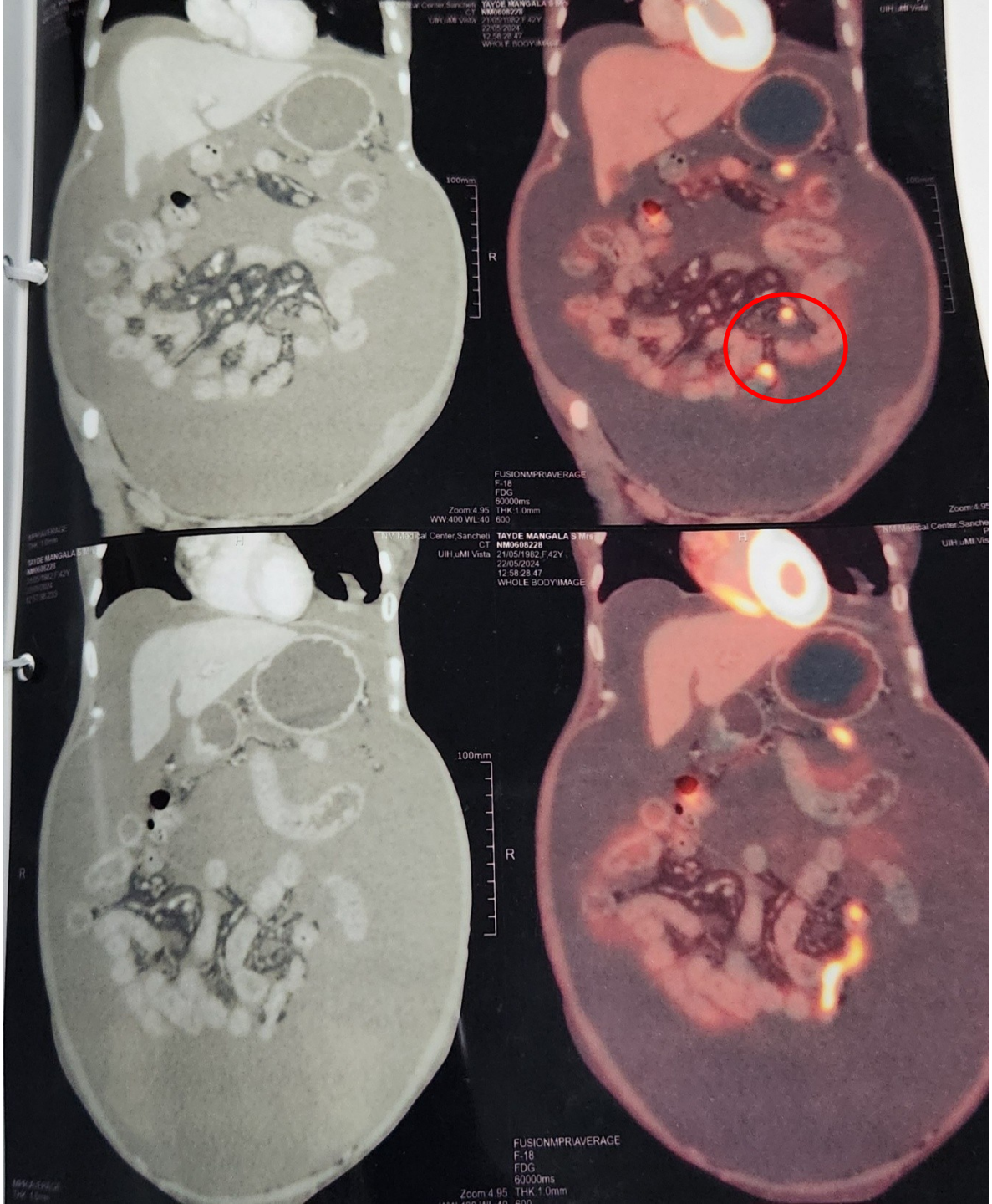
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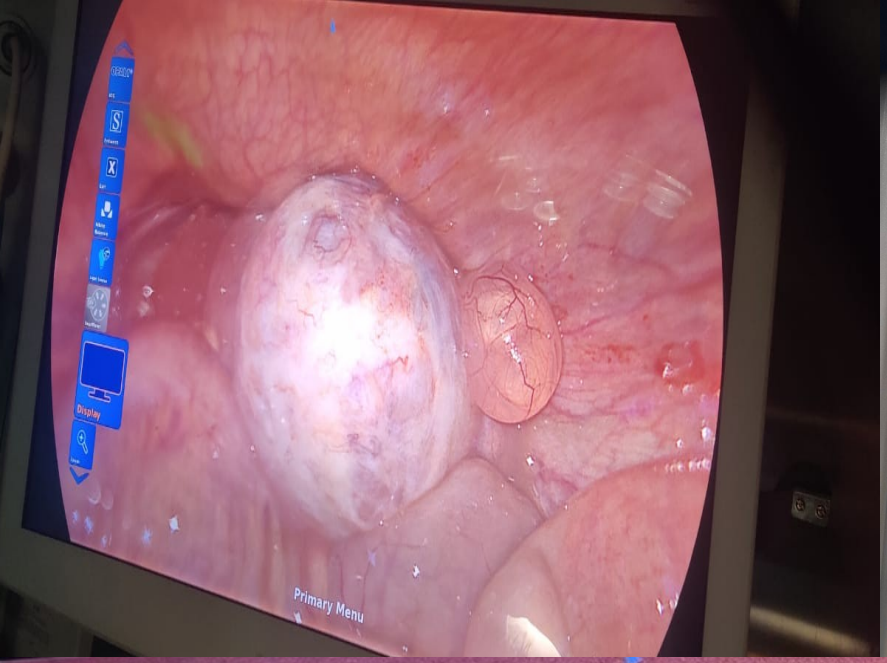
INITIAL OPERATIVE PLAN

