Renal Angiomyolipoma with Tuberous Sclerosis Non Seminomatous Germ Cell Tumor of Testes

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Non Seminomatous mixed germ cell tumor of testis- yolk sac tumour and embryonal carcinoma

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Clinical summary

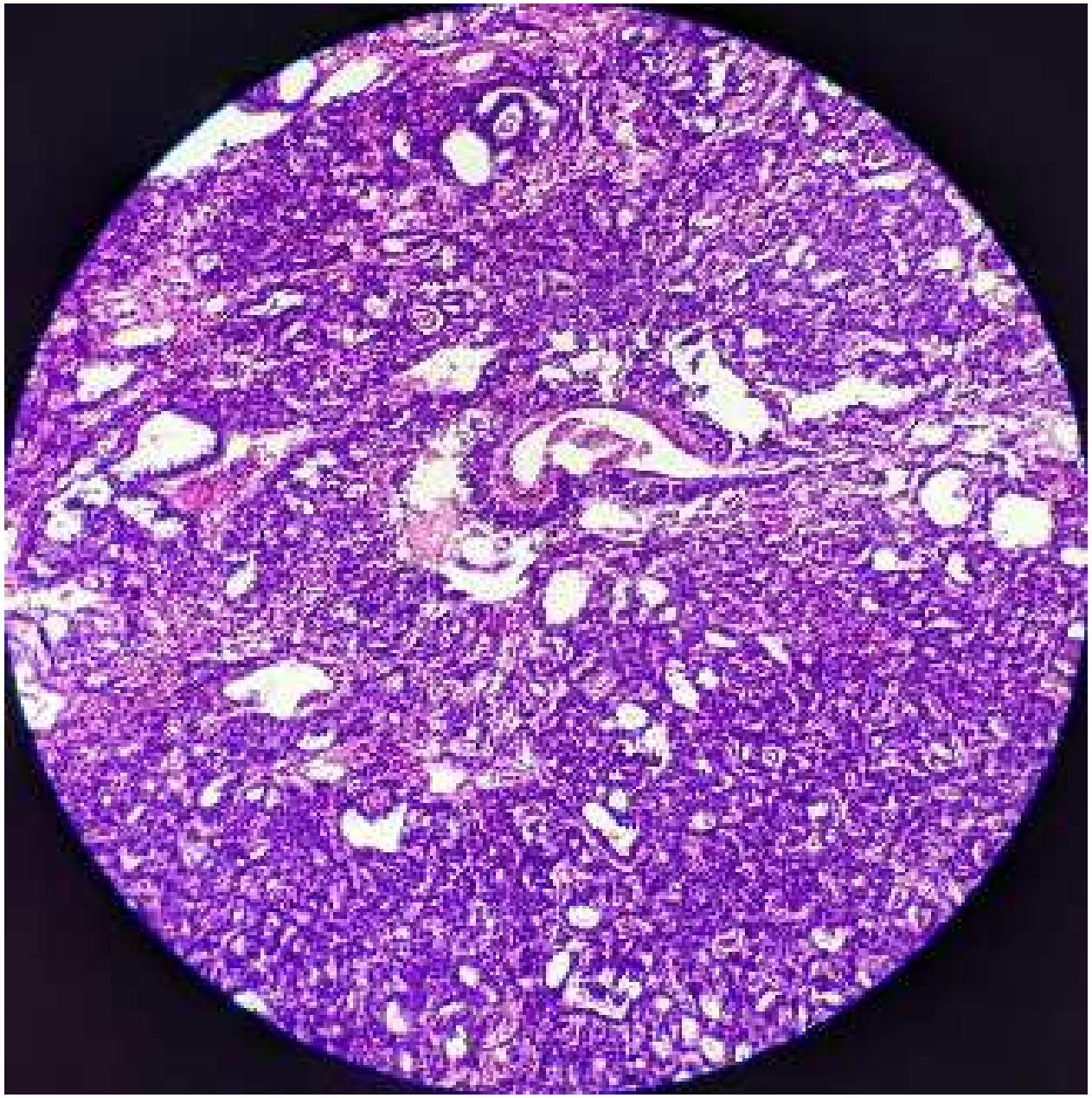
- 21 years/ Male
- Chief complaint – Left Testicular mass
- The mass measured 7x 6.5 cm, with nodular thickening of spermatic cord
- Radiological Findings- show hypo and hyper-enhancing cystic areas, hydrocele, thickening and enhancement of Spermatic cord and enhancement of Scrotal sac.
- Tumor markers:-
- LDH- 339
- AFP- 22904

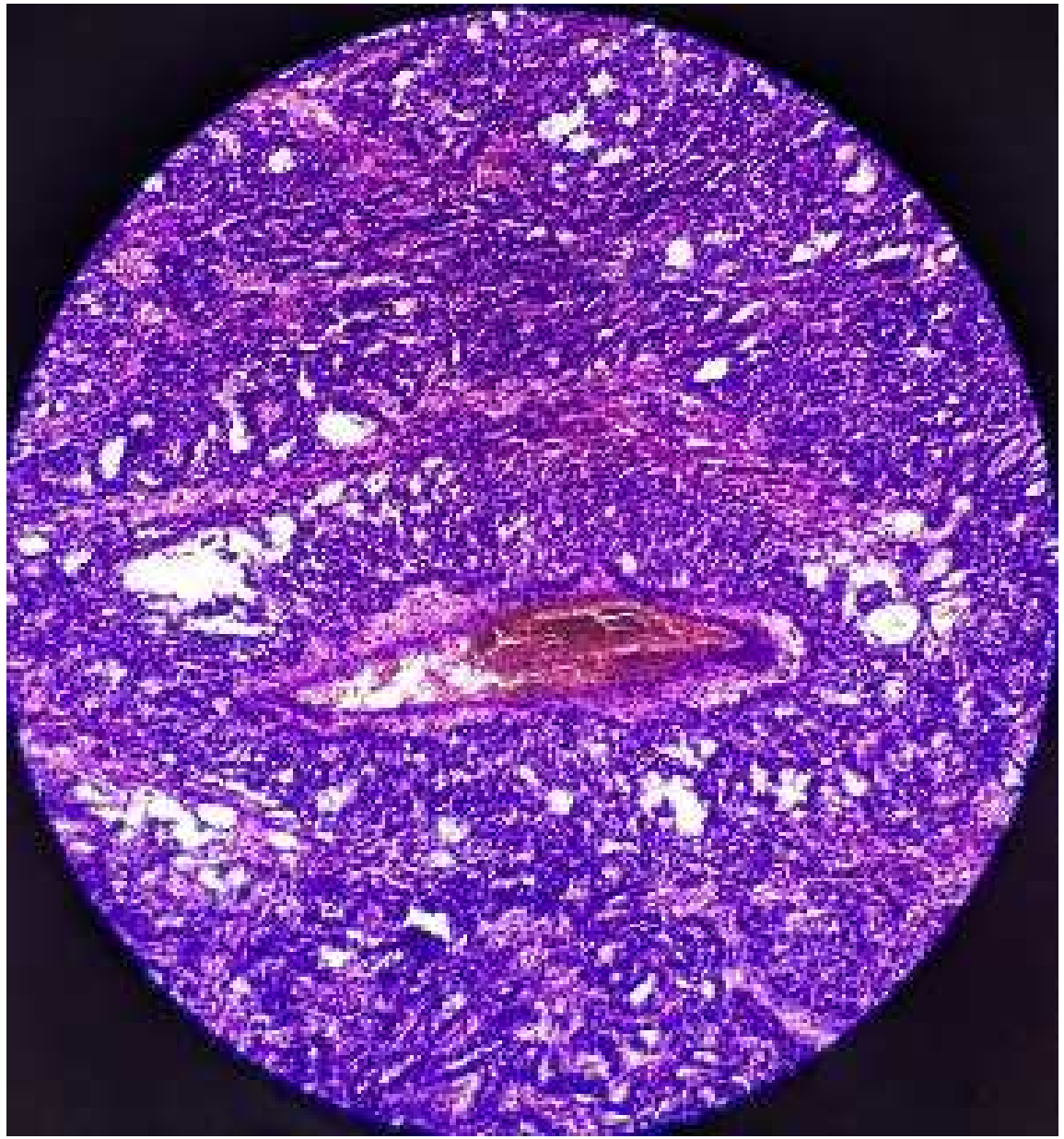
gross

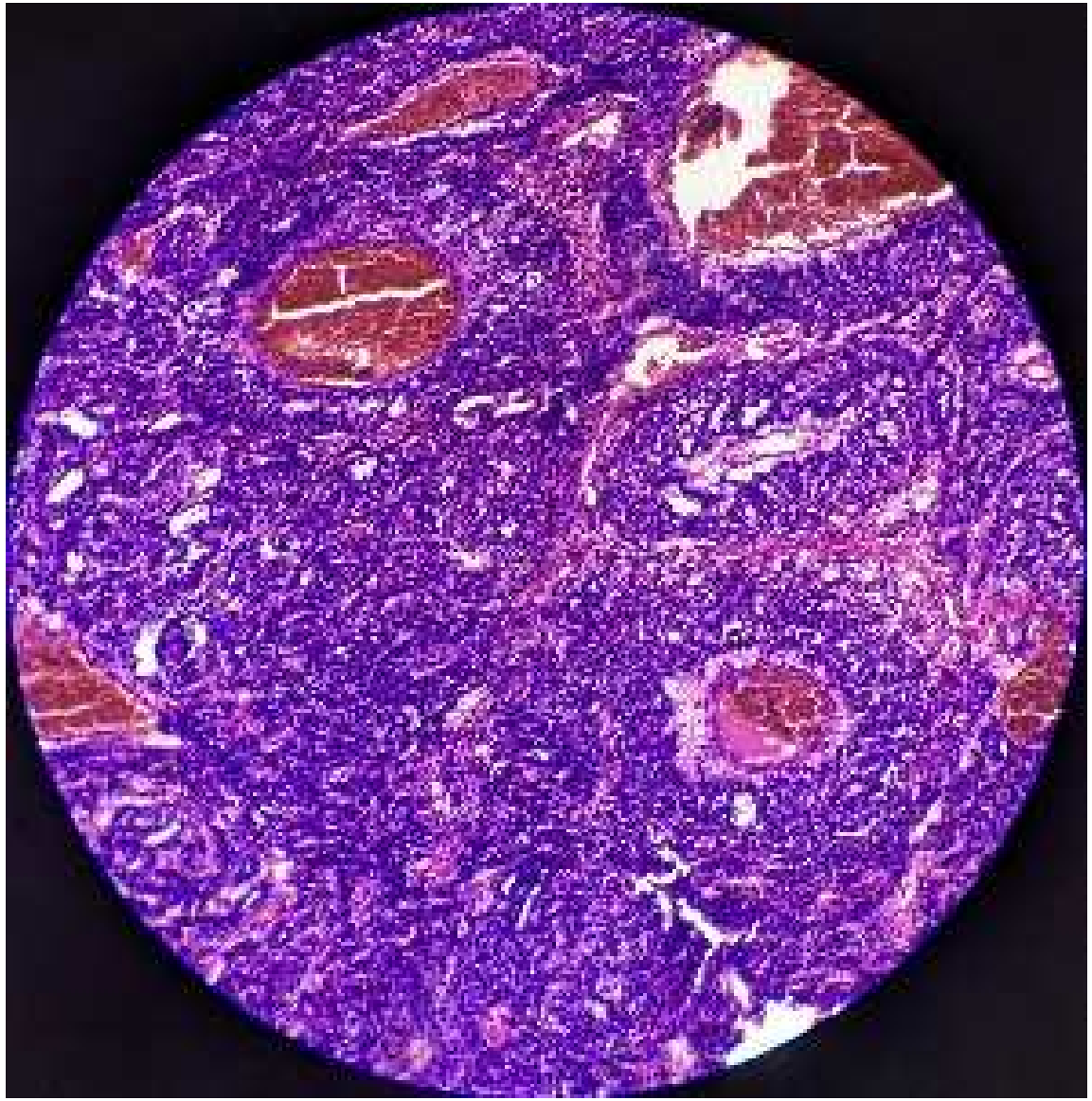
- Received Specimen of Left Testis with Epididymis, entirely measuring 12 x 7 x 7 cm, with Intact tunica.
- The Eternal surface- Smooth and shows a cyst measuring 3cm in diameter. C/S of cyst- filled with yellowish fluid
- C/S Of testis- shows greyish – white, variegated mass, extending throughout the testis, with partly cystic areas and some areas of hemorrhage.

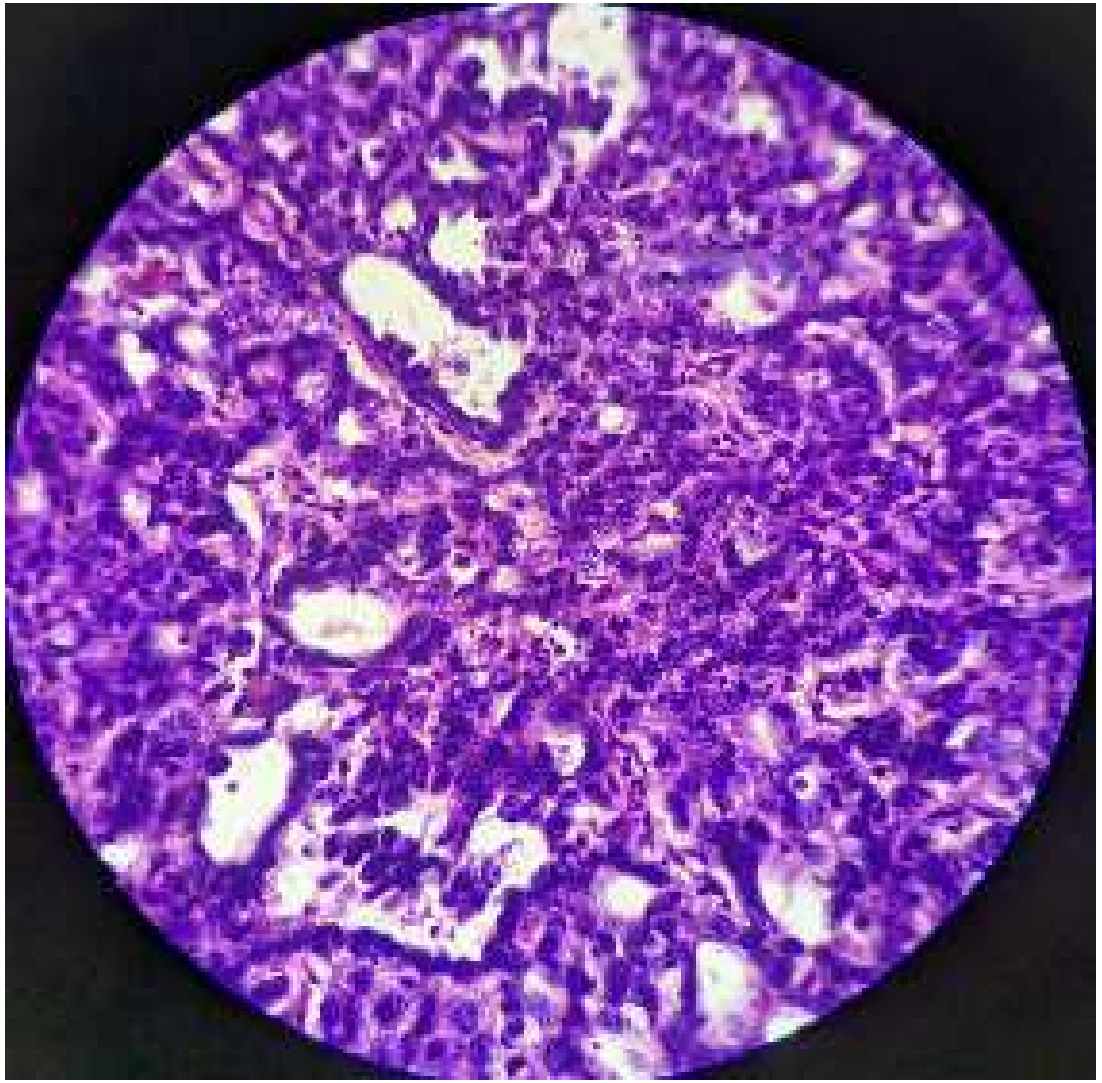
Microscopy- Embryonal Component

- The cells grow in alveolar, tubular and sometimes in papillary folds and more undifferentiated lesions are seen as sheets of cells with cleft like spaces.
- Multiple growth patterns usually present. 3 most common growth patterns: solid (55%), glandular (17%) and papillary (11%)
- Rare patterns: nested, micropapillary, anastomosing glandular, sieve-like glandular, pseudopapillary
- The tumour cells are large and have basophilic cytoplasm, indistinct cell borders, large nuclei, and prominent nucleoli with overlapping of nuclei
- It frequently shows pleomorphic, mitotic figures and tumor giant cells. Lympho-vascular invasion is also common.







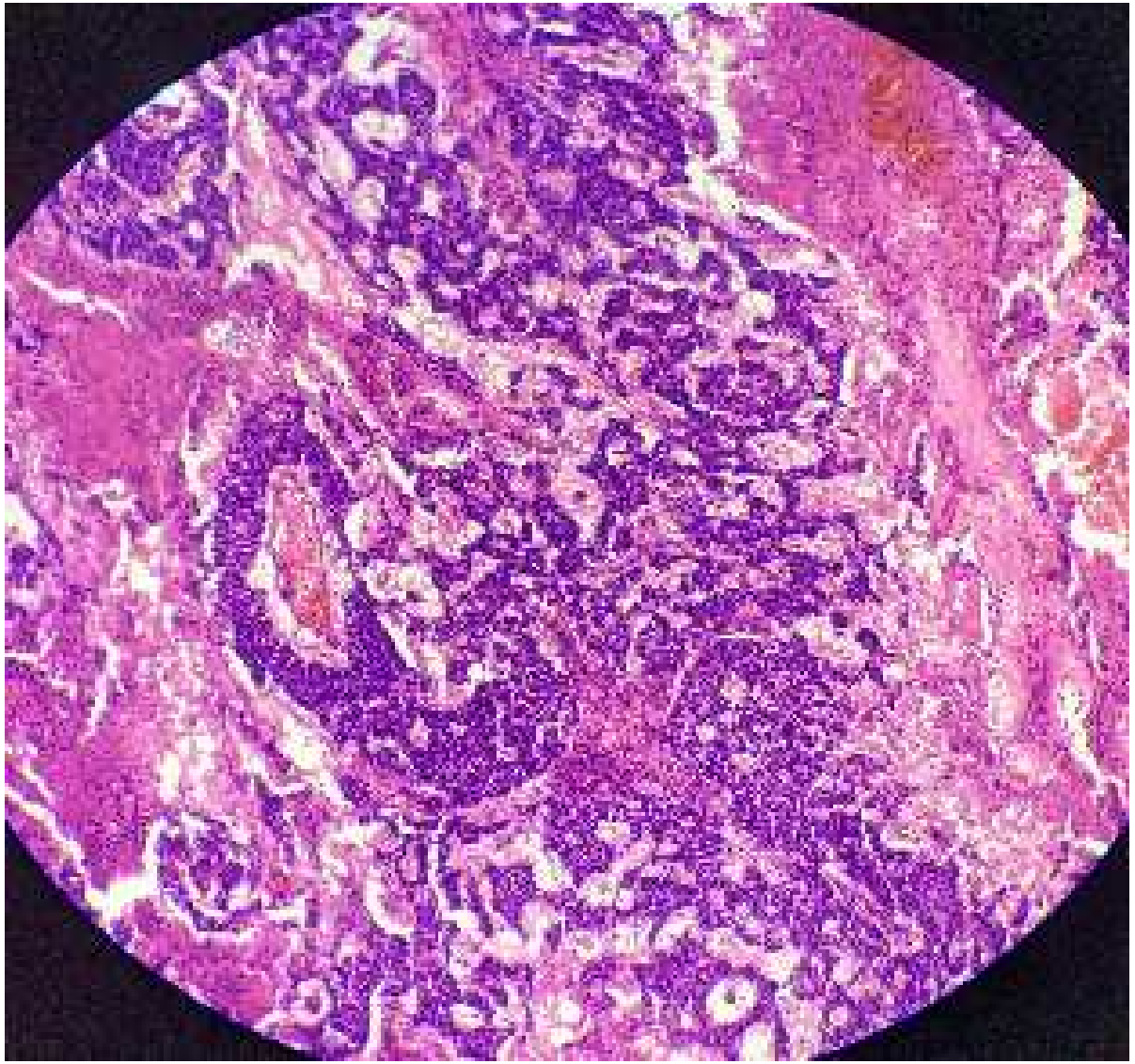


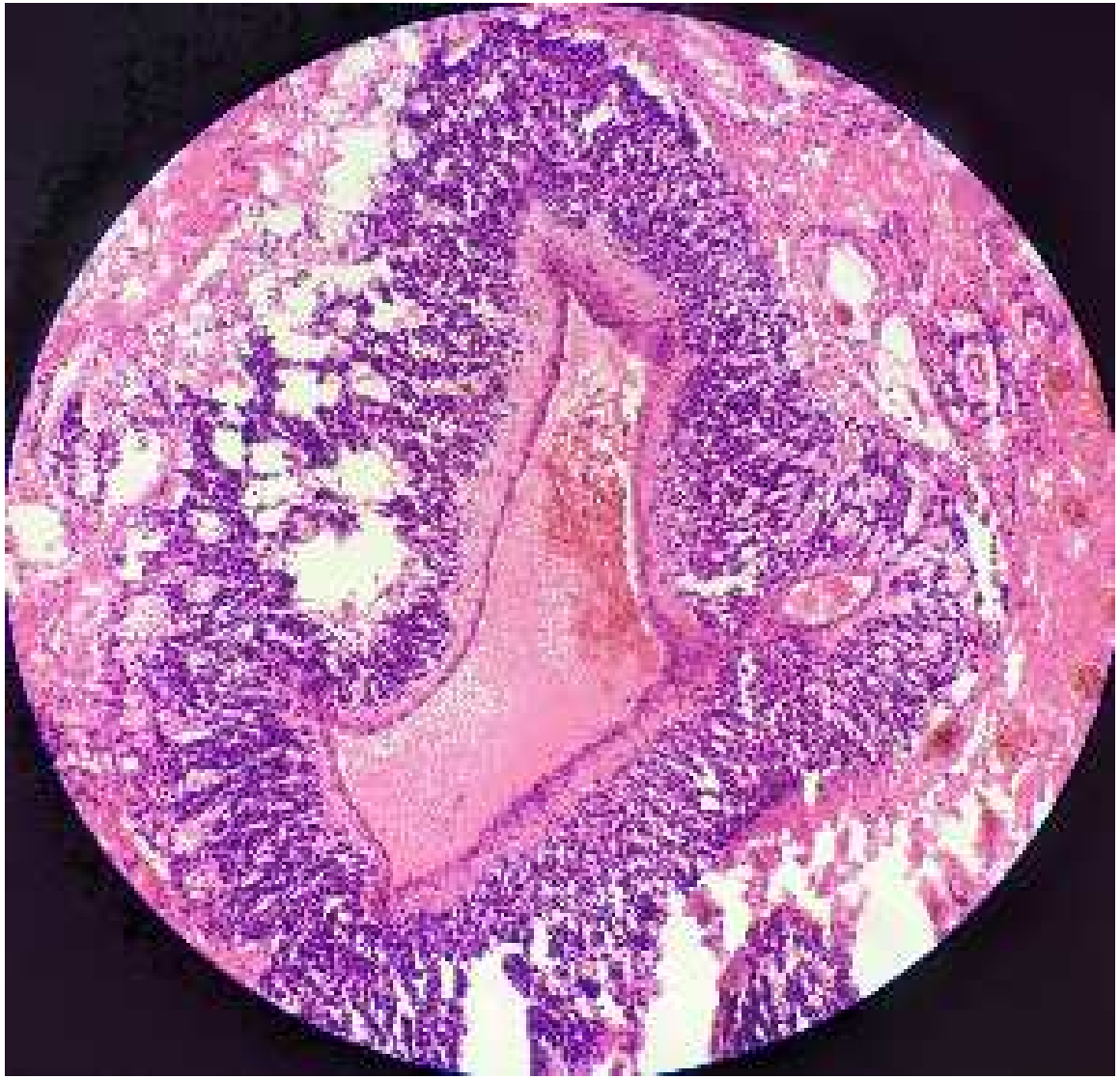
- **Positive stains**
- OCT 3/4 (nuclear and cytoplasmic), CD30 **(**Lost in c/o metastatic Embryonal CA**)**, PLAP**,** SOX2**,** SALL4
- **Negative stains**
- D2-40 / podoplanin, Glypican 3, AFP, CK7, Inhibin, p63, GATA3, Calretinin, B- hCG:

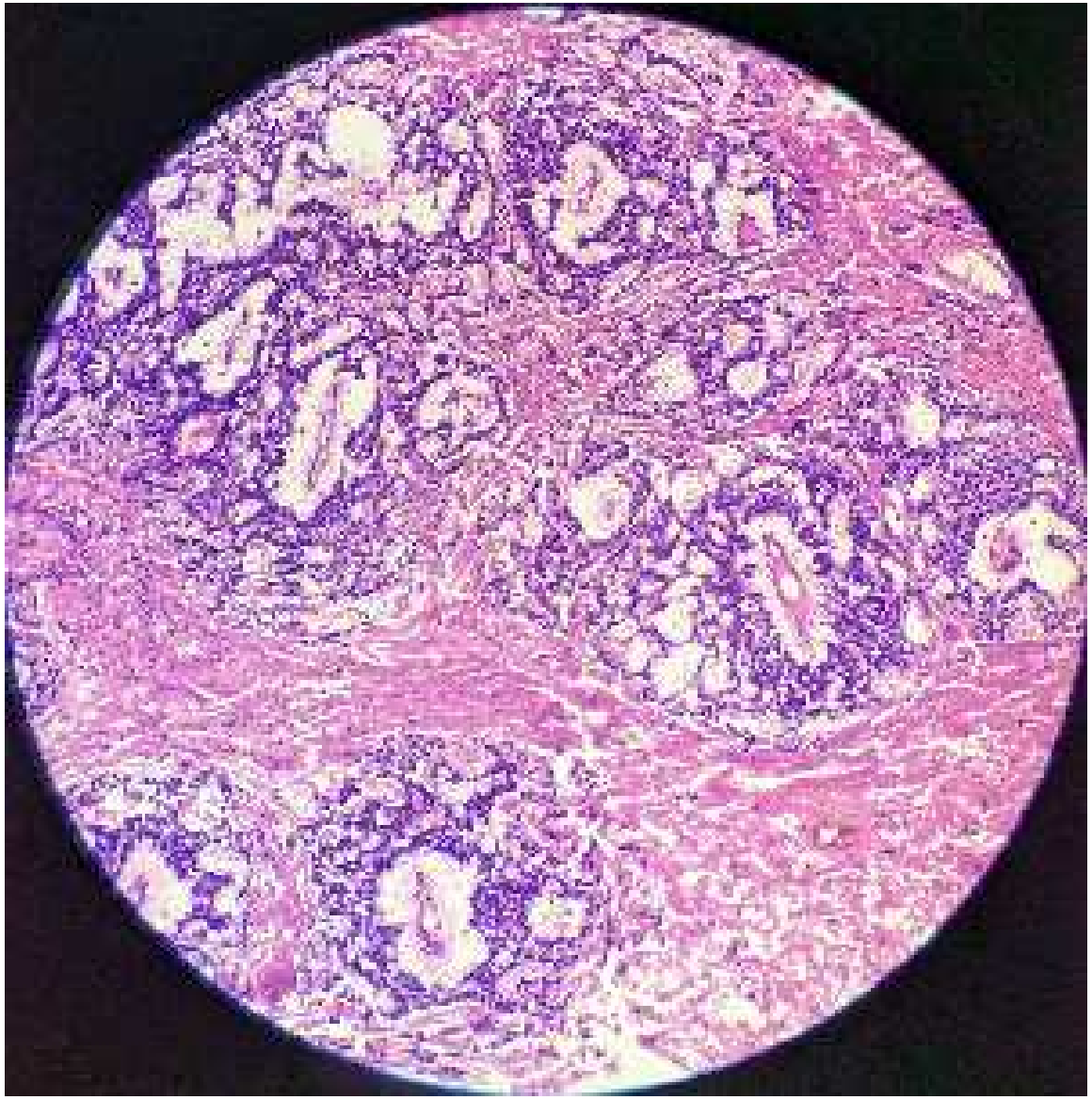
Microscopy- yst Component

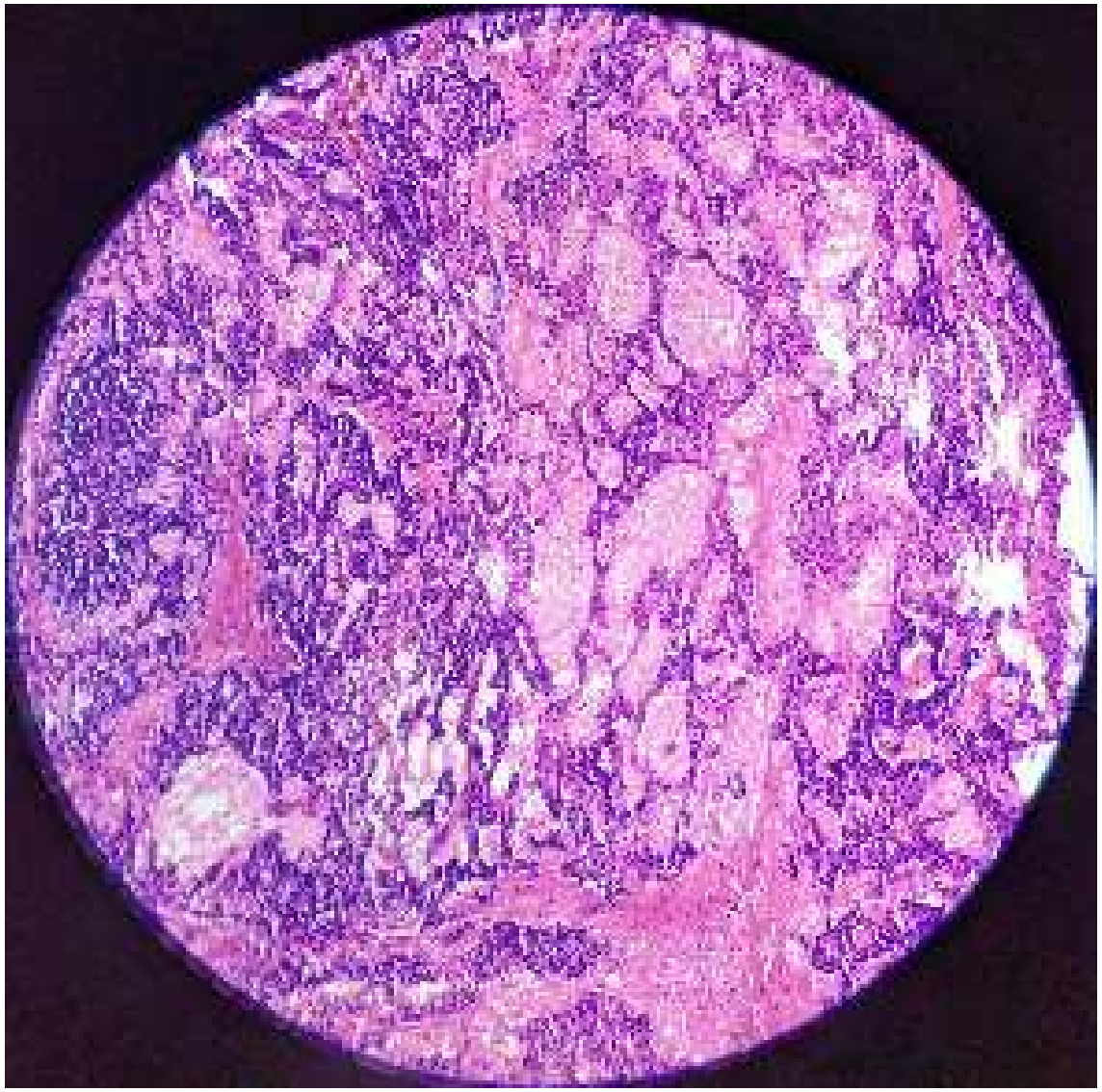
- It is composed of lace like, reticular network of medium sized cuboidal, flattened or spindle cells, which generally show less cytological atypia than Embryonal carcinoma.
- Papillary structures, solid cords of cells and other patterns can be seen.
- A distinctive feature is the presence of structures resembling primitive glomeruli, the so-called **Schiller-Duval bodies** (papillary structures within cystic spaces, lined by cuboidal to columnar cells with a distinct central vessel)

. These tumors often have eosinophilic hyaline globules containing α1-anti-trypsin & AFP, which can be demonstrated by immunohistochemical techniques.









- **Positive stains**
- **Alpha fetoprotein, Glypican 3 , SALL4 , Pancytokeratin, CK7**
- **Negative stains**
- **OCT ¾, CD30, CD117, PLAP, podoplanin, Inhibin, p63, GATA3**

diagnosis

- Non Seminomatous mixed germ cell tumor of testis- with components of Yolk sac tumor and Embryonal carcinoma, showing areas of necrosis and hemorrhage
- The tumor is confined within the tunica
- Vascular emboli are seen
- The Epididymis and margins of resection are free

discussion

Pathogenesis:-

- GCTs predominantly affect Caucasian males in between 15-45 yrs age.
- Various Environmental and genetic factors are implied. e.g., cryptorchidism, dysgenetic gonads increase the risk
- GCTs are believed to arise through abnormal differentiation beginning in fetal life. Undergoes malignant transformation during puberty due to hormonal influence. The Precursor lesion is called **Germ Cell Neoplasia In SItu (GCNIS).**
- Family history is important, relative risk of GCTs is 4x higher in father and sons of affected patient and 8- to 10-fold increased risk in brothers.
- The development of cancer in one testis also is associated with a markedly increased risk for neoplasia in the contralateral testis. Extra copies of the short arm of chromosome 12, usually due to the presence of an isochromosome 12 [i(12p)], are found in virtually all GCTs.
- Several other genetic mutations in gene encoding for ligand for Tyrosine kinase, KIT and BAK have been reported.

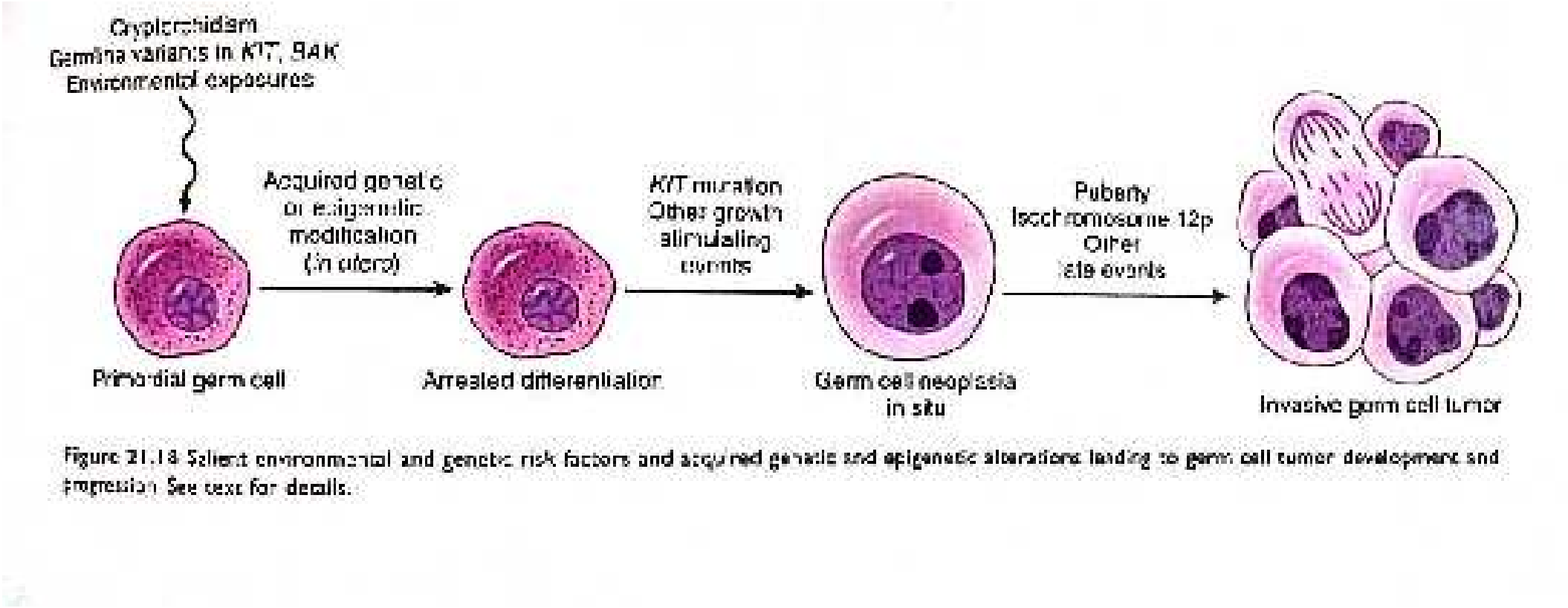


Figure 21.18 Salient environmental and genetic risk factors and acquired genetic and epigenetic alterations leading to germ cell tumor development and progression. See text for details.

GCTs are believed to arise through abnormal differentiation beginning in fetal life. Undergoes malignant transformation during puberty due to hormonal influence. Precursor lesion is **germ cell neoplasia in situ (GCNIS)**.

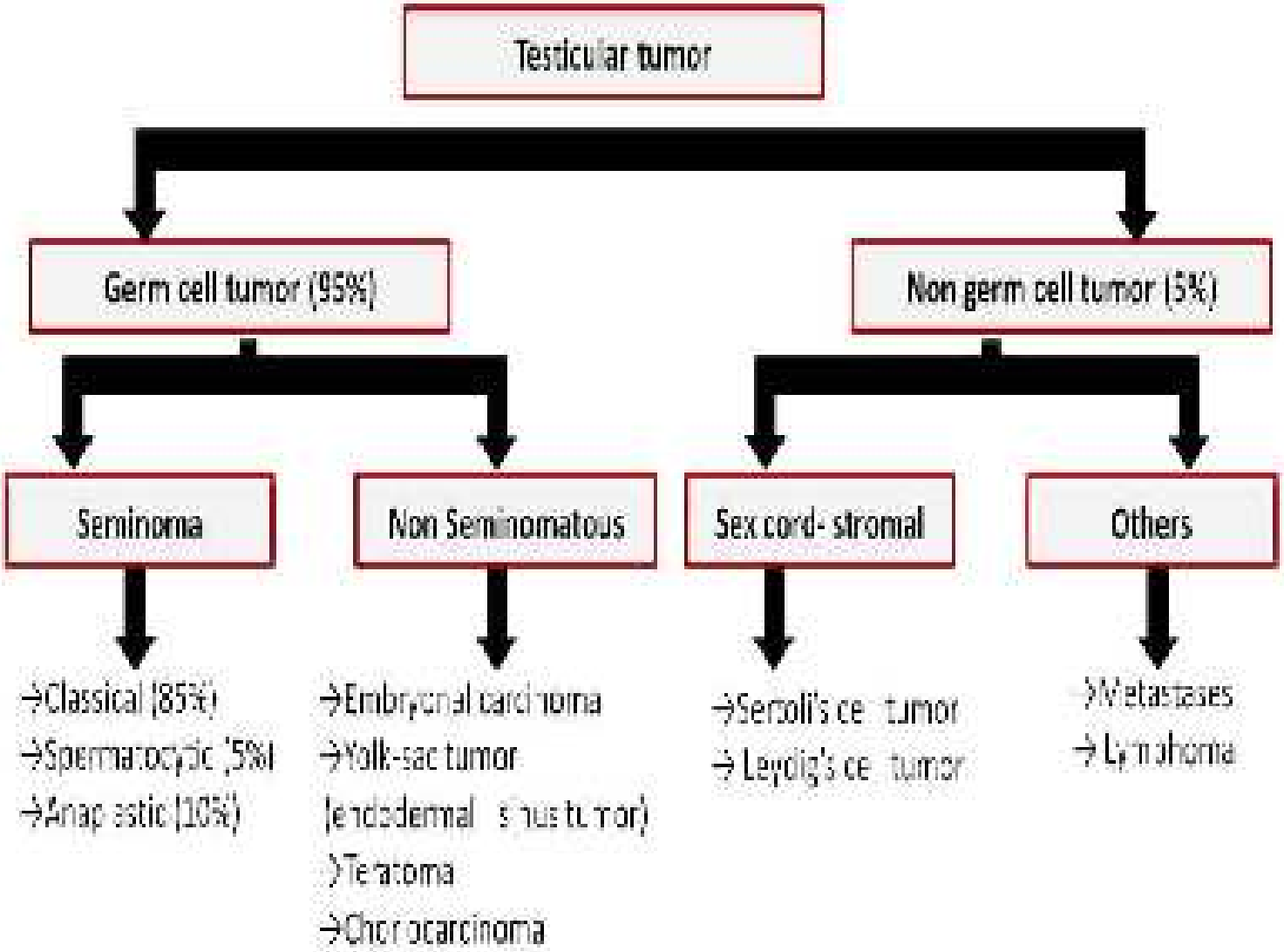
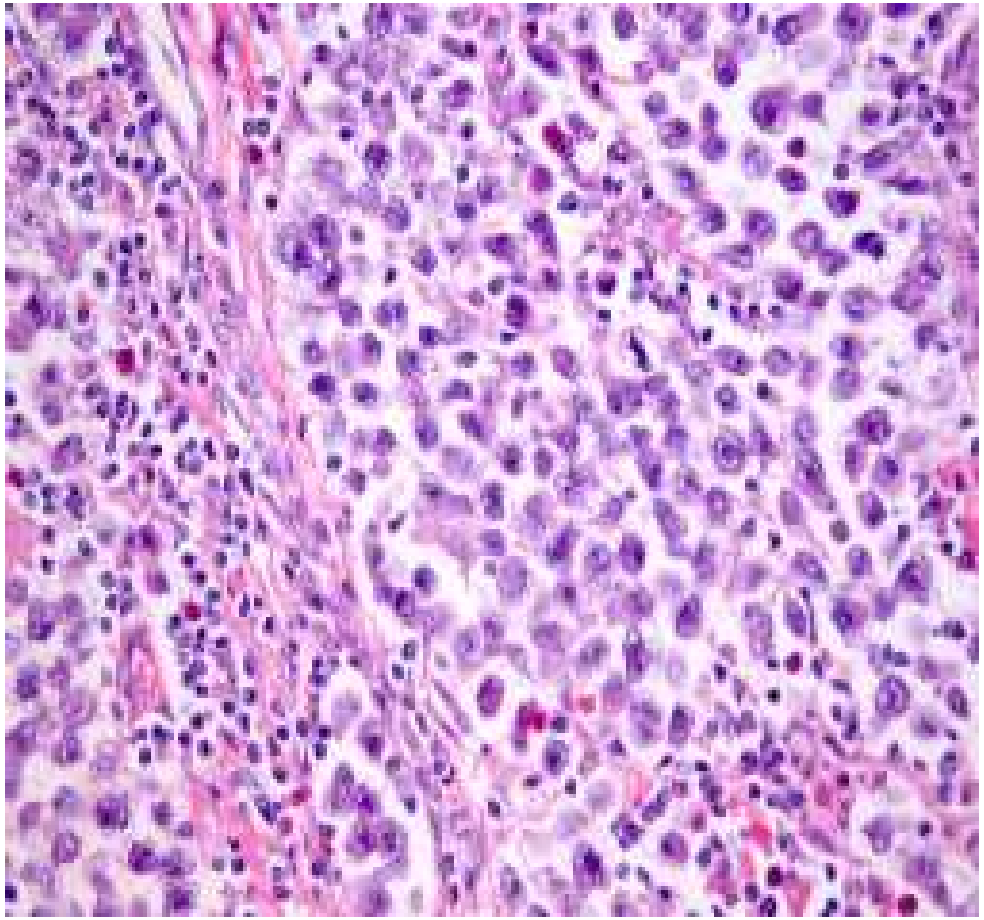


Table 21.7 Pathologic Classification of Common Testicular Tumors

Germ Cell Tumors Derived From Germ Cell Neoplasia in Situ
Noninvasive germ cell neoplasia
Germ cell neoplasia in situ
Tumors of a single histologic type (pure forms)
Seminoma
Nonseminomatous germ cell tumors
Embryonal carcinoma
Yolk sac tumor, postpubertal type
Choriocarcinoma
Teratoma, postpubertal type
Teratoma with somatic-type malignancy
Nonseminomatous germ cell tumors of more than one histologic type
Mixed germ cell tumor
Germ Cell Tumors Unrelated to Germ Cell Neoplasia in Situ
Spermatocytic tumor
Teratoma, prepubertal type
Yolk sac tumor, prepubertal type
Mixed teratoma and yolk sac tumor, prepubertal type
Sex Cord–Stromal Tumors
Pure tumors
Leydig cell tumor
Sertoli cell tumor
Other
Tumor Containing Both Germ Cell and Sex Cord–Stromal Elements
Gonadoblastoma

From World Health Organization (WHO): Histologic Classification of Testis Tumors. Geneva, 1977, WHO.