- Diagnostic Laparoscopy and biopsy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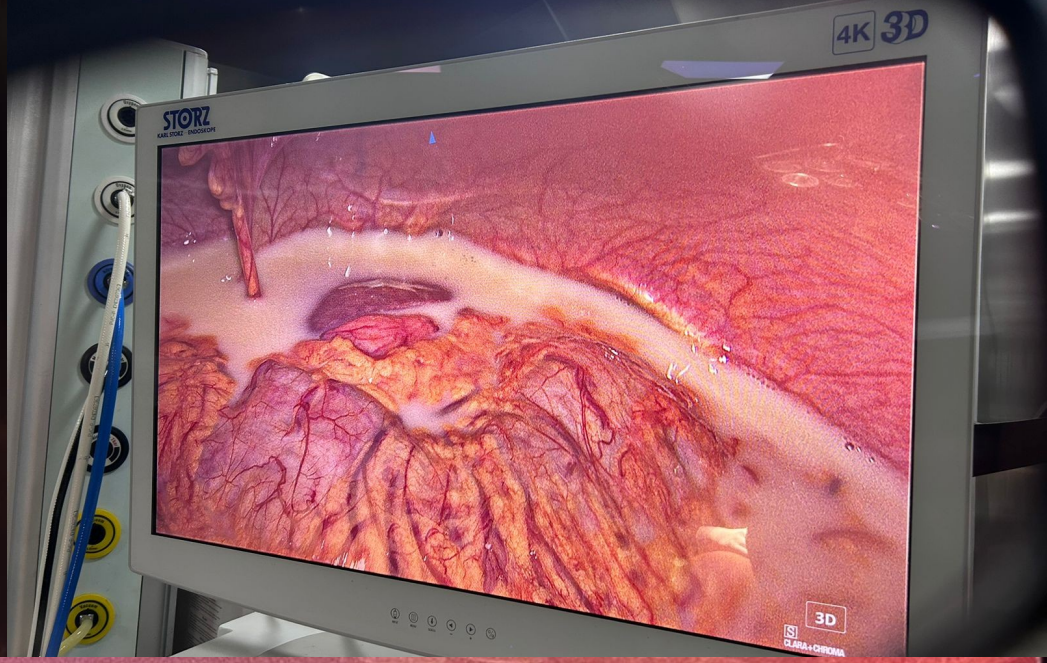
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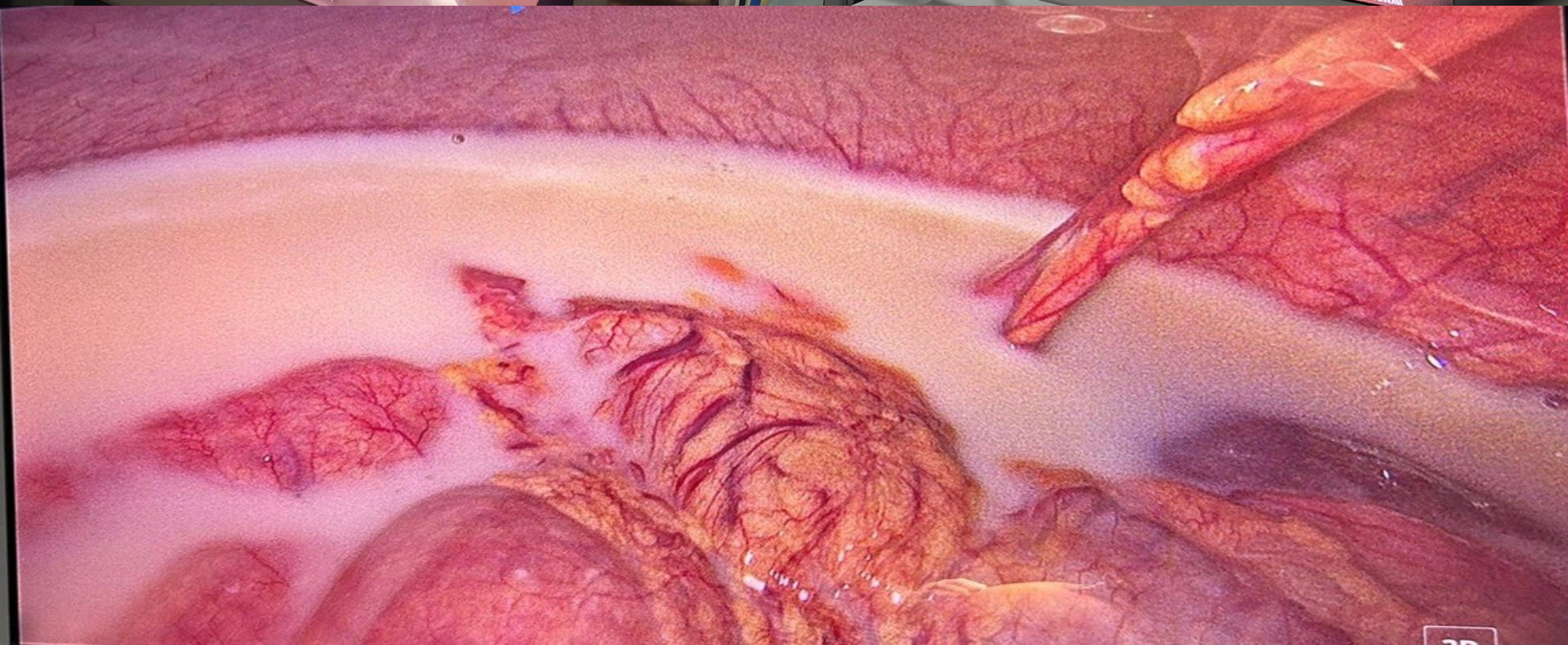
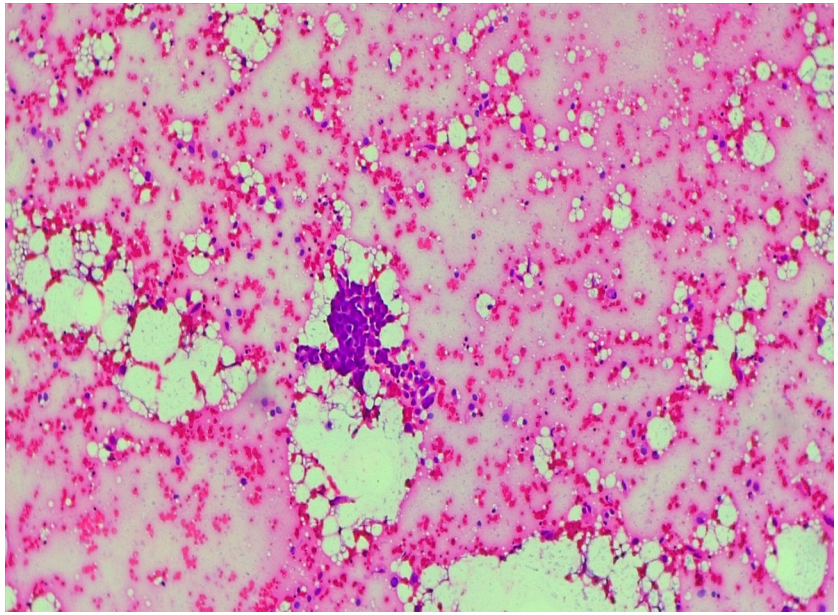


Frozen section for lesion of omental biopsy

Gross : Received 2 fibrofatty tissue pieces measuring 4x3x2 cm & 3x2x2cm.

Frozen section : **Suspicious for metastatic deposits**



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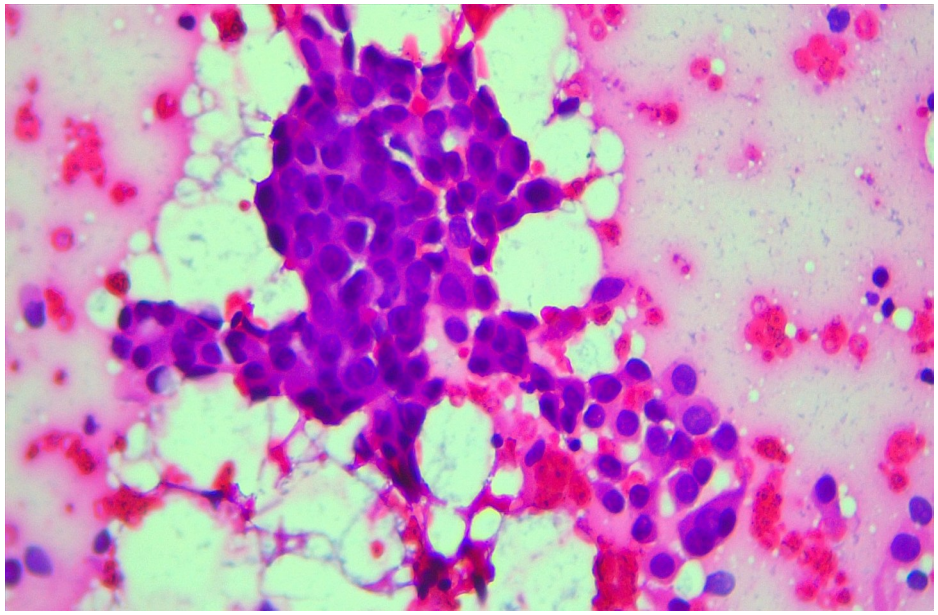