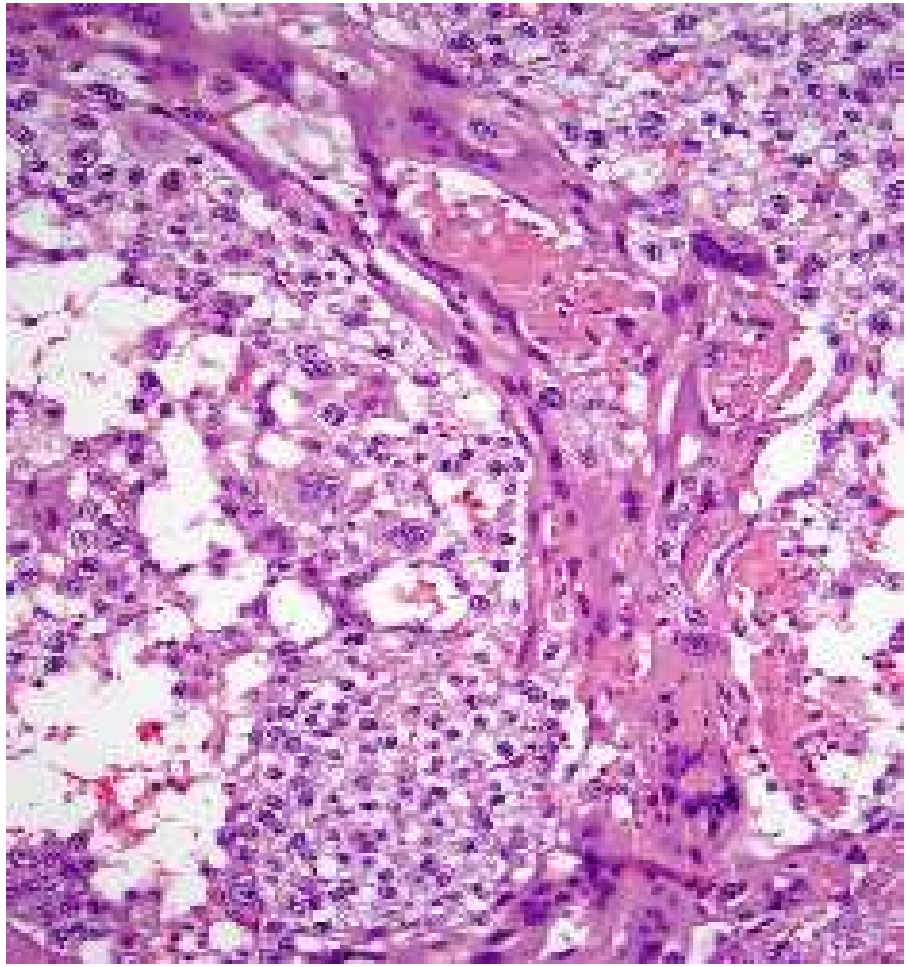
- Except for Seminoma, it is much more common to see combination of non-seminomatous component of germ cell tumor, than the pure ones.
- 69% to 91% of non-seminomatous tumors are of mixed type.
- The components of Germ cell tumor of Testis are as follows.



seminoma

Compact nests of large tumor cells are separated by fibrous septa heavily infiltrated by lymphocytes.

Seminoma, characterized by uniform cells with clear cytoplasm, sharp cell membranes, and centrally located nuclei, some with flattened edges.



choriocarcinoma

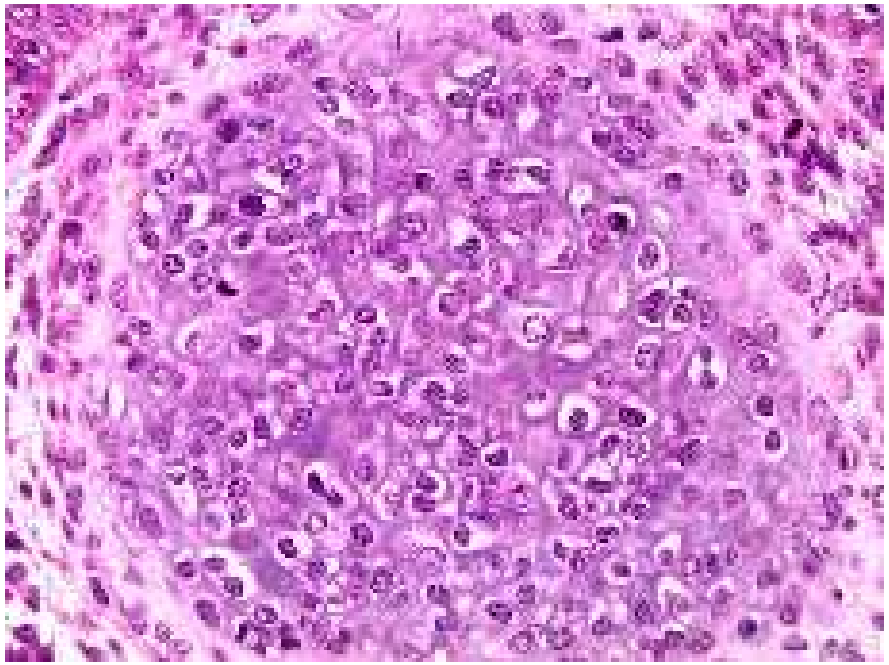
Solid nests and sheets of syncytial cells (syncytiotrophoblasts) and mononucleated trophoblasts (cytotrophoblasts and intermediate trophoblasts)

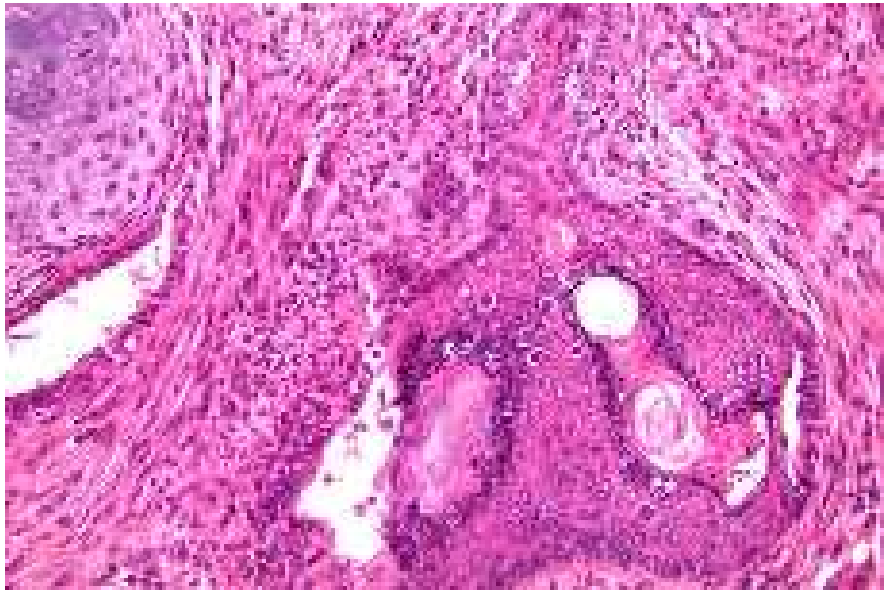
Syncytiotrophoblasts: are Large cells Abundant, dense, eosinophilic cytoplasm Indistinct cell border, Multinucleated, pleomorphic, hyperchromatic nuclei

Mononucleated trophoblasts (cytotrophoblasts and intermediate trophoblasts): are Medium sized cells with Pale, eosinophilic cytoplasm and distinct cell border

Hemorrhage, cyst formation and necrosis are common

Lymphovascular invasion is often present in tumors with pure or predominant choriocarcinoma





teratoma

Demonstrate varying degrees of atypia

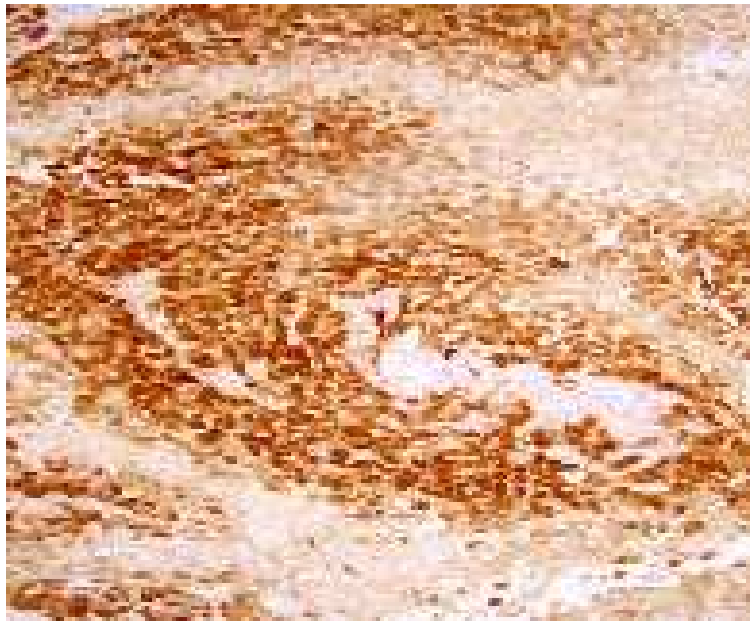
Any type of tissue may be present, such as gastrointestinal glands, respiratory epithelium, cartilage, squamous epithelium with keratinization, primitive undifferentiated spindle cells, or neuroepithelium

Sometimes one of the components of the teratoma (such as cartilage) predominates to the near exclusion of the others.

Areas of cellular monomorphic spindle cells often show circumferential swirling growth around glands, another characteristic feature of post-pubertal teratoma.

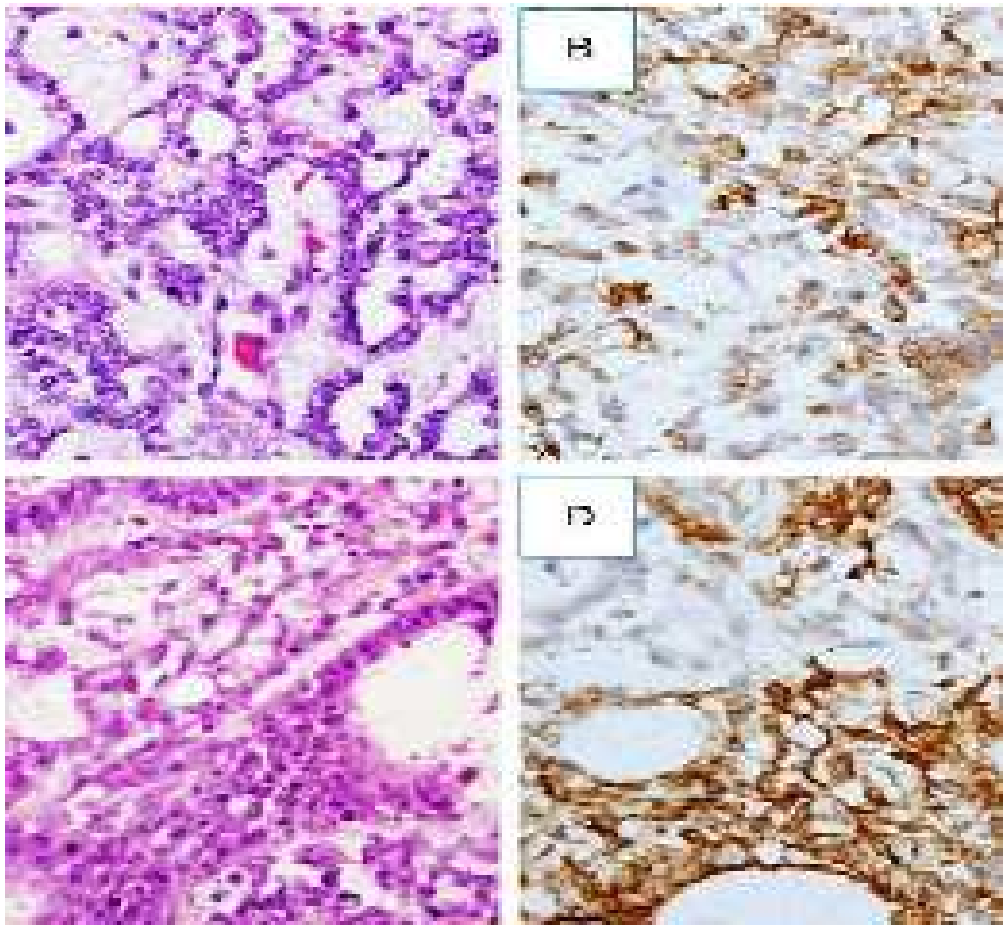
ihc

		Pankeratin	SALL4	OCT3/4	CD30	Glypican 3	CD117
Seminoma	B-hCG: raised LDH: raised AFP: normal	(-)	(+)	(+)	(-)	(-)	(+)
Embryonal carcinoma	B- hCG: normal LDH: raised AFP: raised	(+)	(+)	(+)	(+)	(-)	(-)
Yolk sac tumor	B- hCG: normal LDH: normal AFP: raised	(+)	(+)	(-)	(-)	(+)	(-)
Chorio-carcinoma	B- hCG: raised LDH: normal AFP: normal	(+)	(-)	(-)	(-)	(-)	(-)
Teratoma	B- hCG: normal LDH: normal AFP: normal	(+) in epithelial elements	(-) in mature components	(-) in mature components	(-)	(-)	(-)



Embryonal ca (+) for oct3/4

EMBRYONAL CA (+) for CD 30



Yst (+) for glypican 3

RENAL ANGIOMYOLIPOMA

Dr.Guru

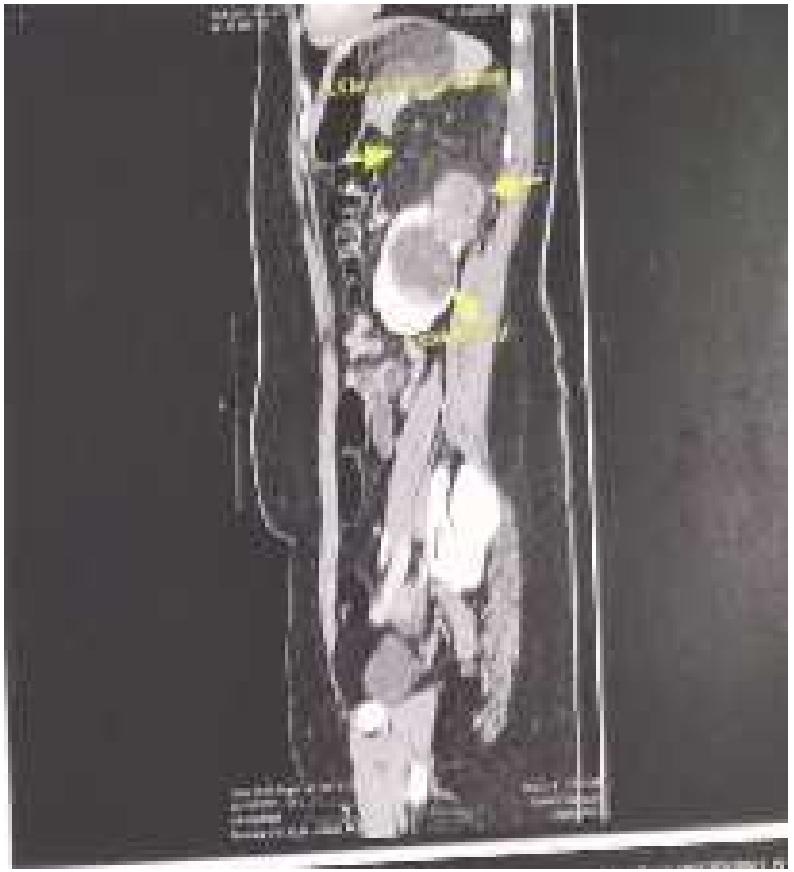
Rebecca barretto

- 19yr, female
- No comorbidties
- Presented with pianless hematuria with passing of occasional clots since 2 months
- No h/o renal calculi disease
- No hiotroy of weight loss

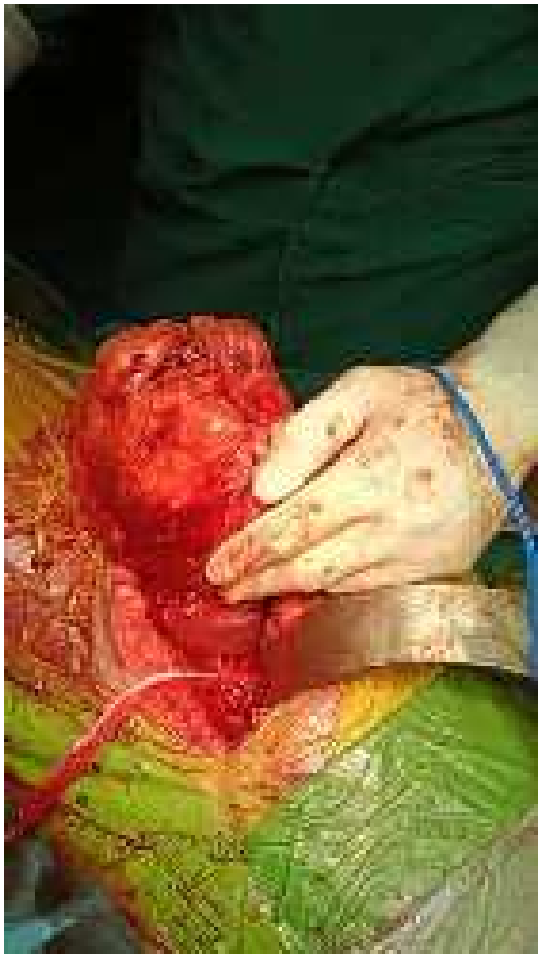
- General physical examination: normal
- Per abdomen : soft no organomegaly
- foley insitu – hematuria

investigations

- Cect abdomen: 13x 9.5x10cm arising from upper pole interpolar region of left kidney
- Complex cyst 5x5x4cm in midpole of left kidney



Operative procedure: left nephrectomy



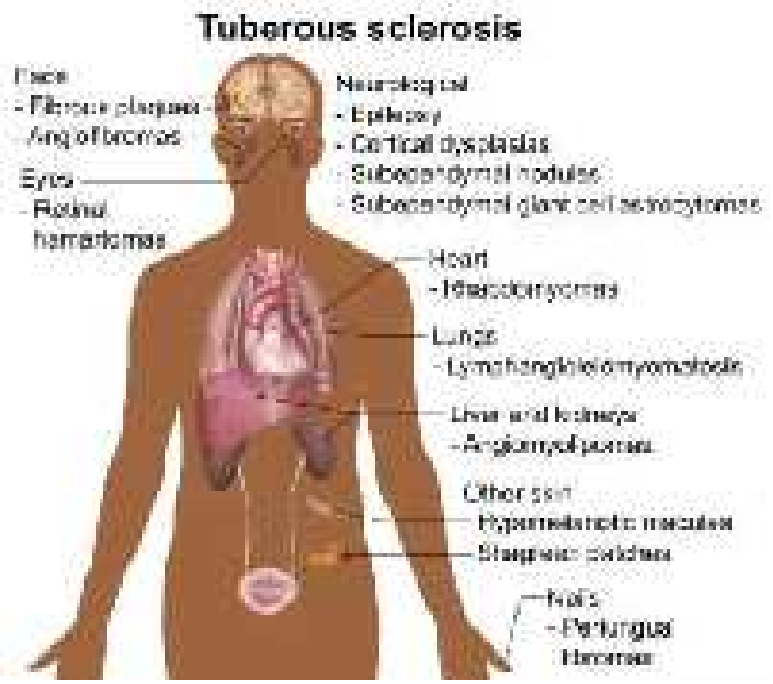
HISTOPATHOLOGY REPORT

Introduction

- Angiomyolipoma is benign entity consist of dysmorphic blood vessels, smooth muscle & adipose tissue.
- Prevalence is 0.13% in general population.
- Perivascular epithelioid cells.
- Sporadic AML more common female peak in 4-5 decade.
- Stain strongly for esotrogen receptor, progesteron & androgen explaining postpubertal female preponderance