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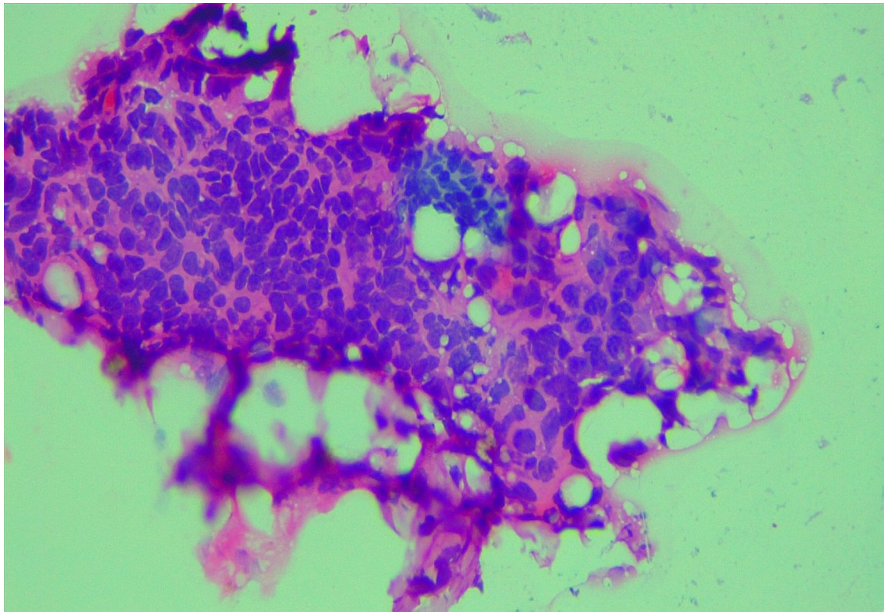

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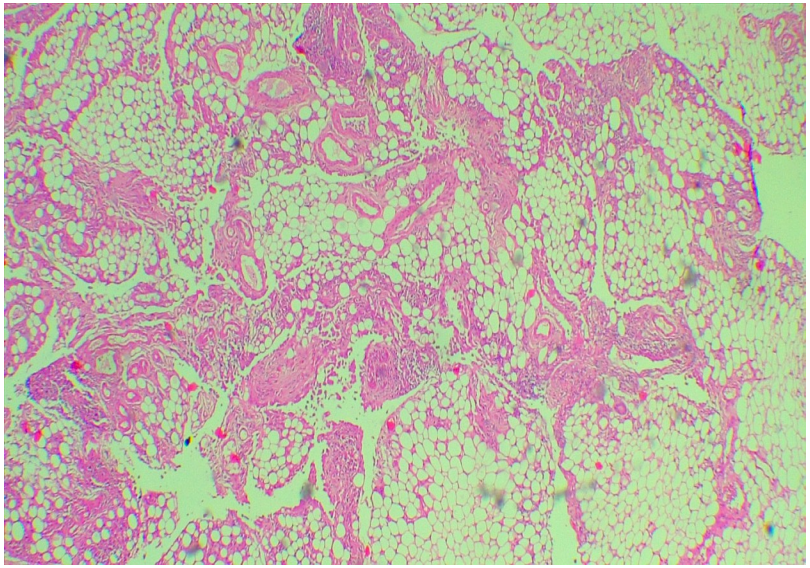
Final diagnosis:

Mesothelial hyperplasia, negative for malignancy



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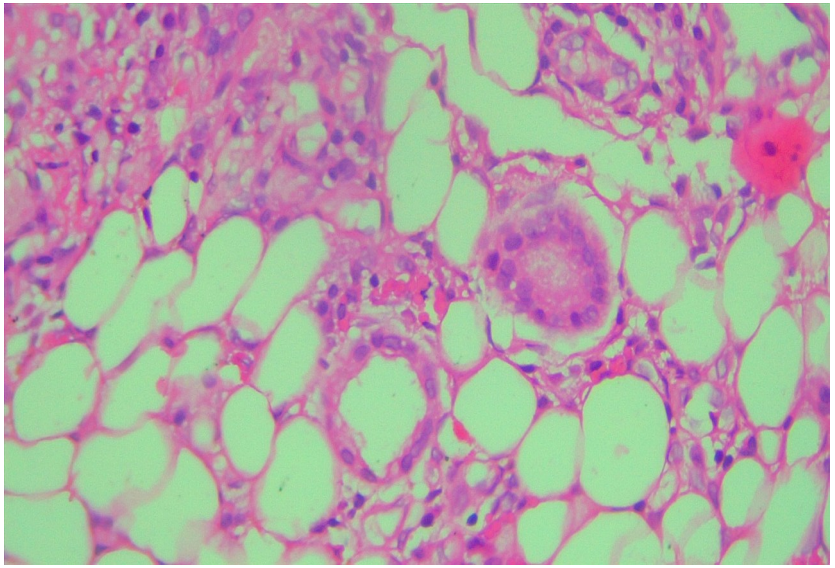

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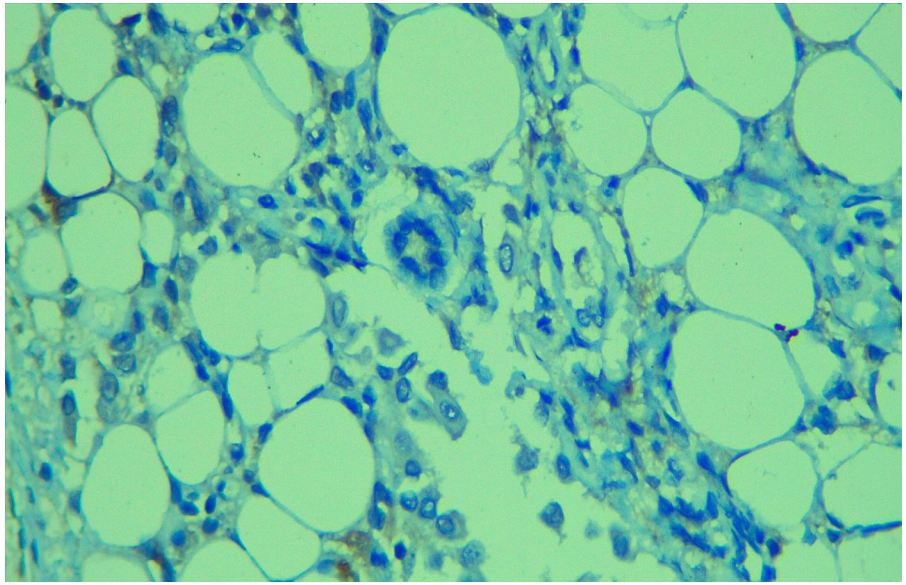