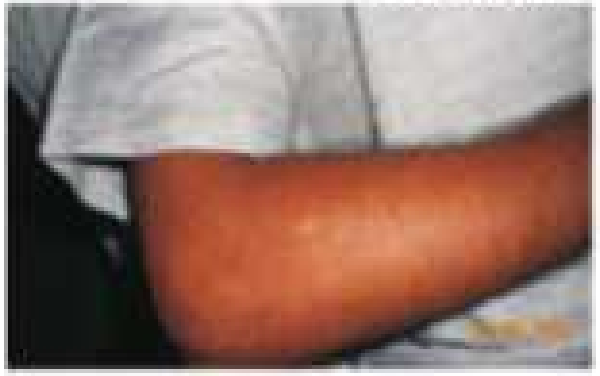
Syndromic association: Tuberous Sclerosis

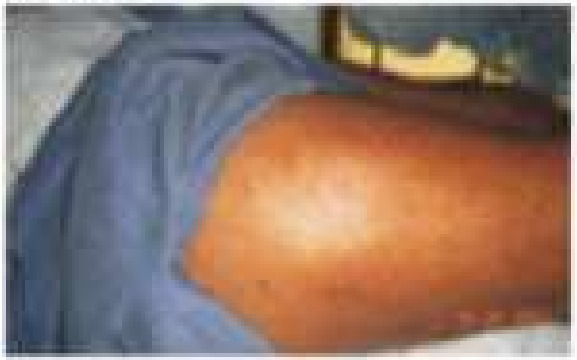
- In TSC prevalance may be as high as 55% - 90%
- With early presentation
- TSC1(hamartin) on 9q34
- TSC2(tuberin) on 16p13
- Unregulated mTOR activation



CLINICAL FEATURES

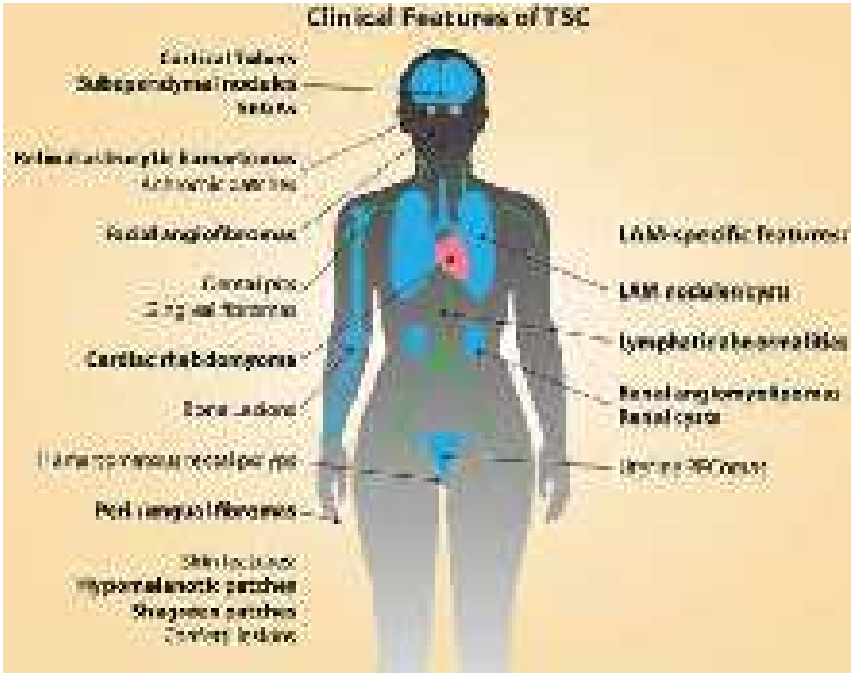
Adenoma sebaceum





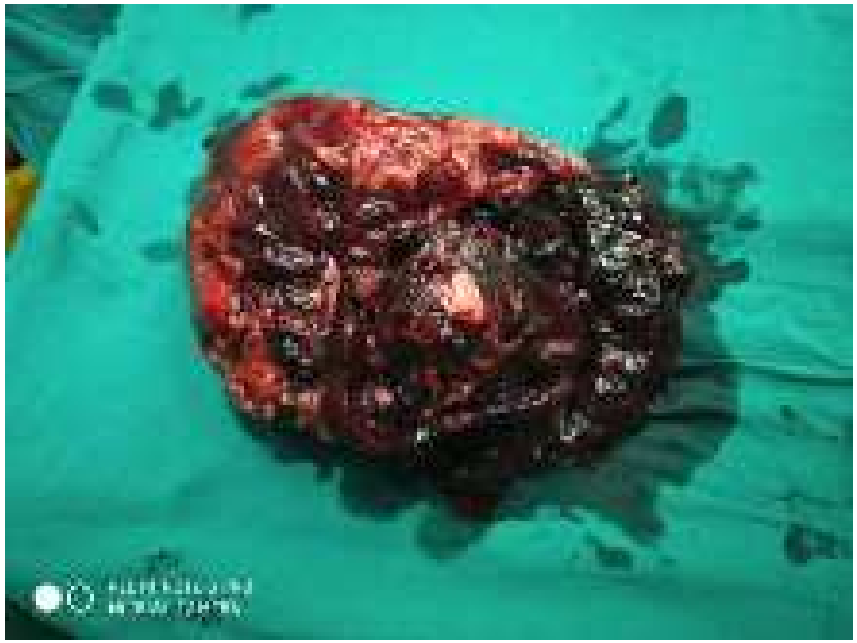
Ash leaf shaped hypopigmented macules

- Lymphinagioleomyoli pomatosis (LAM)
  - Cystic lung lesions
  - Lymphangioleiomyom as
  - Chylous pleural effusion
- Commonly with TSC & rarely in isolation



Presentation

- Diagnosed incidentally
- Upto 15% present with wunderlich syndrome – atraumatic spontaneous retroperitoneal hemorrhage.



Epithelioid AML

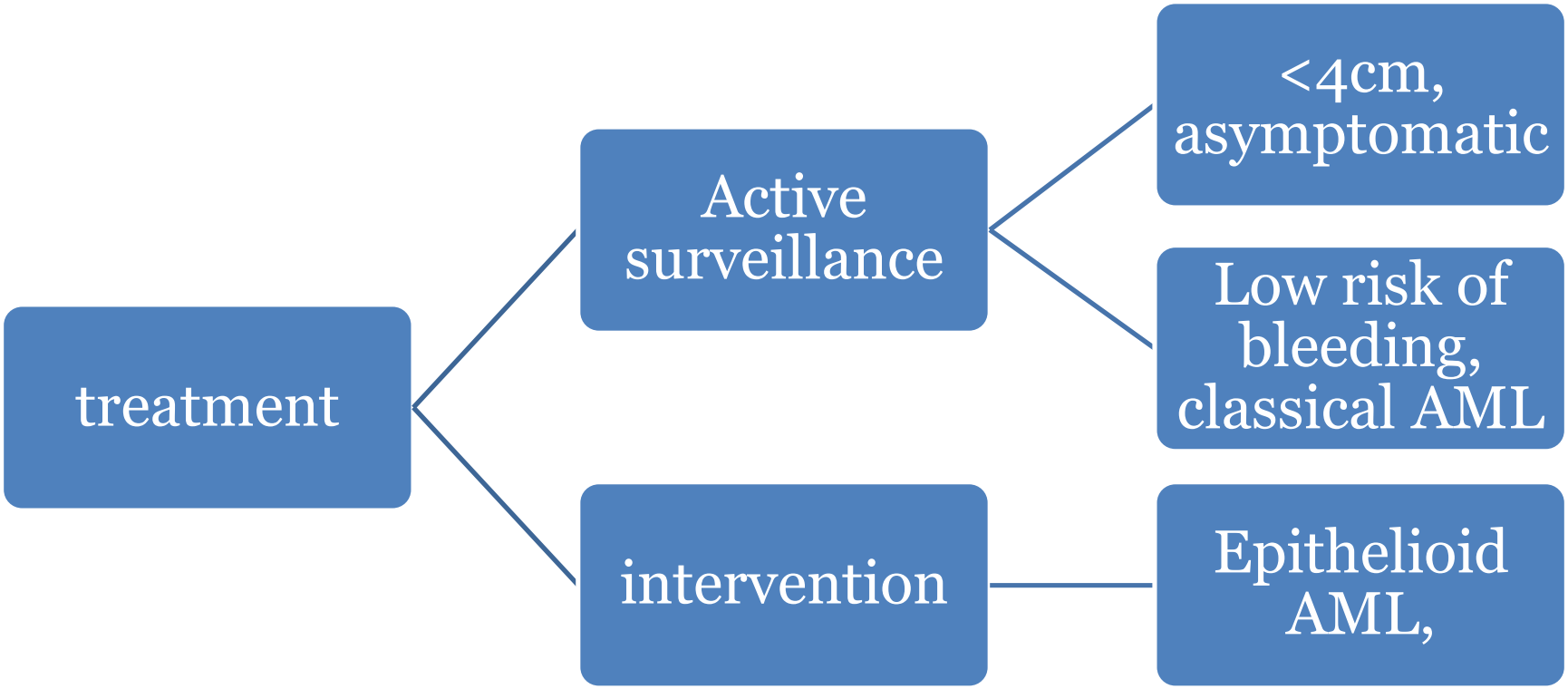
- Minimal fat content & abundance epithelioid cells.
- Atypia within epithelioid cells, presence of mitotic figures & necrosis are common & suggest more aggressive course
- Metastatic disease reported in one third of cases.

Biopsy ?

- Classical angiomyolipoma on imaging doesn’t require biopsy

- Biopsy may be useful in fat poor AML

Treatment


treatment
Active surveillance
intervention
<4cm, asymptomatic
Low risk of bleeding, classical AML
Epithelioid AML,

Risk of bleeding

- Large size of tumor
- Pregnancy
- Intralesional aneurysm larger than 5mm in diameter

Intervention options

- Surgery: nephron sparing approach.
- radiofrequency & cyroablation more research required
- Selective arterial embolization – acute hemorrhage in AML
- mTOR inhibitors: everolimus is fda approved for AML in TSC, it has respose rate of 42%(atleast 50% reduction in volume) & 80% achieve atleast 30% reduction in size

Total nephrectomy

- AML with RCC
- AML with complex cyst
- AML with hemorrhage

Nephron sparing resection

NON SEMINOMATOUS GERM CELL TUMOUR OF TESTES

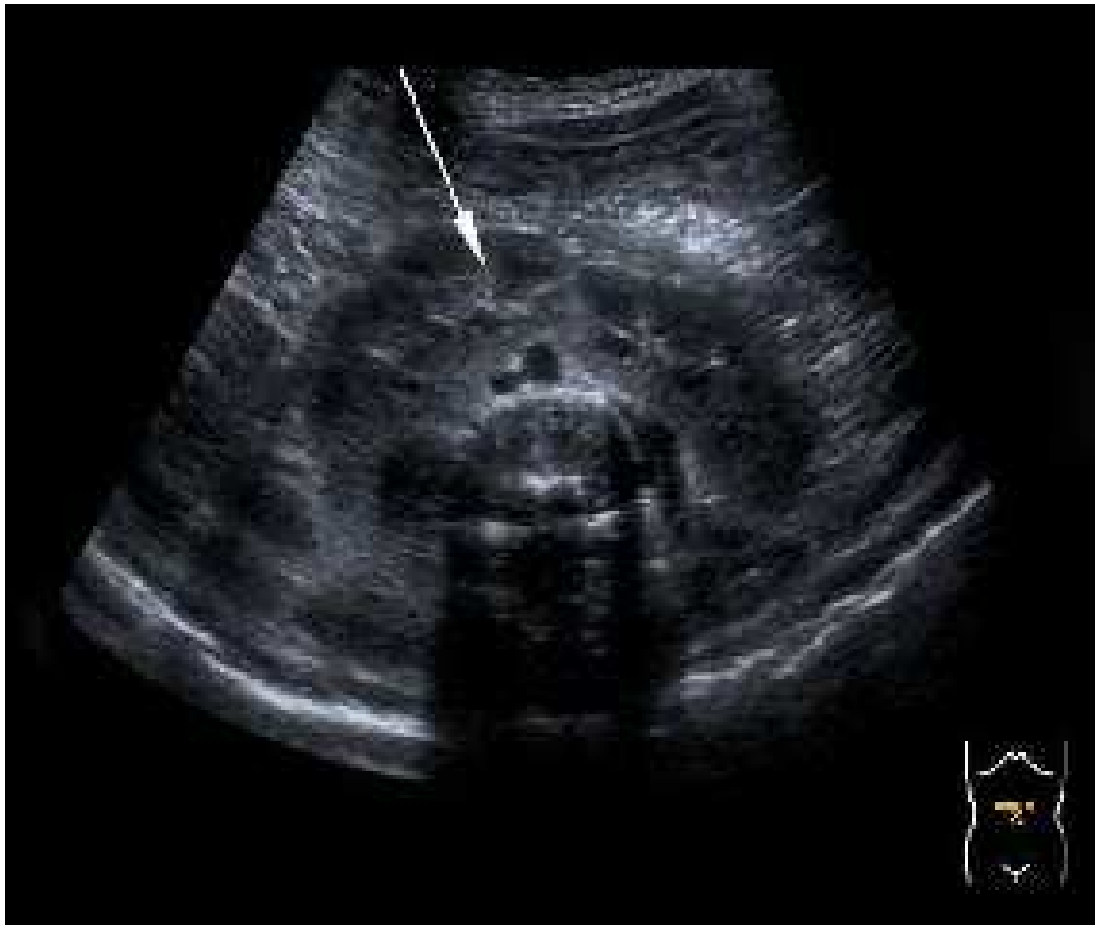
DR VEDANT KUNDE

JUNIOR RESIDENT
DEPATMENT OF
RADIODIAGNOSIS

GOA MEDICAL COLLEGE

USG ABDOMEN

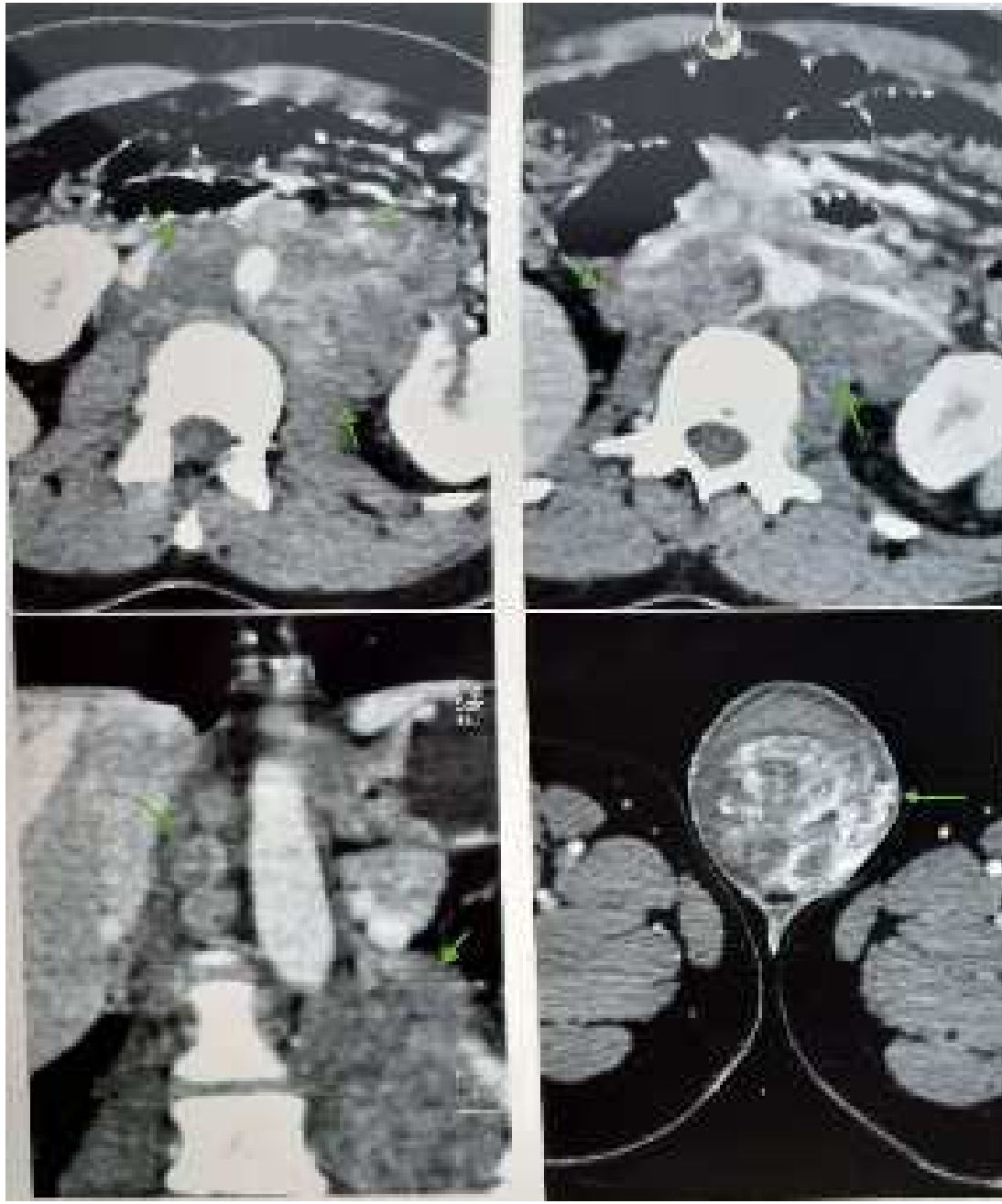
- MULTIPLE ENLARGED LYMPH NODES ARE NOTED IN THE BILTERAL PARA-AORTIC AND IN THE RETROCAVAL LOCATION.
- LOWER POLE OF BOTH THE KIDNEYS APPEAR DEVIATED MEDIALLY WITH ITS FUSION IN THE MID-LINE SUSPICIOUS FOR HORSHOE CONFIGURATION OF THE KIDNEY.
- REST OF THE ABDOMINAL STRUCTURES REVEALED NO SIGNIFICANT ABNORMALITY ON USG



CECT ABDOMEN AND PELVIS

- WELL-MARGINATED
- HETEROGENOUSLY ENHANCING MASS
- ARISING FROM LEFT TESTES MEASURING (~ 7 X 6.2 CM) BOTH HYPO AS WELL AS HYPERENHANCING AREAS WITHIN THE MASS.
- MODERATE HYDROCOELE.
- SCROTAL WALL SHOWS DIFFUSE ENHANCEMENT.
- SPERMATIC CORD APPEARED THICKNED WITH NODULAR ENHANCEMENT.

- RIGHT TESTES -NORMAL.
- MULTIPLE ENLARGED HOMOGENOUSLY ENHANCING ENLARGED LYMPH NODES ARE NOTED
- HORSE SHOE CONFIGURATION OF KIDNEY CONFIRMED.



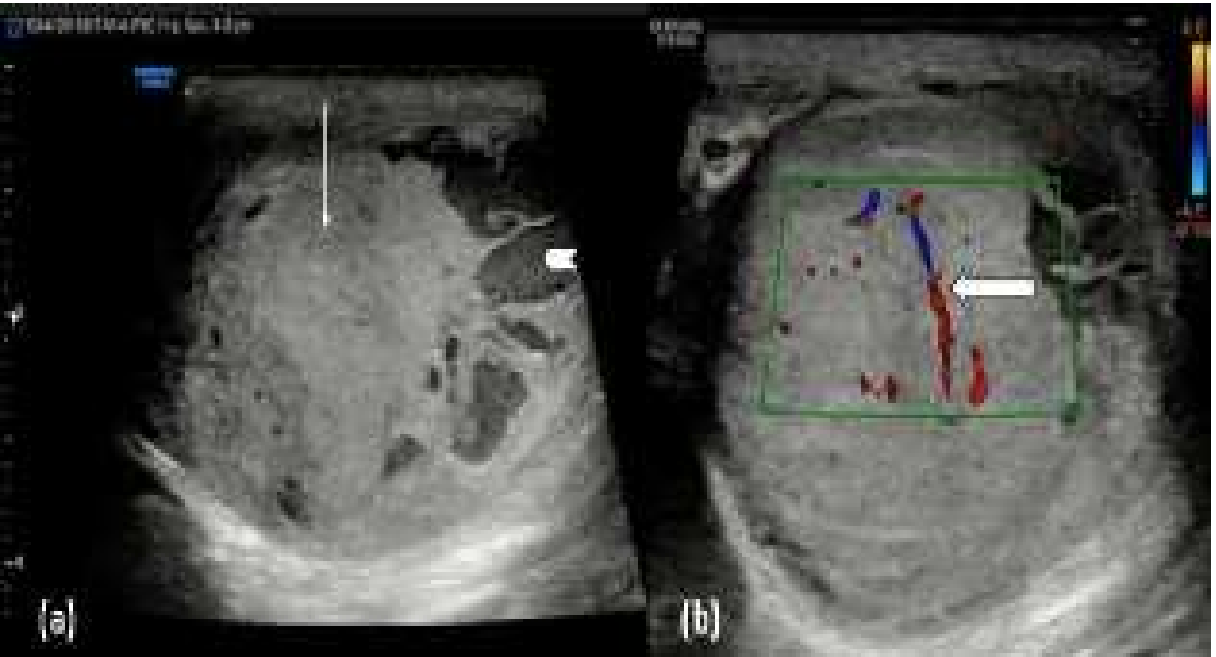
DIAGNOSIS

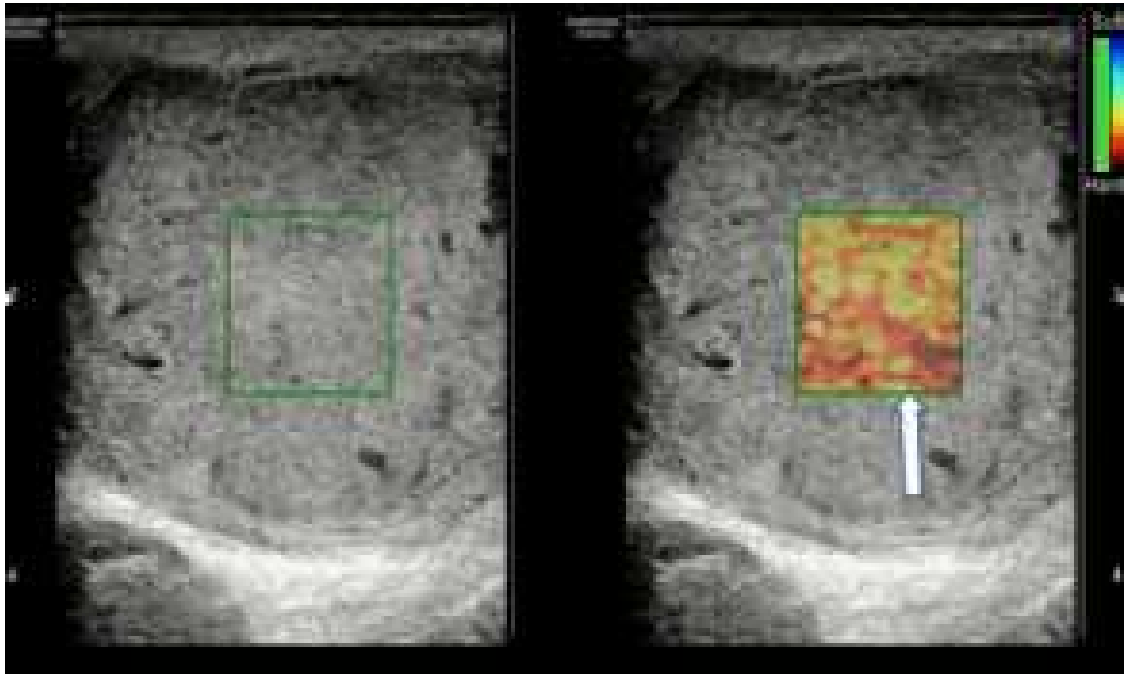
- LEFT TESTICULAR NON –LIKELY NON SEMINOMATOUS GERM CELL TUMOUR
- RETROPERITONEAL LYMPHADENOPATHY.

DISCUSSION

- All the types of non seminomatous germ cell tumours have similar imaging characteristics on CT/ MRI as well as ultrasound.

- On Ultrasound:
- well-defined
- heterogeneous lesion
- solid and cystic components.
- On color Doppler, the lesion showed increased vascularity.



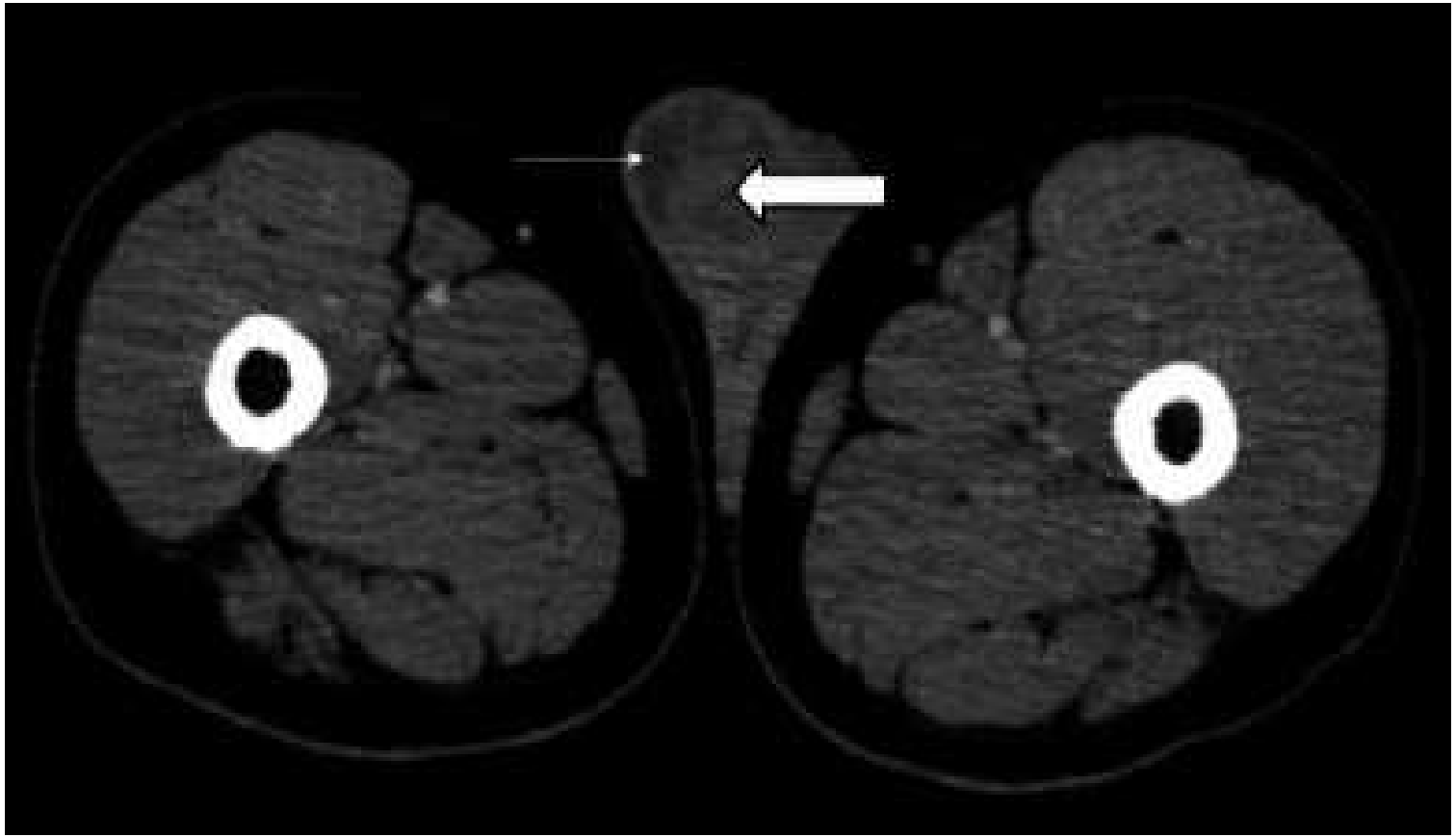


Contrast-enhanced:

Computed tomography

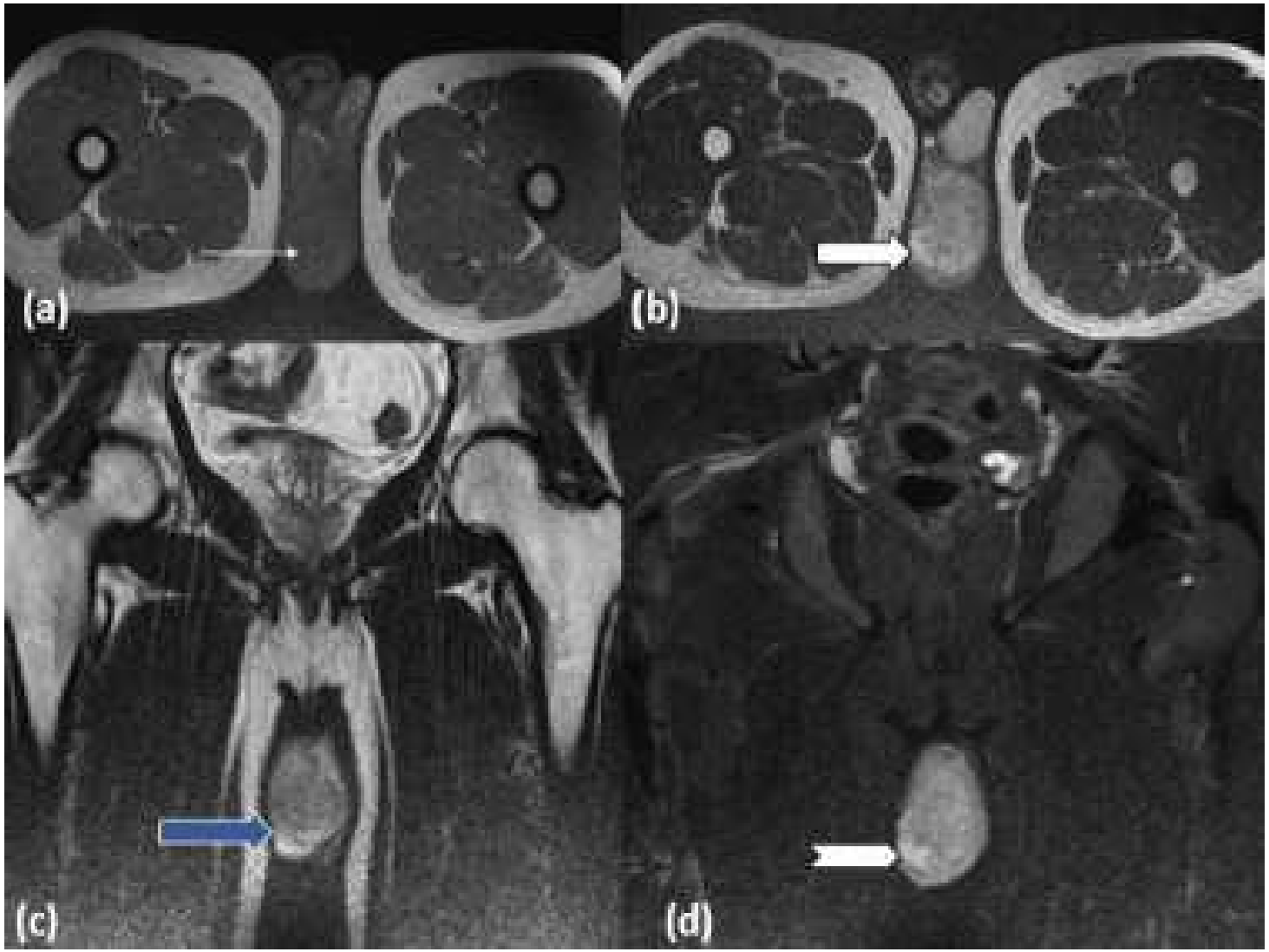
Well-defined heterogeneous density lesion

both solid and cystic components.



MRI

- Well-defined heterogeneous
- iso to hypointense lesion on T1-weighted imaging
- T2-weighted hyperintense lesion
- T2-weighted imaging-showed multiple cystic spaces suggestive of necrotic space



CPCR

May 02, 2024

Dr Ekansh Gupta

SR Urology

Dept. of Urology, Goa Medical College

CHIEF COMPAINTS

- Presented to Dept. of Urology, GMC on 15/March/2024 with complaints of
  - **Left scrotal swelling x 2 months**
  - **Left lumbar region pain** *(dull aching mild)* **x 6 months**

HISTORY OF PRESENTING ILLNESS

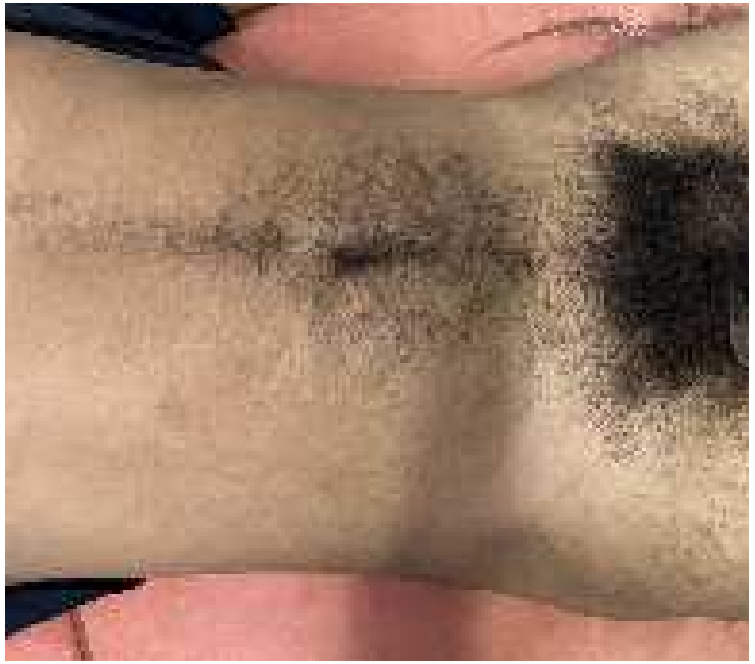
- 18-year-old gentleman presented with Left scrotal swelling x 2 months
    - Insidious onset
    - Attributed by patient to injury to left hemi-scrotum(?cause of trauma)
    - Gradually progressive in size: From 4x3 cm to 15 x 7 cm over 4 months
    - A/w nausea and occasional (2 / week) episodes of non-bilious emesis
- A/w left lumbar region pain x 2 weeks
        - Insidious onset, non radiating in nature
        - Character: Dull, aching
        - Aggravating / relieving factors: None
- A/w significant weight loss (~ 10 kg (~ 20%) over past 1 year)

GENERAL PHYSICAL

- Conscious, cooperative
- Oriented to time, place and person
- Normal built
- Hemodynamically stable
- No Icterus / edema/ generalized LAD

ABDOMINAL EXAMINATION

- Non-distended, abdomen with no scars or visible fullness
- Hernial orifices intact (no evidence of hernia)
- No abdominal tenderness
- No abdominal lump
- Normal percussion / auscultation findings



INGUINOSCROTAL EXAMINATION

Inspection:

- An ovoid smooth well defined swelling in left scrotum of size 15x8 cm
- Not reducible, No cough impulse.
- Skin over scrotum appears stretched with loss or rugosity, no visible veins, scars or sinuses.
- Penis- normal in position; Opposite scrotum and B/L groin normal.

INGUINOSCROTAL EXAMINATION

Palpation:

- No local rise of temperature / tenderness.
- An **ovoid , hard , swelling in left scrotum of size 15 x 8 cm with well defined margins and smooth surface.**
- Not reducible, able to get above the swelling.
- No fluctuation/ transillumination.
- Testis not separately palpable.
- Swelling not fixed to skin.
- Spermatic cord bulky
- BCR +
- Cremasteric reflex of affected side diminished
- Right Testes, Penis and Prepuce normal

Radiology

EVALUATION AND MANAGEMENT OF THE CASE

- Subsequent evaluation revealed raised serum AFP and serum LDH levels
- USG and CT findings s/o heterogenous 5.5 x 3 cm lesion in left testes
- CT s/o metastatic adenopathy involving retroperitoneal and mediastinal LN
- HPE from Radical Orchidectomy Specimen: s/o Yolk Sac Tumor
- Patient counselled and referred to Medical Oncology for initiation of chemotherapy.

Discussion

Histological classification

95%

Germ cell tumours

GCNIS-derived

- **Seminoma**
- **Nonseminoma**
  - **Embryonal carcinoma**
  - **Yolk sac tumour**, post pubertal
  - **Choriocarcinoma**
  - **Teratoma**, post pubertal
  - Teratoma with somatic type malignancies
  - **Mixed germ cell tumours**

Non GCNIS-derived

- **Spermatocytic tumour**
- Yolk sac tumour, pre pubertal
- Mixed germ cell tumour, pre pubertal

5%

Sex cord/stromal tumors

- **Leydig cell tumor**
- **Sertoli cell tumor**
- **Granulosa cell tumor**
- Thecoma/fibroma
- Gonadoblastoma (contain both germ cell & sexcord/stroma)
- Others- mixed, unclassified

Miscellaneous non-specific stromal tumours

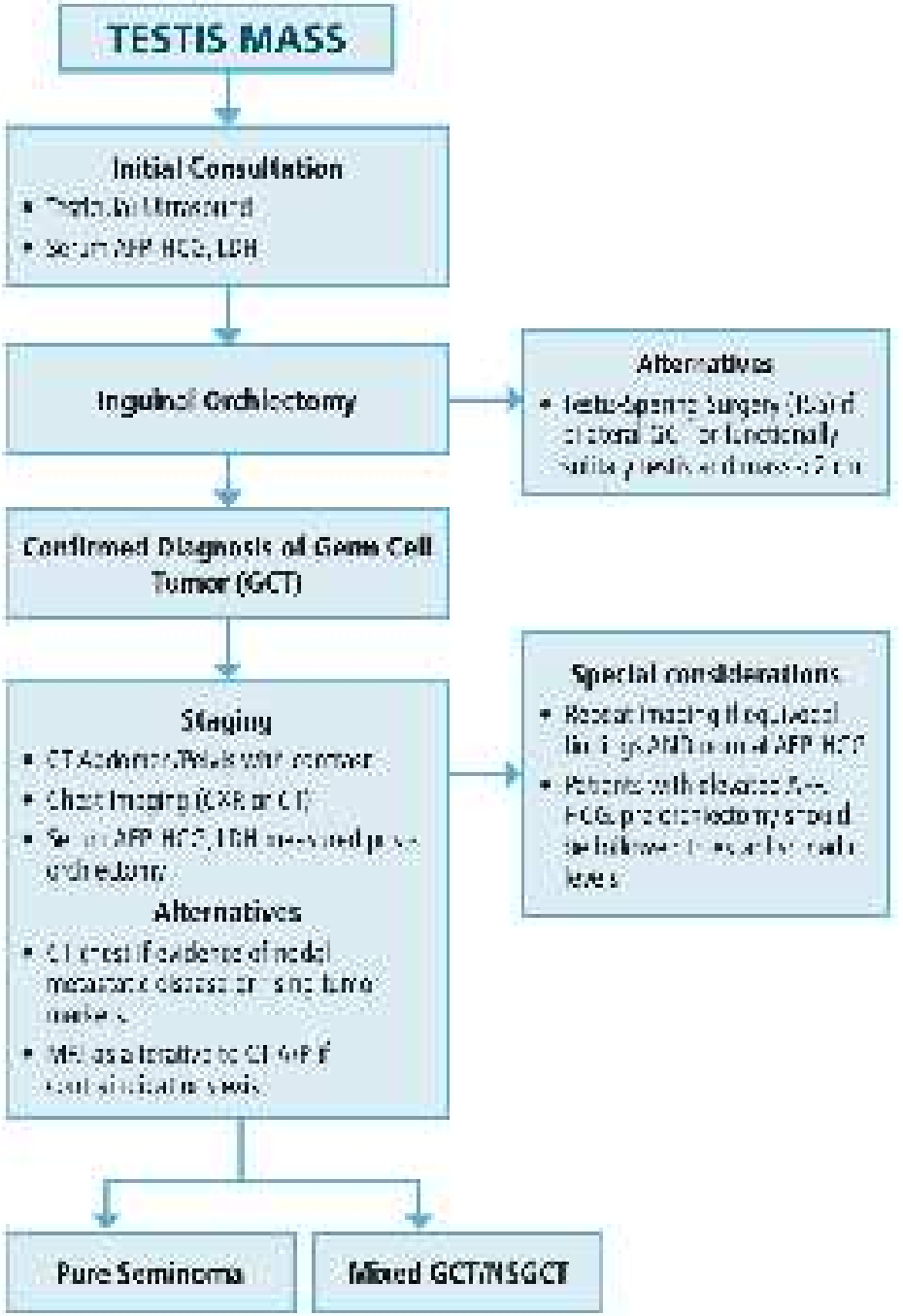
- Ovarian epithelial tumours
- Tumours of collecting ducts and rete testis
  - -Adenoma
  - -Carcinoma
- Tumour of Para testicular structure
  - -Adenomatoid tumour
  - -Mesothelioma
  - -Epididymal tumour
- Cysteadenoma of epididymis
- Papillary cystadenoma
- Adenocarcinoma of the epididymis
- Mesenchymal tumours

Contrasting seminoma & non-seminoma GCT (NSGCT)

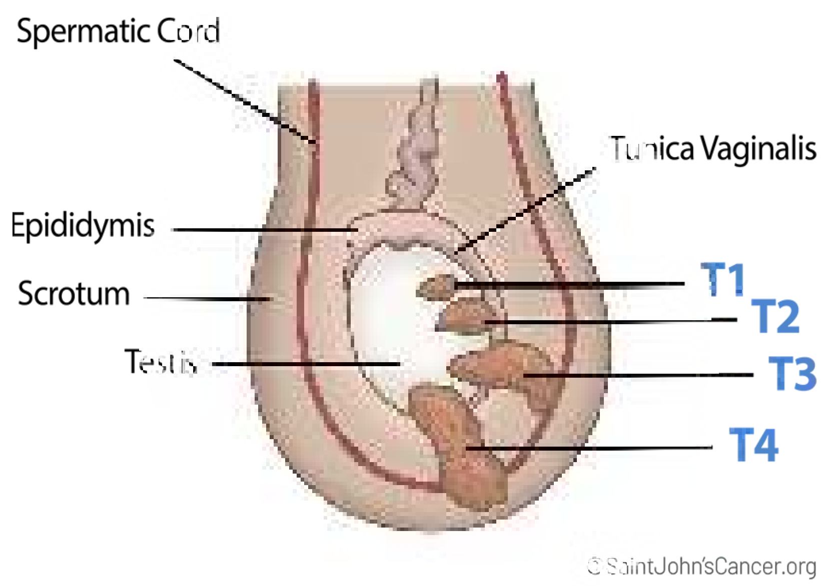
- Favourable natural history
- Less aggressive
- Predictable spread along lymphatics
- Less likely to spread hematogenously
- Lower incidence of occult metastasis
- Lower risk of relapse
- Serum markers are not too high (Pure Seminoma: Never Positive for AFP)
- Exquisitely sensitive to RT and platin-based chemo
- The risk of teratoma at metastatic site is generally not a consideration for advanced seminoma
- Seminoma may transform into NSGCT is an important consideration