PAX 8

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DIFFERENTIAL DIAGNOSIS

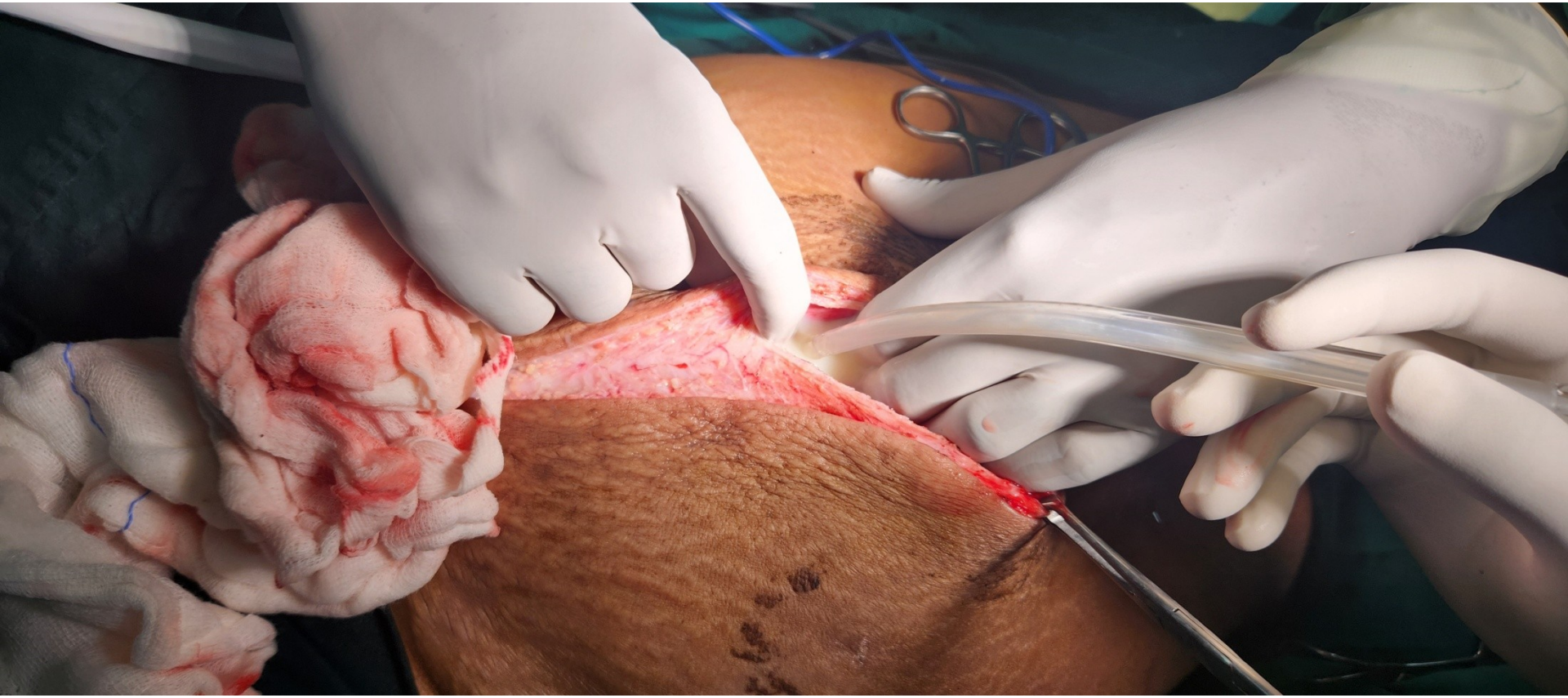
- CHYLOUS ASCITIS:

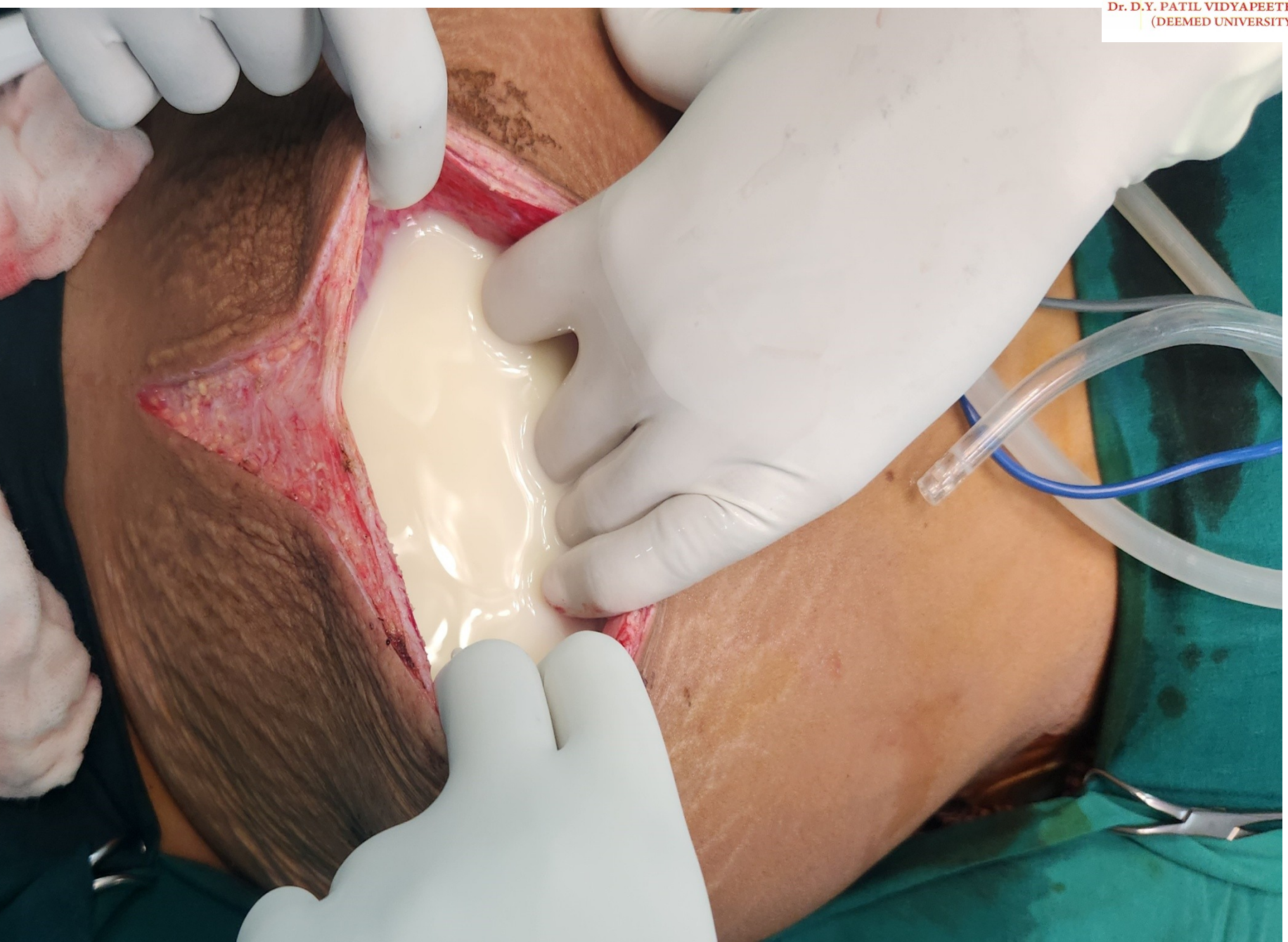
-Malignancy
-Tuberculosis
-Pancreatitis
-Lymphoma
- Filariasis

MULTIDISCIPLINARY BOARD MEETING

- **Surgical staging for the diagnosis of CA ovary**
- **Repeat frozen section and proceed accordingly**

- **Patient was planned for exploratory laparotomy**






Quali surge

INTRAOPERATIVE PLAN

Bilateral Ovaries were sent for frozen section

↓

Frozen reported- Negative for malignancy

↓

Right external iliac node and mesenteric node sent for histopathology

(were FDG avid on PETCT)

↓

Surgery performed- TAH+BSO+external iliac and mesenteric node sampling

HPE right ovary

- Gross: Received right ovary of size 7x6.5x4 cm with attaches Fallopian tube 6cm in length.

- E/S : Ovary mildly enlarged with intact capsule. No capsular breach or surface deposits seen

- C/S : Solid-cystic. The cystic area measured 3x2x2 cm, was multiloculated separated by thin fibrous septae. The cyst wall was smooth, uniform. No papillary excrescences or nodules seen. The solid area appeared to normal ovary.
- Diagnosis:
  -Benign serous cystadenoma of right ovary.

  -Negative for malignancy

HPE- left ovary

- Gross: ovary measured 2.8x1.5x1.4 cm and attached fallopian tube measured 3.5 cm in length.

- External and cut surface were unremarkable.

- Diagnosis:
  Normal ovary with follicular cyst
  Bilateral fallopian tubes- Unremarkable.
  No malignancy.

Total abdominal hysterectomy

- Gross: Specimen measured 8.5x7.5x2.5cm. Uterus – 7x7.5x2.5cm. Cervix – 1.5cm in length.

- E/S: uterus was mildly bulky with intact external surface. No surface deposits.

- C/S : endometrial canal – 5cm, endometrial thickness 0.2cm, myometrial thickness 2 cm. No polyp or any growth identified.
- Diagnosis:
  -Proliferative endometrium with intramural leiomyoma and chronic cervicitis

  -Negative for malignancy.

Received mesenteric and right external iliac lymphnodes

Gross: Received 2 tissue pieces labelled as mesenteric and 1 tissue piece labelled as external iliac lymphnode.

Multiple lymphnodes were dissected largest measuring 1.2x1x0.5cm.

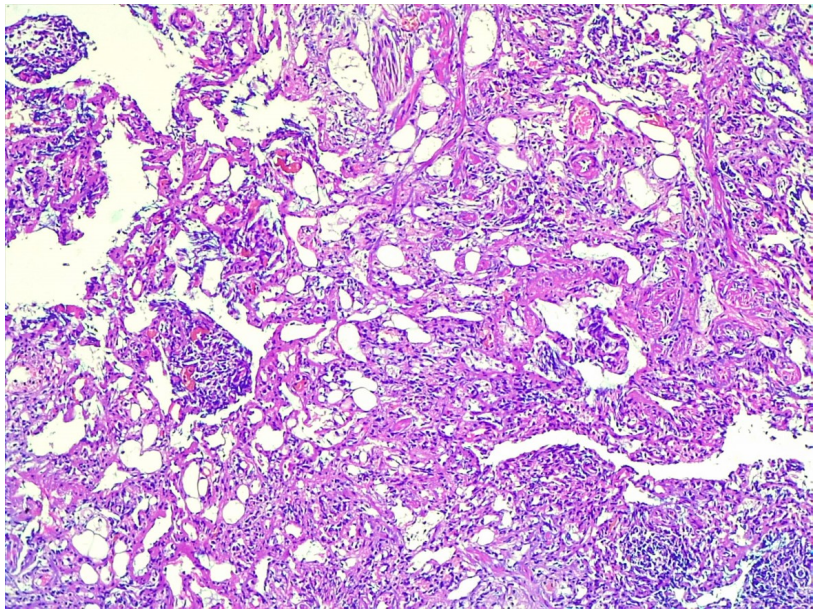
Diagnosis:

-On clinicopathological correlation

- Lymphangioleiomyomatosis of lymphnodes is favoured.

Microscopy in lymphnode involvement:

- Haphazard proliferation of spindle/epitheiloid cells around the lymphatics.
- Lipid droplets in the fluid within the lymphatic channels
- Extranodal extension & proliferation of smooth muscle cells
- IHC: SMA & HMB 45 positive.
- In cases where multiple lymphnodes in a chain are involved, HMB45 positive cells may not be present in all the nodes.



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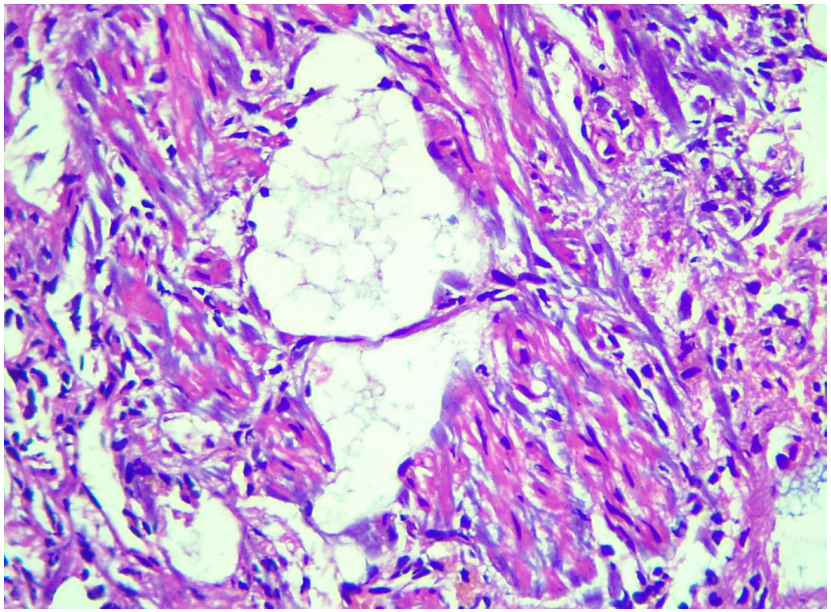

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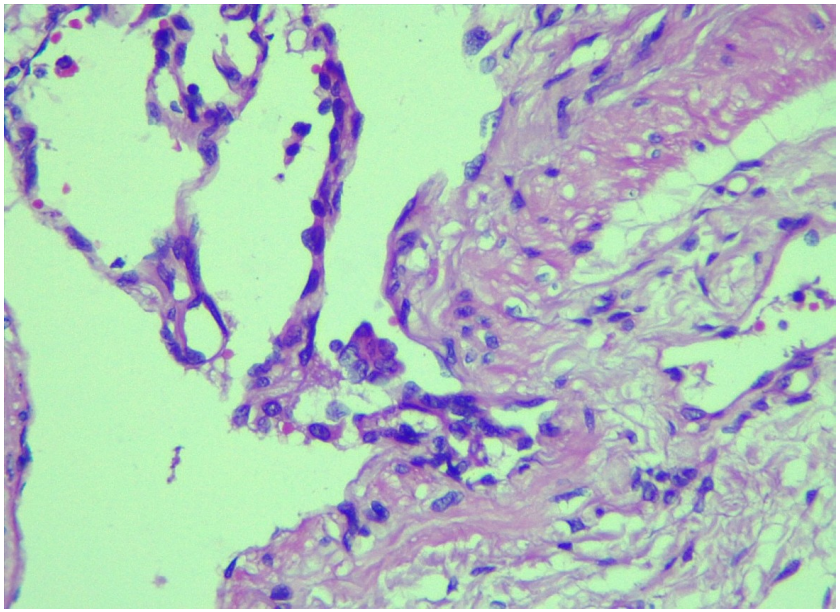