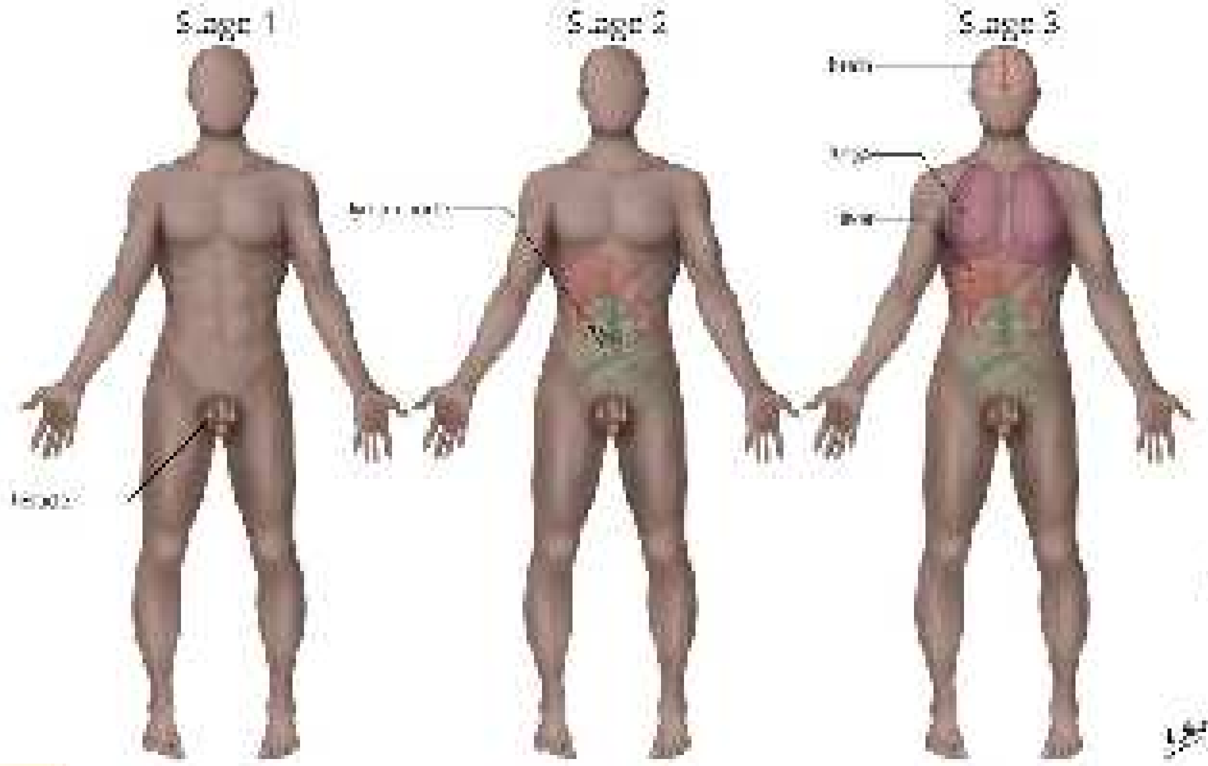
Staging Testicular Cancer

AUA 2023 Guidelines for Testicular Cancer



Staging Testicular Cancer





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EUA 2023 Guidelines for Testicular Cancer

Managing Testicular Cancer

AUA & EUA 2023 Guidelines for Testicular Cancer

Stage I disease

Stage II Seminoma

Stage II NSGCT

Stage III disease

Seminoma

Table 4 – Recommendations for the management of stage I seminoma

Recommendation	Strength rating
Fully inform the patient about all available management options, including surveillance or adjuvant therapy (i.e. orchidectomy as well as treatment-specific recurrence rates and acute and long-term side effects.	Strong
Offer surveillance as the preferred management option if resources are available and the patient is compliant.	Strong
Offer one dose of carboplatin at an AUC of 7 as adjuvant chemotherapy is considered.	Strong
Do not recommend adjuvant treatment in patients at very low risk of recurrence (no risk factors).	Strong
Do not routinely administer adjuvant radiotherapy.	Strong
Adjuvant radiotherapy should be reserved for highly selected patients not suitable for surveillance and with a contraindication for chemotherapy.	Strong

NSGCT

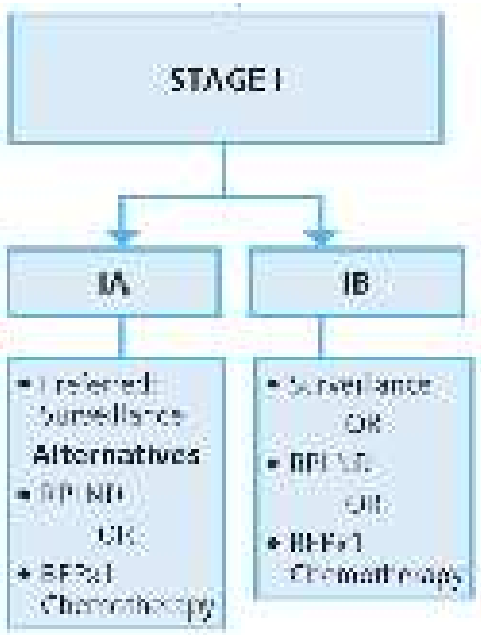


Table 5 – Recommendation for the management of stage I NSGCT

Recommendations	Strength rating
Inform patients about all management options (surveillance, adjuvant chemotherapy, and retroperitoneal lymph node dissection), as well as treatment specific recurrence rates and acute and long-term side effects	Strong
Offer surveillance or risk-adapted treatment based on lymphovascular invasion (see below).	Strong
Discuss one course of cisplatin, etoposide, bleomycin as an adjuvant treatment as alternative to stage I NSGCT if patients are not willing to undergo or comply with surveillance.	Strong

NSGCT = nonseminomatous germ cell tumour.

Managing Testicular Cancer

EUA 2023 Guidelines for Testicular Cancer

Stage I disease

Stage II Seminoma

Stage II NSGCT

Stage III disease

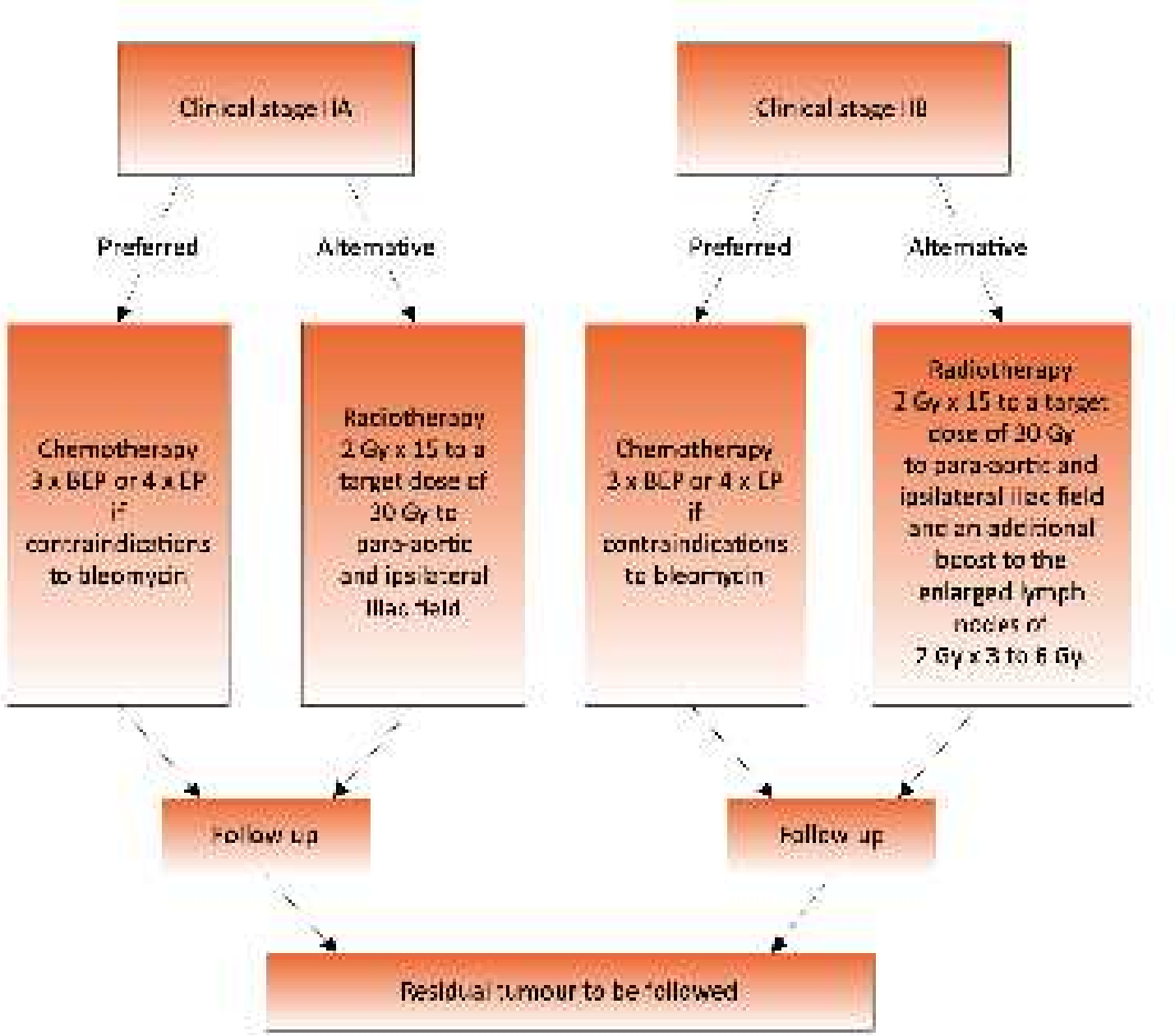


Fig. 1 – Treatment options for patients with clinical stage IIA or IIB seminoma*. BEP = cisplatin, etoposide, and bleomycin; EP = etoposide and cisplatin. *When enlarged retroperitoneal lymph nodes are <2 cm and markers are normal, treatment should not be initiated unless metastatic disease is unequivocal on the basis of biopsy, increasing nodal size/number, or subsequent marker rise.

Managing Testicular Cancer

EUA 2023 Guidelines for Testicular Cancer

Stage I disease

Stage II Seminoma

Stage II NSGCT

Stage III disease

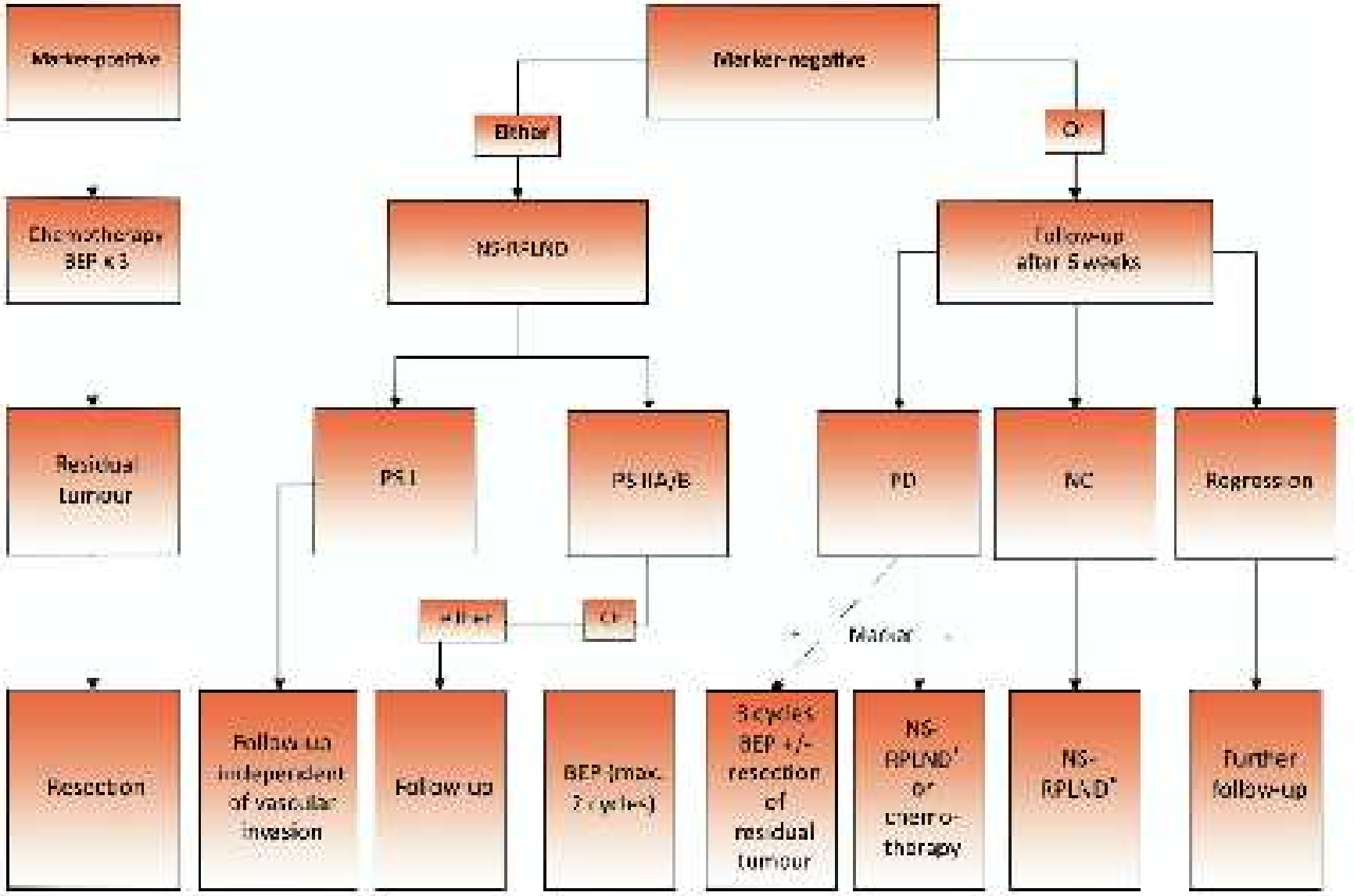


Fig. 2 – Treatment options for patients with clinical stage IIA nonseminoma. BEP = cisplatin, etoposide, and bleomycin; NS = nerve-sparing; RPLND = retroperitoneal lymph node dissection; PS = pathological stage; PD = progressive disease; NC = no change. *In cases of pathological stage IIA/B, patients can be followed after receipt of adjuvant chemotherapy (maximum of 2 cycles).

Managing Testicular Cancer

Stage I disease

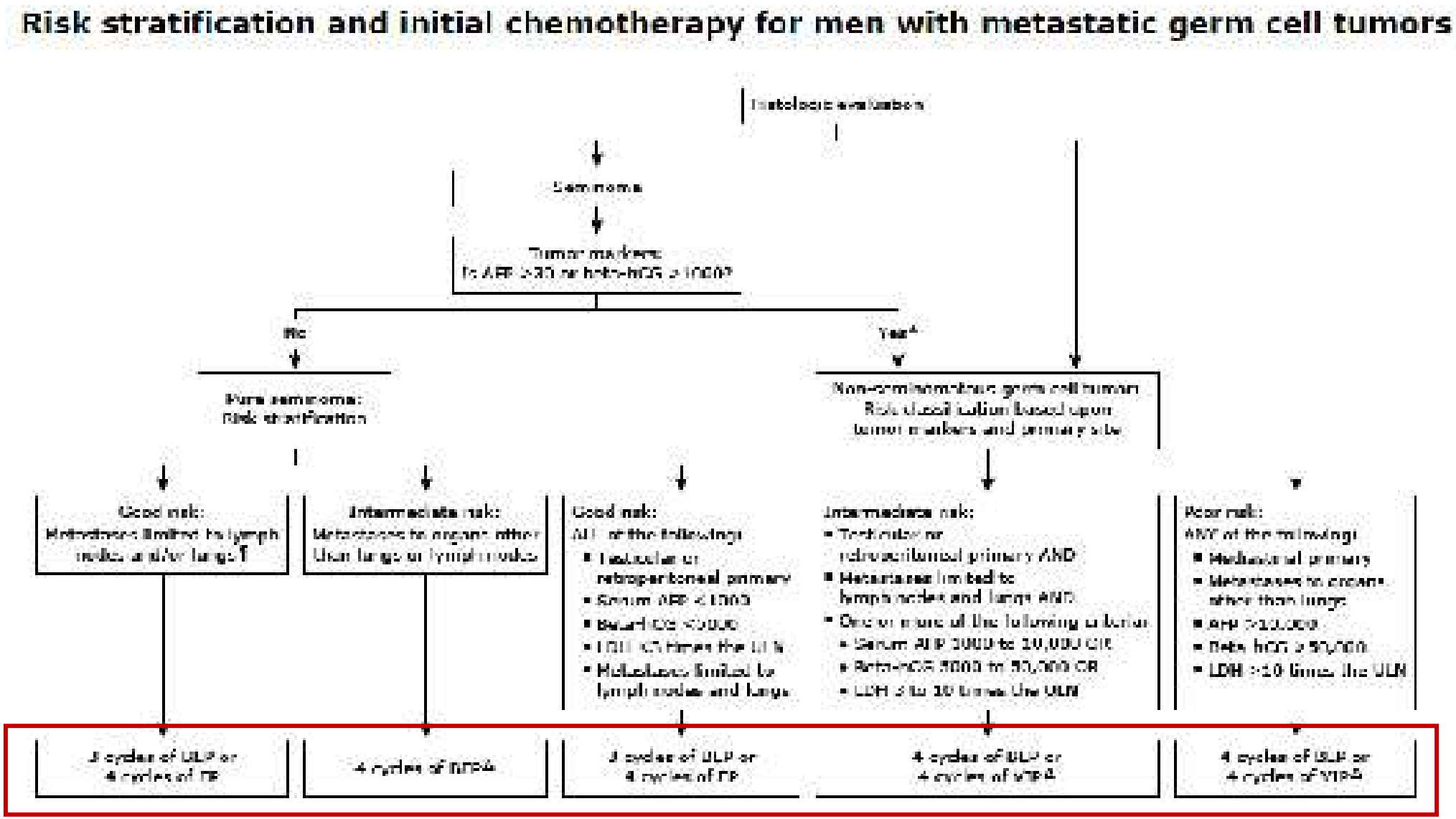
Stage II Seminoma

Stage II NSGCT

Stage III disease

Risk Stratification

Therapeutic choice



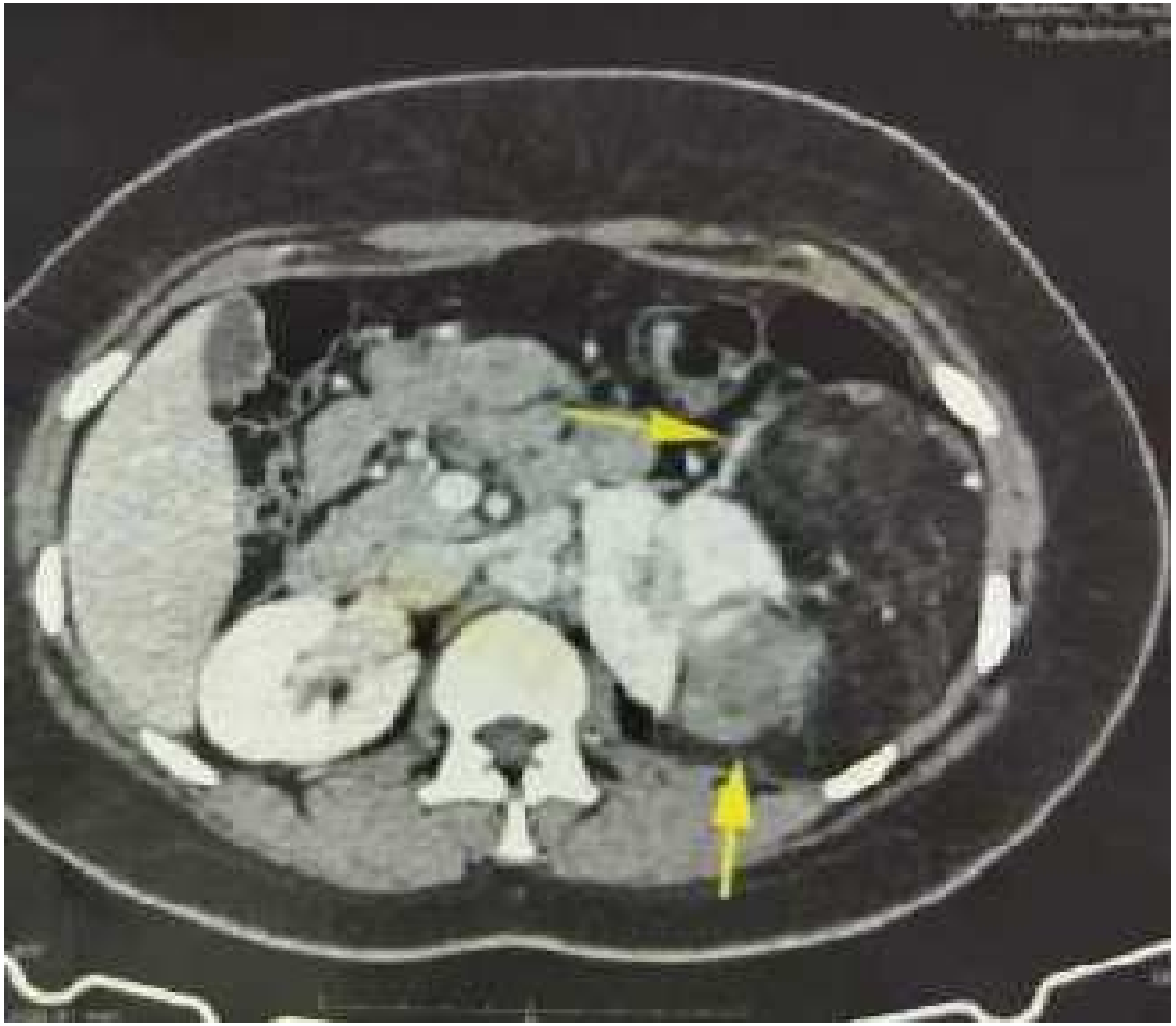
UpToDate Guidelines for Testicular Cancer