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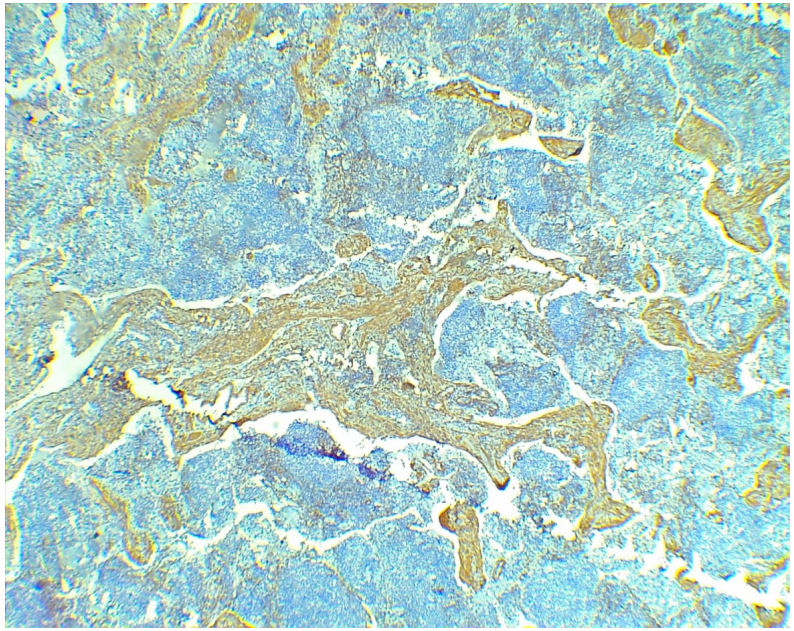
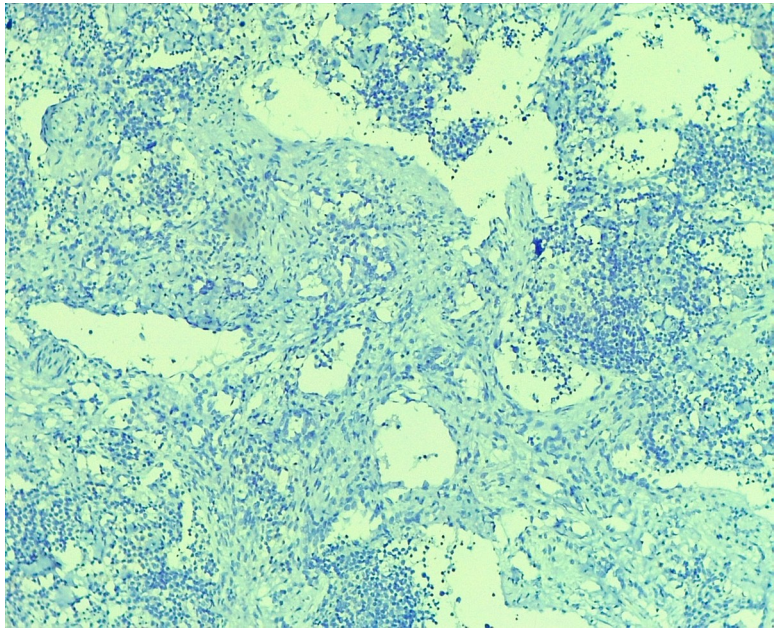
SMA

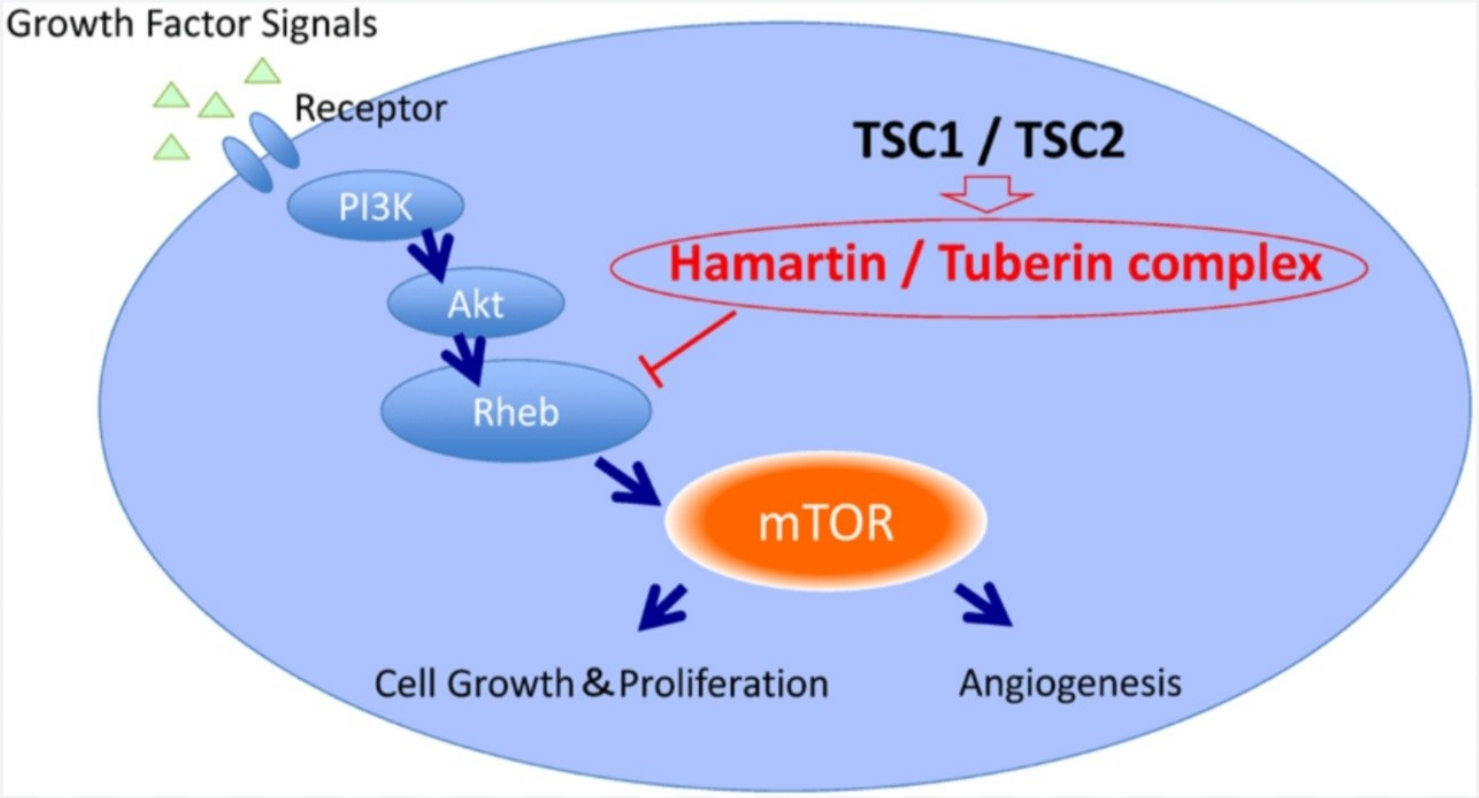


HMB 45

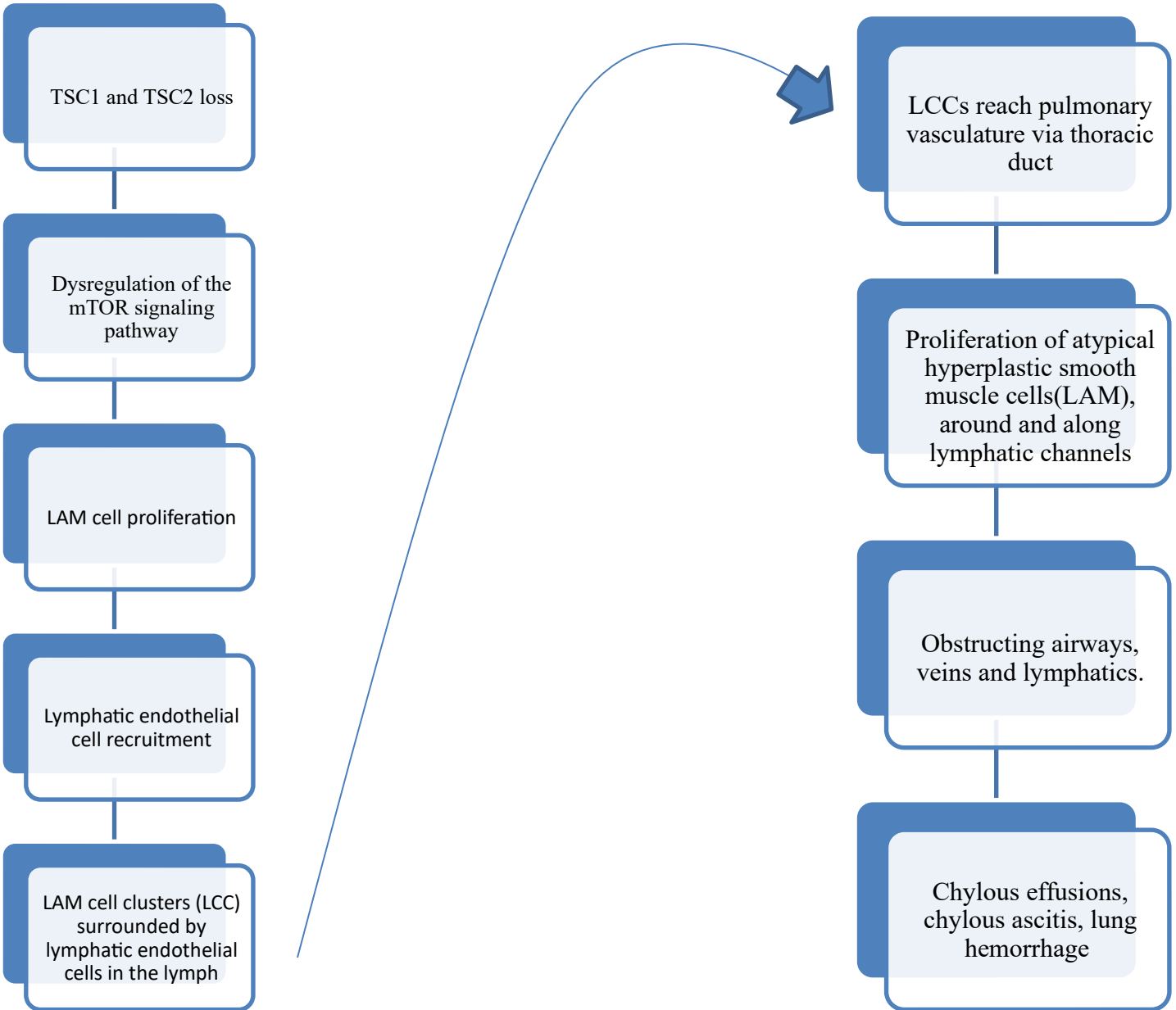


- Lymphangioleiomyomatosis(LAM) is a rare, progressive systemic disease affecting the lymphatic system.
- Overall rare (5 cases per 1 million)
- Women of childbearing age, 3rd decade, reported in males with tuberous sclerosis complex- rare
- Usually presents with exertional dyspnoea and spontaneous pneumothorax
- **low-grade metastasizing neoplasm** by the WHO classification of lung tumors.
- LAM comes under the category of **Mesenchymal tumors,** belonging to the class of **PEComatous tumors(Perivascular epithelial cells)**
- *TSC1* and *TSC2* genes encode two proteins, hamartin and tuberin, together these inhibit the mechanistic Target of Rapamycin (mTOR) signaling pathway

Cudzilo CJ, Szczesniak RD, Brody AS, et al. Lymphangioleiomyomatosis screening in women with tuberous sclerosis. Chest. 2013;144:578–85.


Growth Factor Signals
Receptor
PI3K
Akt
Rheb
TSC1 / TSC2
Hamartin / Tuberin complex
mTOR
Cell Growth & Proliferation
Angiogenesis

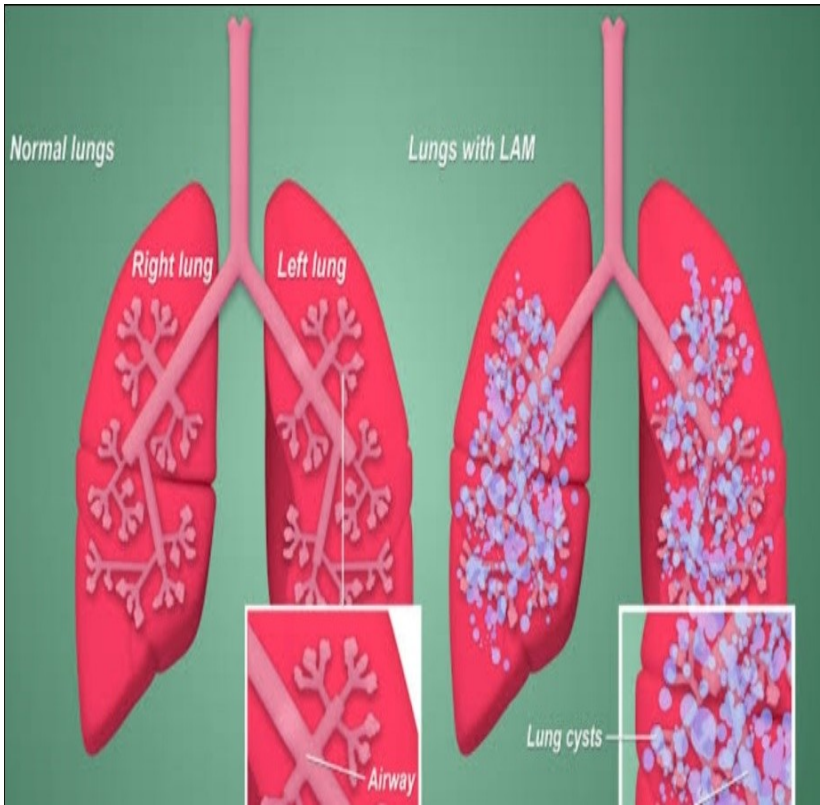
PATHOPHYSIOLOGY



- Clinical features:

	Sporadic LAM	TSC-LAM
Dyspnea	73 %	71 %
Pneumothorax	57 %	47 %
Abdominal angiomyolipomas	41 %	96 %
Chylous effusions	20 %	14 %
Lymphangioleiomyomas	38 %	13 %
Hemoptysis	10 %	3 %

Enlargement of the air spaces is associated with the proliferation of type II pneumocytes and destruction of elastic and collagen fibers in the walls of the cysts.



- **Also reported in patients:**

- **chyluria,**
- **chyloptysis,**
- **Posterior mediastinal, retroperitoneal and pelvic lymphangioleiomyomas**