A CASE OF RENAL ANGIOMYOLIPOMA

DR VEDANT KUNDE

JUNIOR RESIDENT
DEPATMENT OF
RADIODIAGNOSIS

GOA MEDICAL
COLLEGE



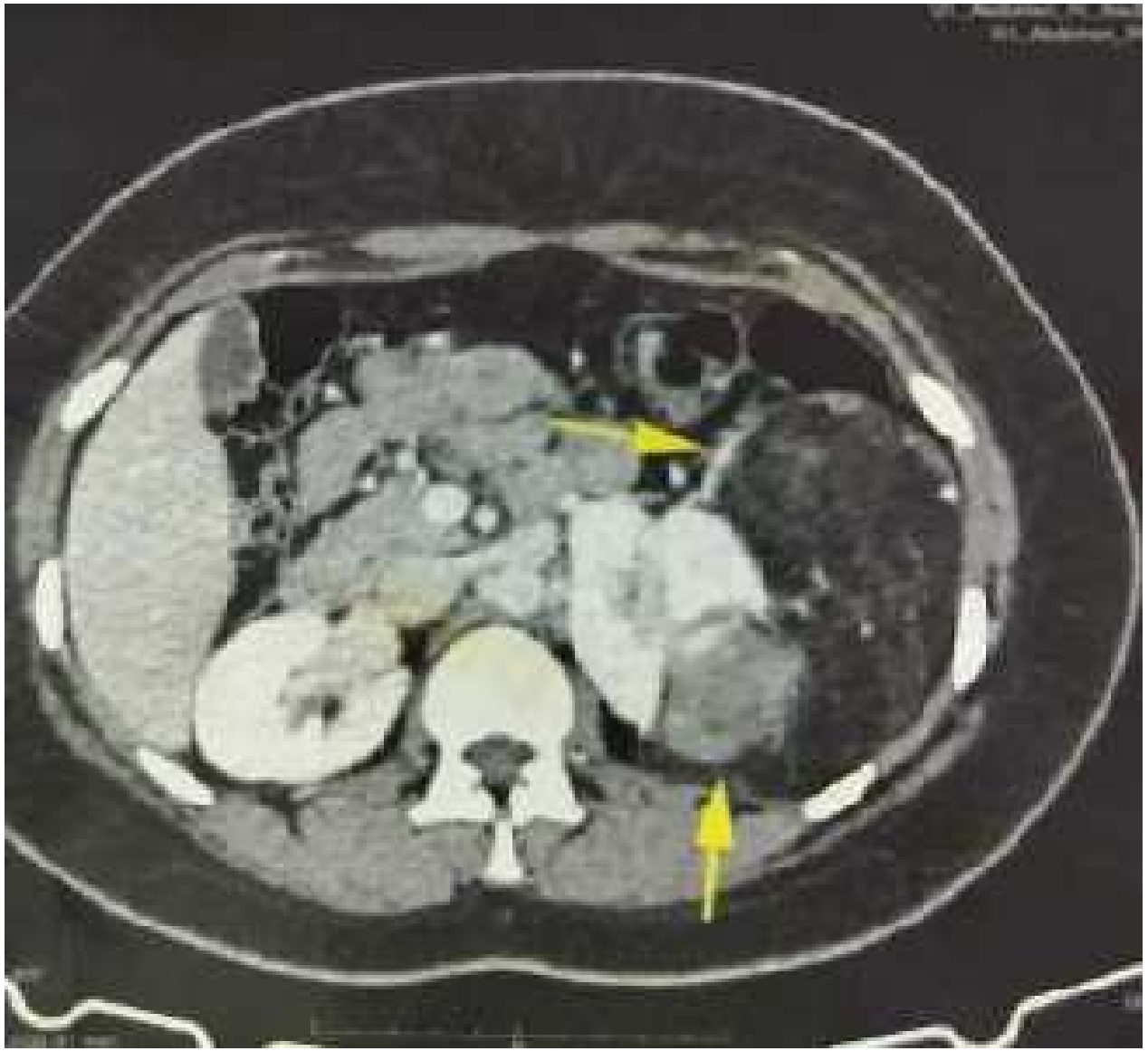
Large Well marginated
Partly exophytic
heterogeneously enhancing
mass ~ (13 x 9.5 x 10 cm)

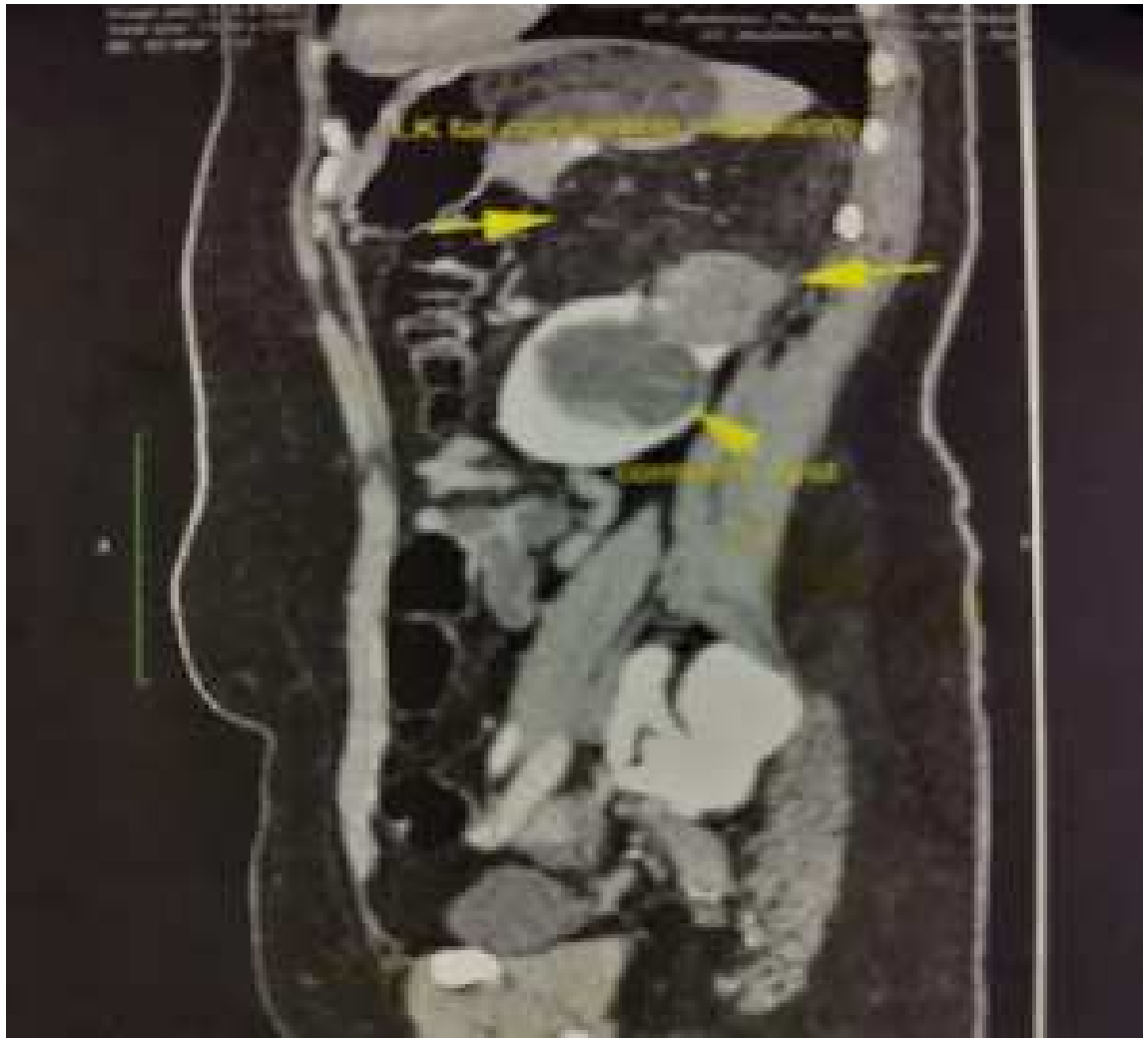
Posterior cortex of upper and mid pole of the left kidney

Two components
Larger component- fat attenuation (~ 8.9 x 7.6 x 8 cm) in size -
Smaller- soft tissue attenuation(~ 3.6 x 3.2 cm in size)
Multiple vessels are seen coursing through the mass

Relations of the mass

- Anteriorly -indenting the splenic flexure of colon
- splenic vessels are seen coursing along the anterior margin of the mass.





Superiorly -indenting the spleen and the left hemidiaphragm

Inferiorly -displace the left kidney infero-medially.

Posteriorly extend into the posterior para-renal space and in close proximity with posterior abdominal wall displacing the left adrenal gland.

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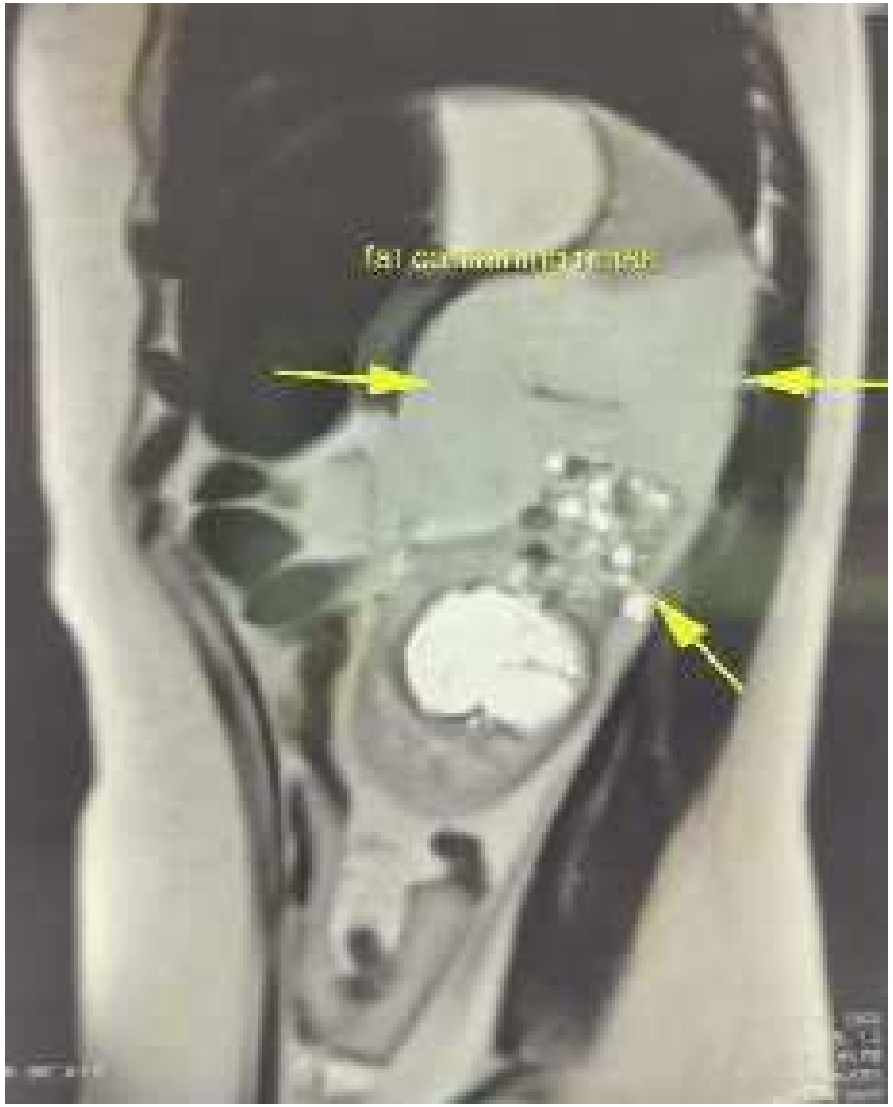
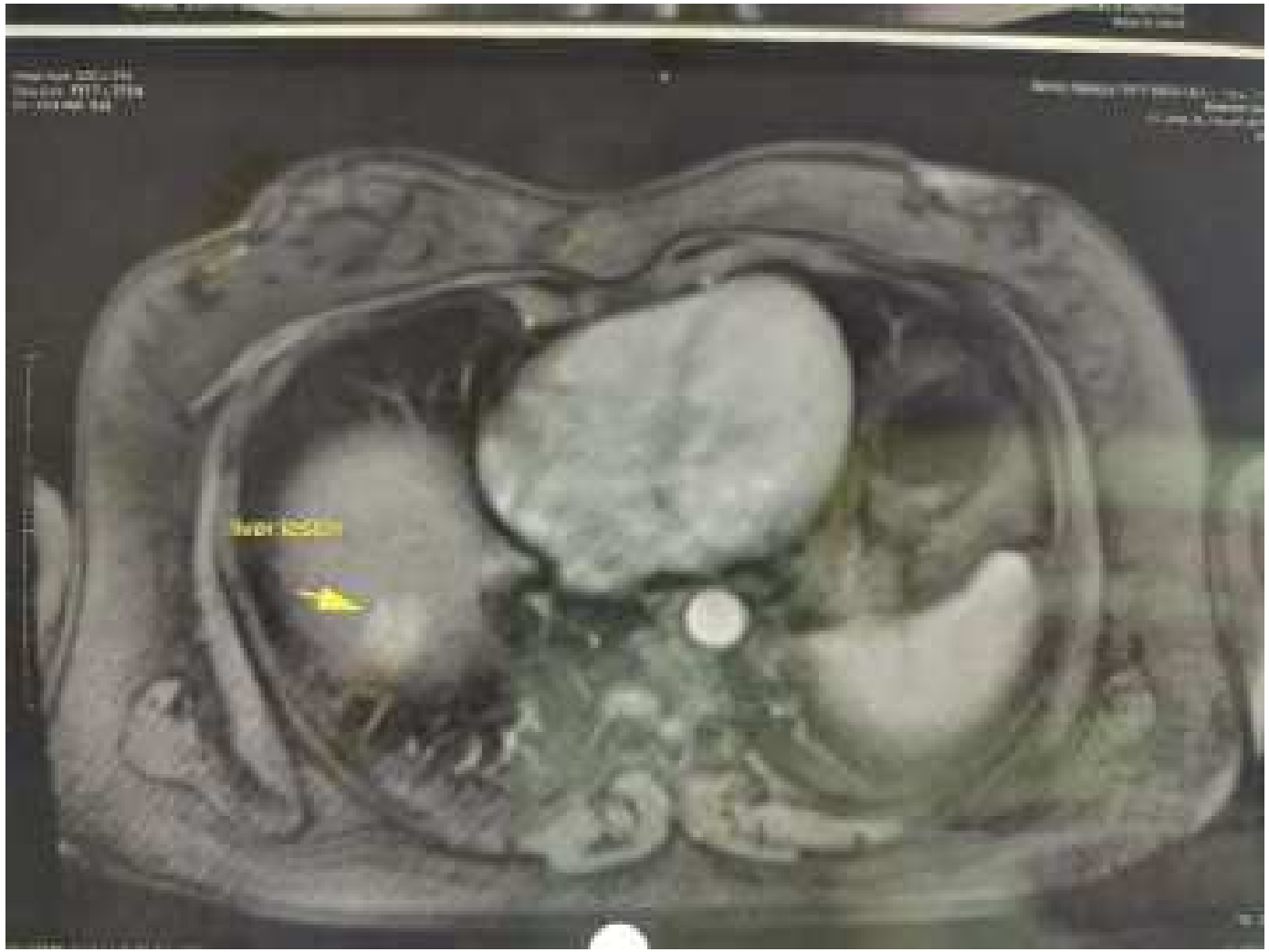
MRI

- On T2 weighted imaging
- A well marginated exophytic fat containing lesion was noted arising from the upper and mid pole of the left kidney
- A small soft tissue component was noted along its lower aspect.

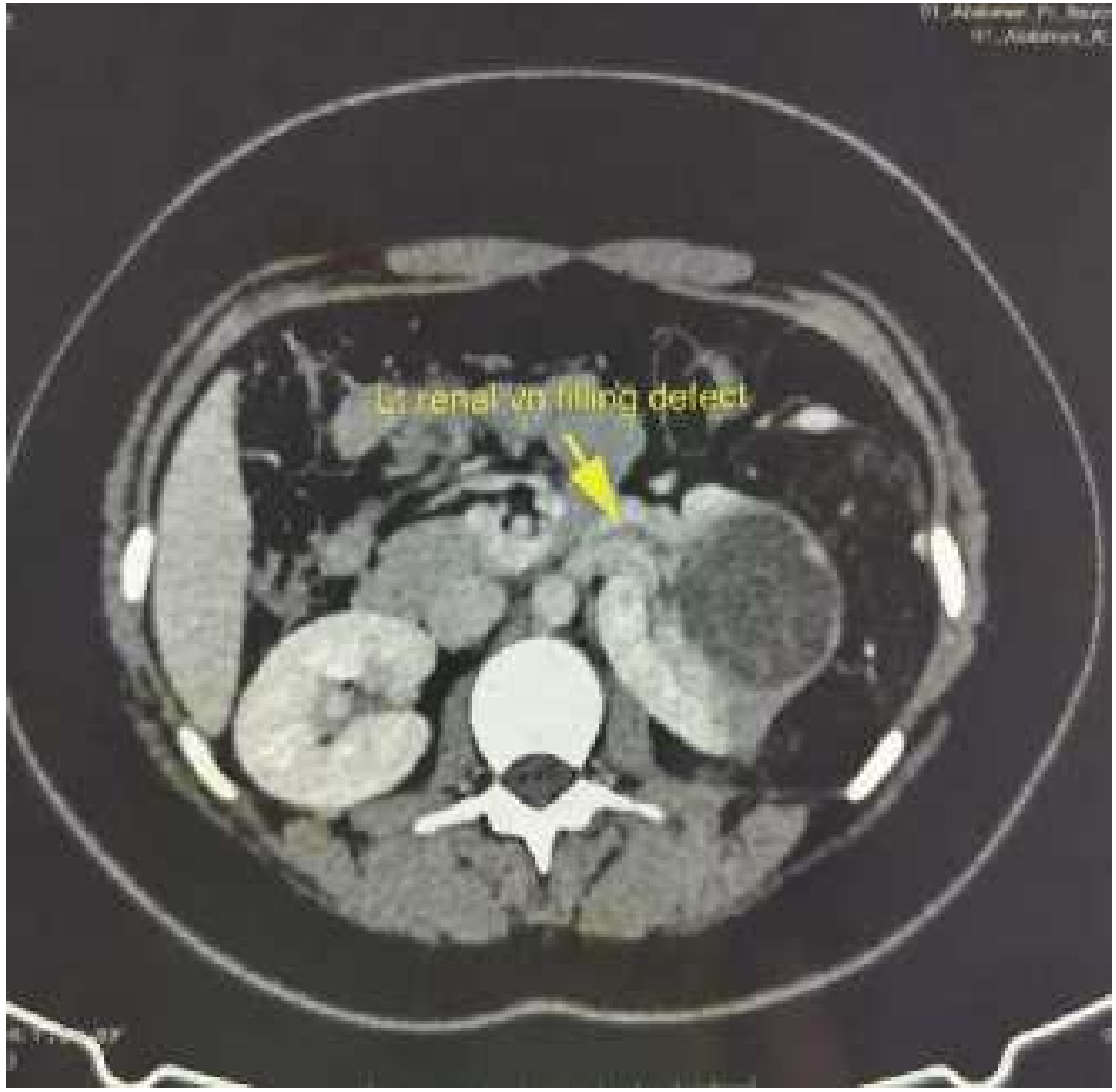


OTHER FINDINGS

- Enhancing nodular lesion in segment VIII of the liver likely suggestive of an hemangioma



- Left renal vein thrombosis



DIAGNOSIS

- LEFT RENAL NEOPLASM MOST LIKELY- ANGIOMYOLIPOMA.

- DIFFERENTIAL:
- FAT CONTAINING RCC
- RETROPERITONEAL LIPOSARCOMA WITH RENAL INVASION.