TREATMENT

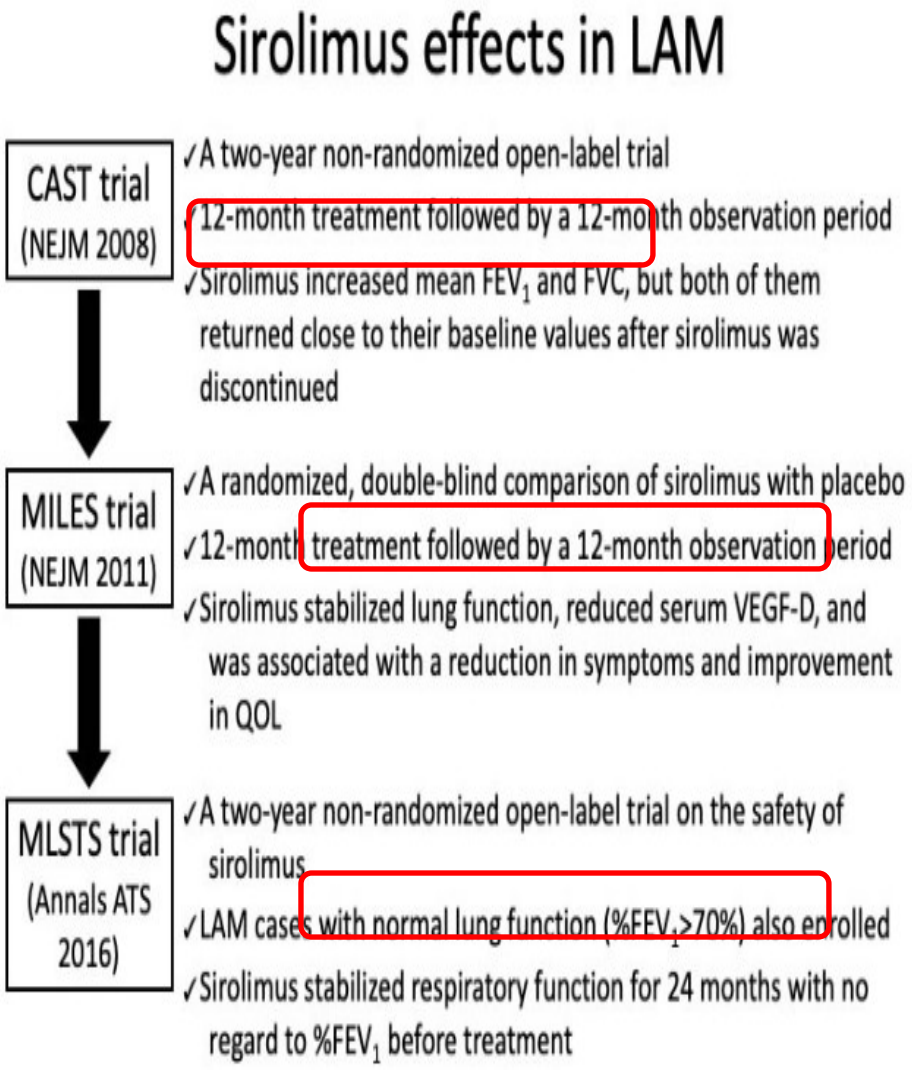
- ROLE OF SIROLIMUS:

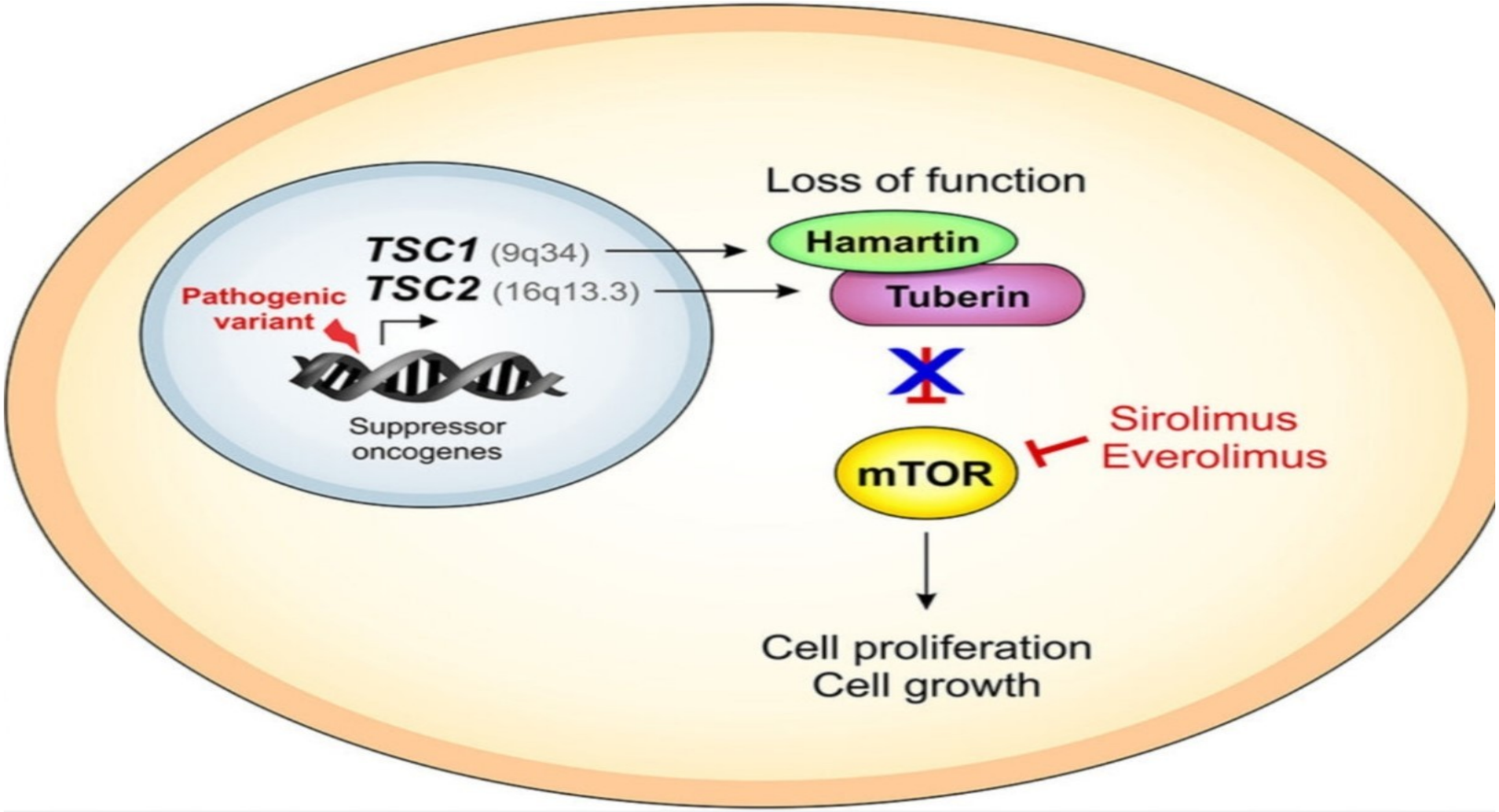
- mTOR inhibitor

- In 2008, Bissler *et al*. published the first clinical trial on the use of sirolimus for renal AMLs in patients with TSC as well as sporadic LAM.

- Sirolimus therapy :

- Stabilized lung function
- Improve quality of life
- Reduce the size of chylothorax
- Decrease the volume of renal AMLs
- Decrease serum VEGF-D level.




Loss of function
TSC1 (9q34)
TSC2 (16q13.3)
Pathogenic variant
Suppressor oncogenes
Hamartin
Tuberin
mTOR
Sirolimus
Everolimus
Cell proliferation
Cell growth

- Dosage: 1–2 mg per day ("low dose") to achieve a serum level of around 5 ng/mL.

- In cases of treatment failure, combination of sirolimus and hydroxychloroquine (an autophagy inhibitor) and demonstrated the safety of this combination therapy .

- There is a role of Peritoneovenous shunting in cases of relapses or treatment failure

Makino, Y., Shimanuki, Y., Fujiwara, N., Morio, Y., Sato, K., Yoshimoto, J., Gunji, Y., Suzuki, T., Sasaki, S., Iwase, A., Kawasaki, S., Takahashi, K., & Seyama, K. (2008). Peritoneovenous shunting for intractable chylous ascites complicated with lymphangioleiomyomatosis. *Internal medicine (Tokyo, Japan)*, *47*(4), 281–285. https://doi.org/10.2169/internalmedicine.47.0475

- This Patient was on Sirolimus for 6 months – with moderate decrease in symptoms

TAKE HOME MESSAGE

- A differential diagnosis of Lymphangioleiomyomatosis(LAM) should be kept in mind in cases of chylous ascitis or effusion.

- Awareness should be created regarding this condition and its association with tuberous sclerosis.

THANKYOU