DISCUSSION

- **Renal angiomyolipomas (AML)- Benign renal neoplasm**
- Most common
- **Benign solid renal lesion**
- **Fat containing lesion of the kidney.**

- Sporadically
- Phakomatosis (m/c **tuberous sclerosis).**

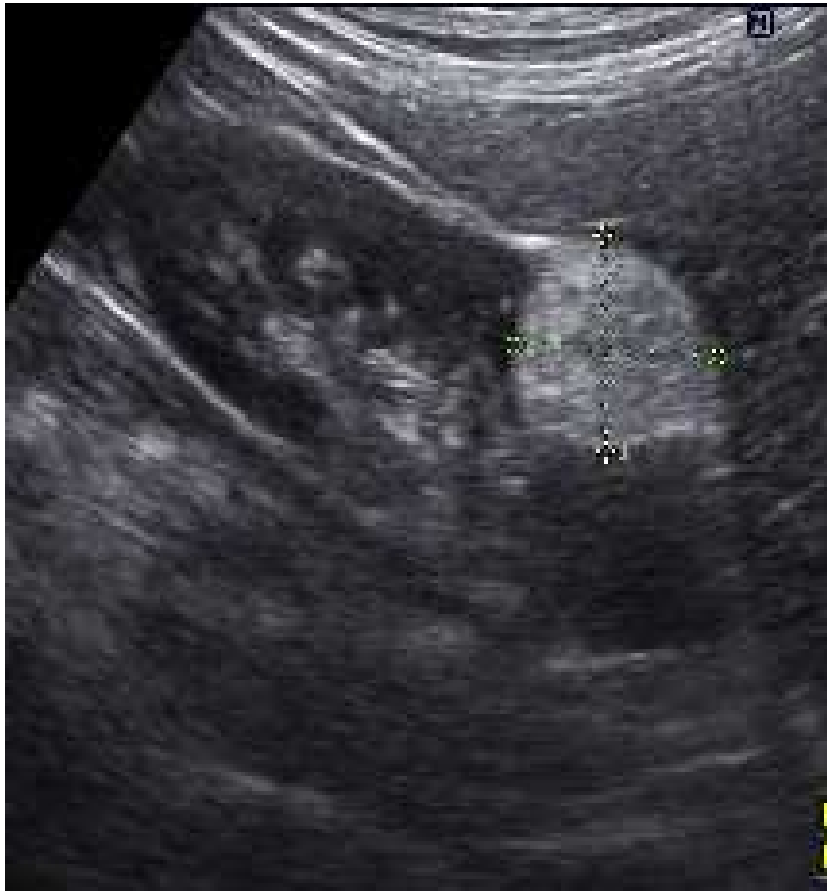
Cornerstone of diagnosis of AML

- **Demonstration of macroscopic fat**

- Distinguishing an angiomyolipoma from a **RCC becomes difficult in presence of** hemorrhage, or when lesions happen to contain little fat.

Ultrasound

- Location : Cortex
- single/ multiple
- Well marginate hyperechoic lesions
- No significant vascularity demonstrated on doppler study.
- Tuberous sclerosis, numerous –affecting the entire kidney (appearing echogenic with the loss of normal corticomedullary differentiation)

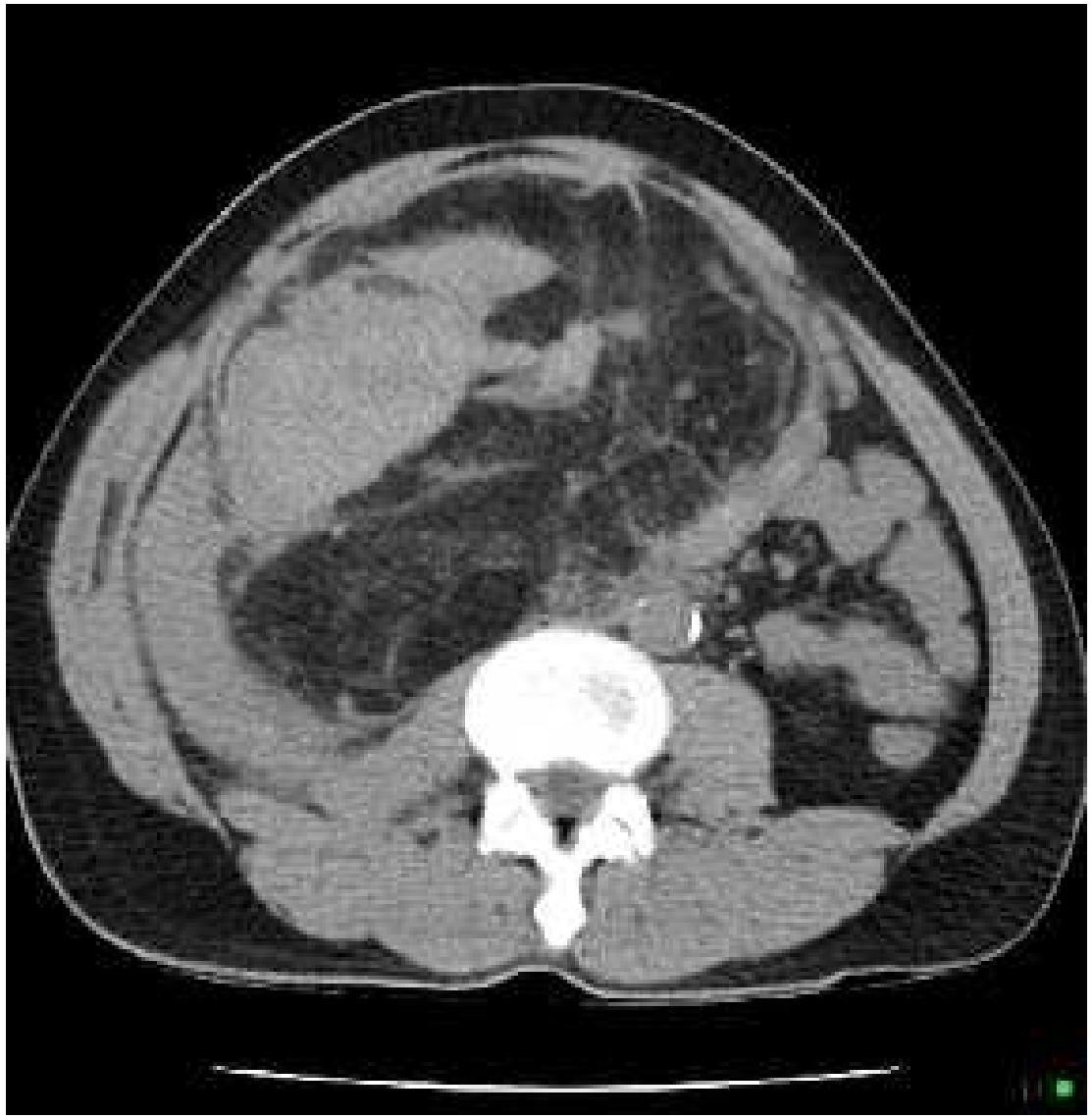


NCCT

- **Demonstrate macroscopic fat (less than -20 HU),** the presence of fat is strongly indicative of an angiomyolipoma, .

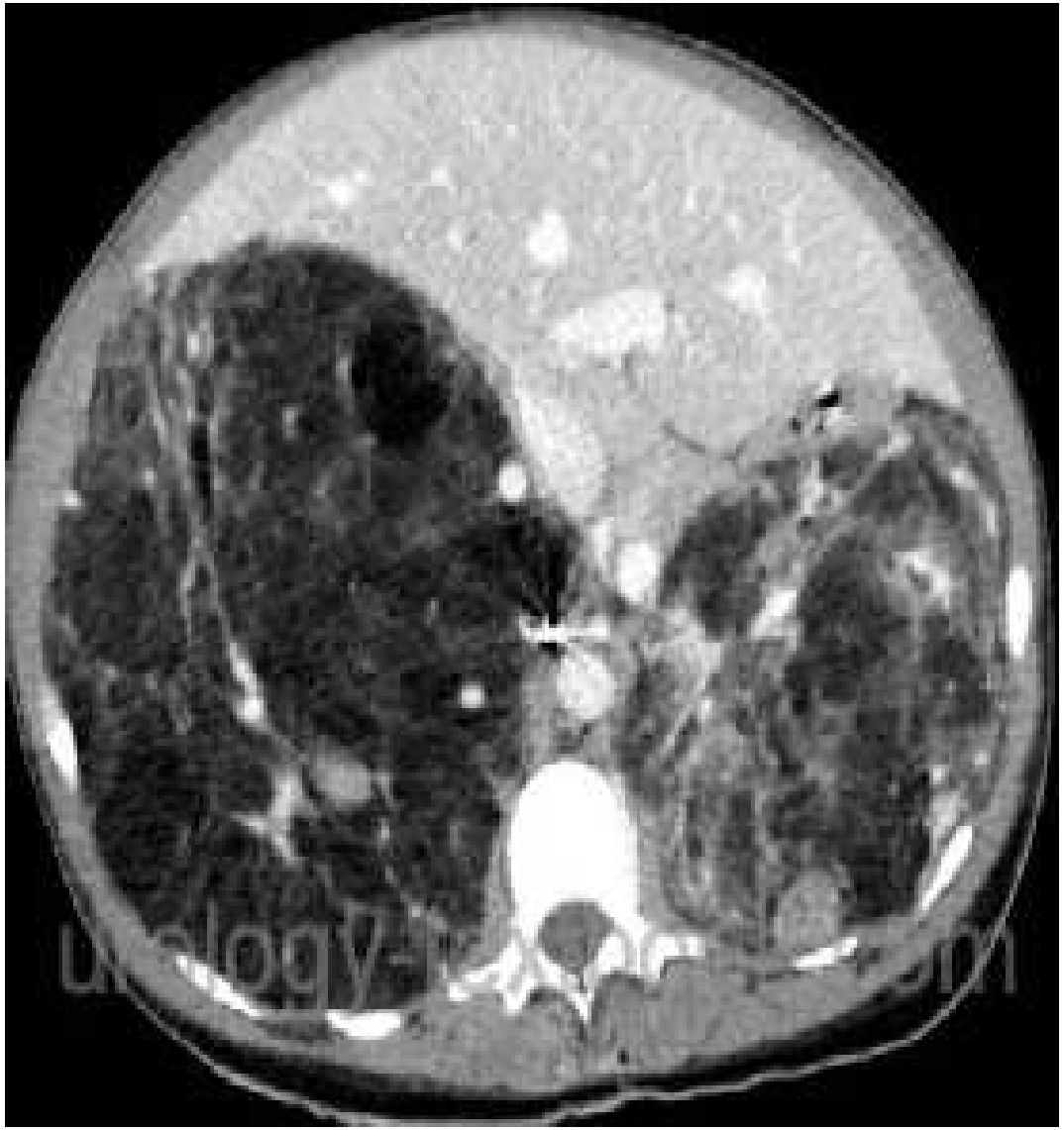
- Rarely (RCC) may have macroscopic fat components
- ~5% of angiomyolipomas are fat-poor

Absence of ossification/calcification on imaging is in favor of AML.



CECT

- Angiomyolipomas are hypervascular lesions often demonstrating characteristic features:
- Arterial phase: **Sharply marginated hypervascular mass with a dense early arterial network, and tortuous vessels giving the "sunburst" appearance**
- Venous phase: **whorled "onion peel" appearance of peripheral vessels**
- **micro- or macro-aneurysms**
- **absent arteriovenous shunting**



MRI

- **MRI is excellent evaluating fat-containing lesions.**
- **Fat-saturated techniques**
- Non-fat-saturated-high signal intensity Fat saturation- loss of signal
- In-phase and out-of-phase imaging, which generates India ink artifact at the interface betwee fat and non-fat components.
- Interface between the angiomyolipoma and surrounding kidney or between fat and non-fat components of the mass.

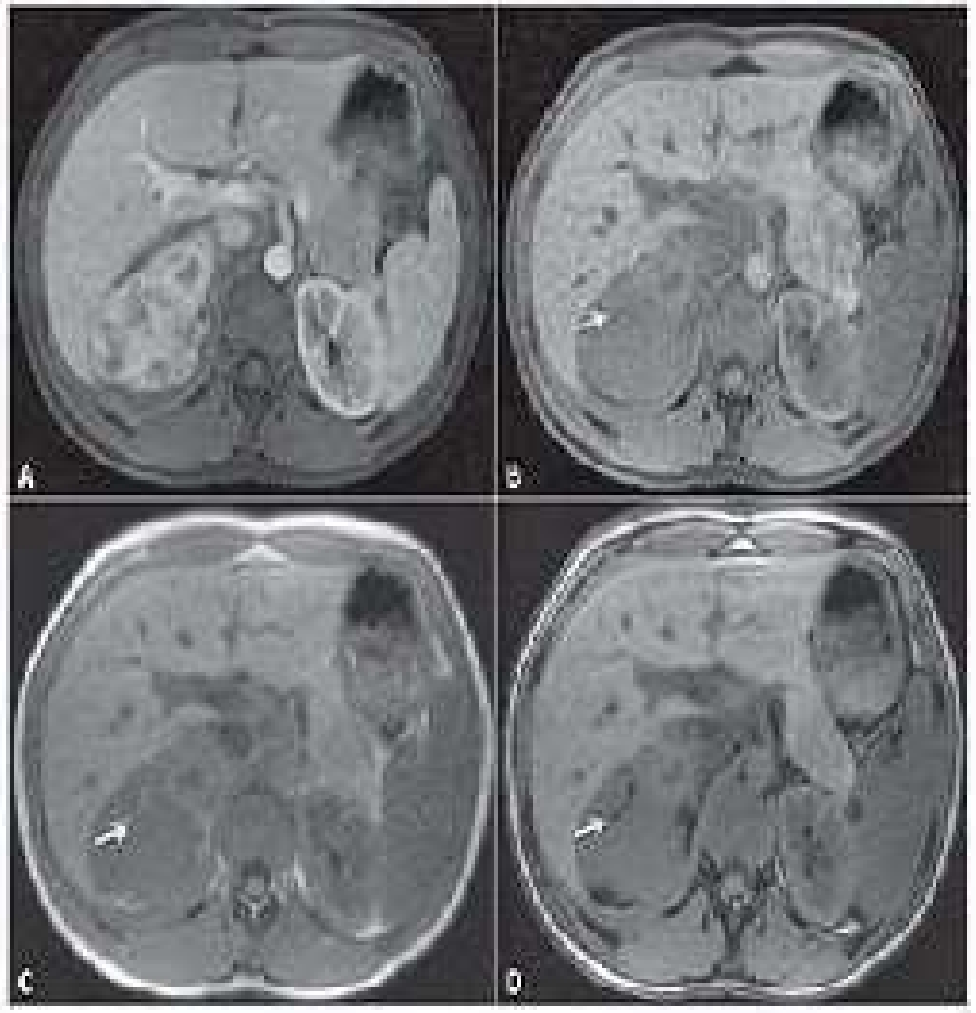
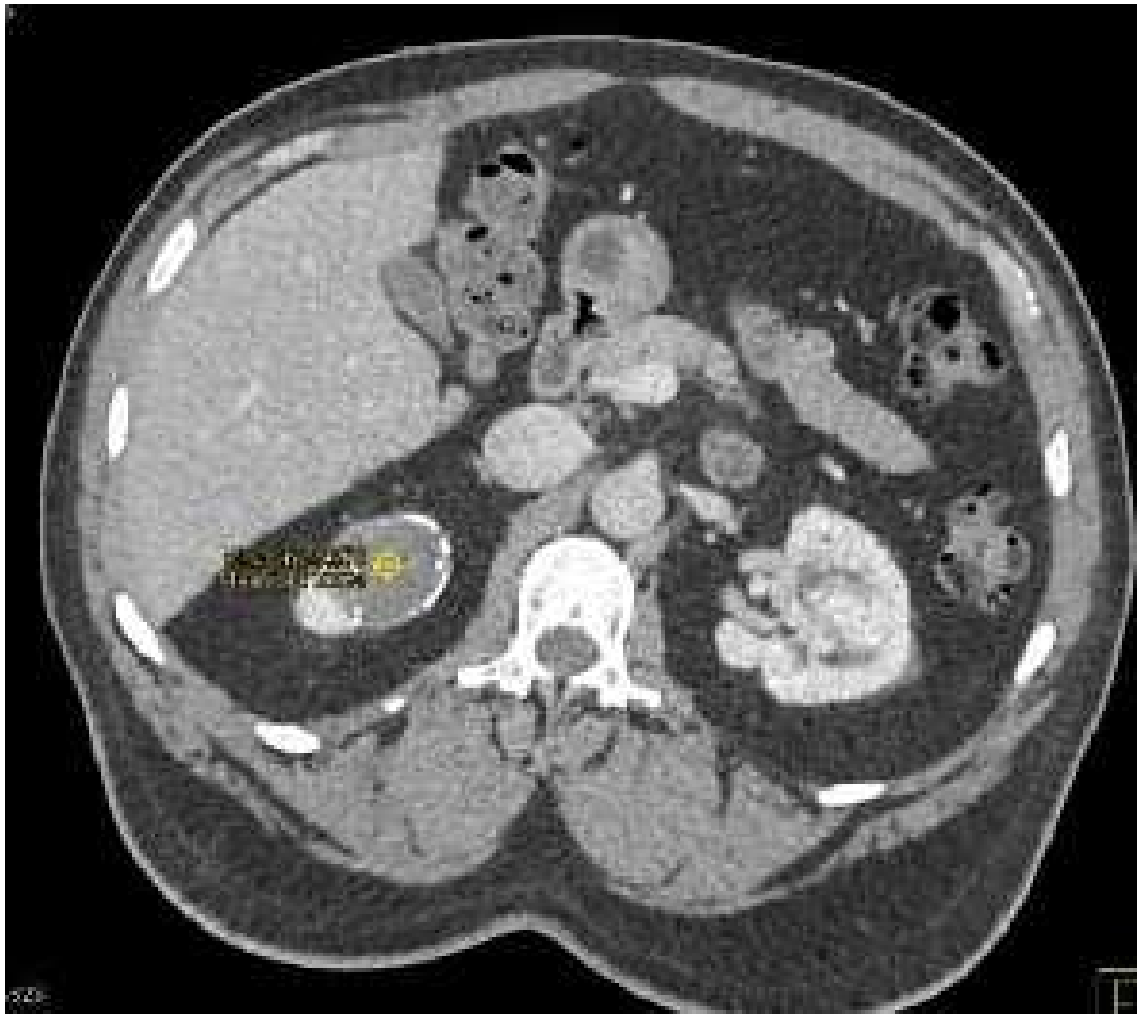


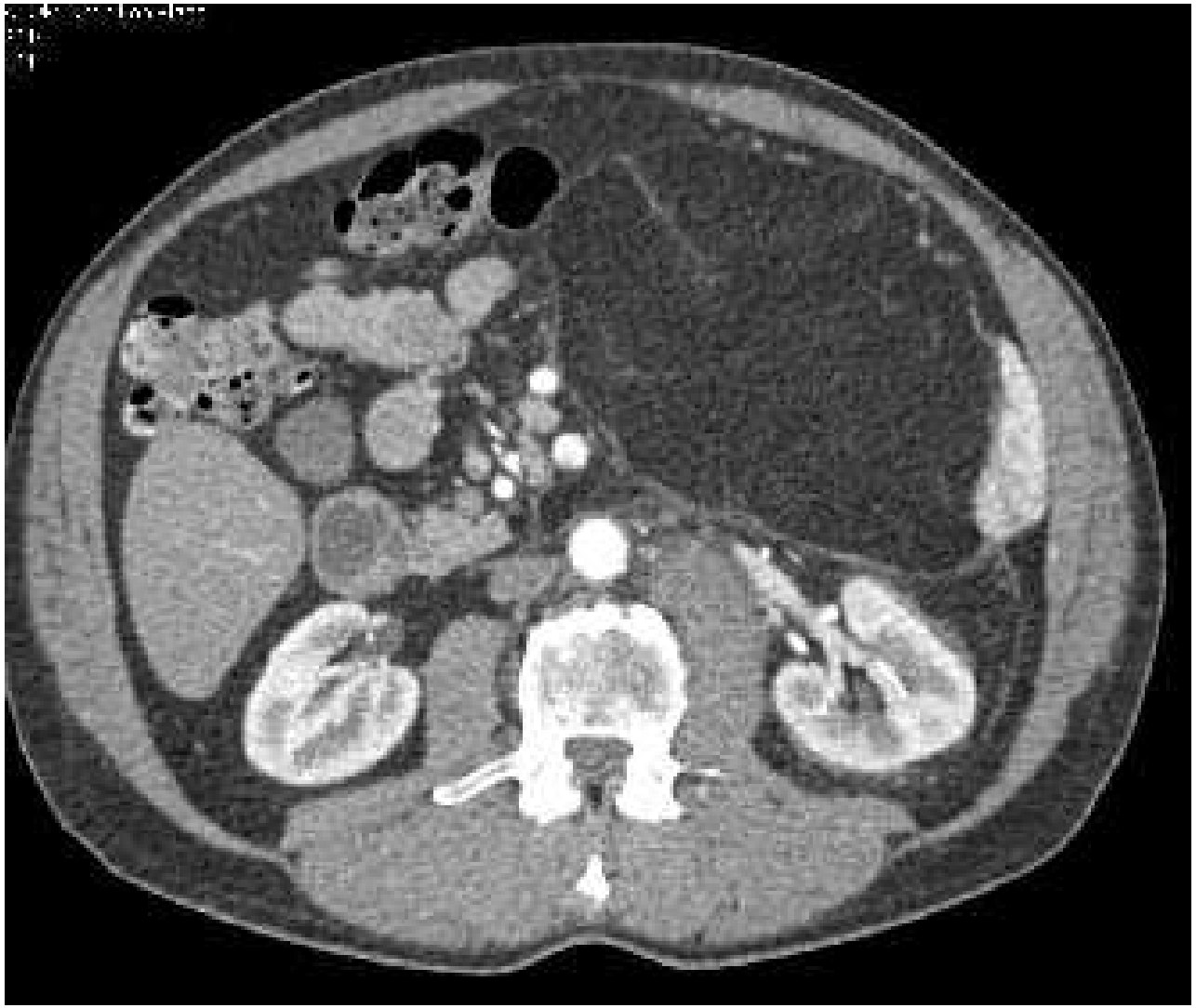
Figure 12 MRI of angiomyolipoma. Postcontrast T1 weighted sequences [A] show a hypervascular mass in kidney. Macroscopic fat is present in a solid renal mass, which is seen as loss of signal intensity between fat-suppressed precontrast T1 weighted image [B] and the in-phase non-fat-suppressed gradient echo [C]. Alternatively, opposed-phase gradient echo imaging [D] shows an India ink artifact at the water/fat interface

Differential diagnosis

- Renal cell carcinoma (RCC)
  - large irregular tumors
  - Areas of ossification/calcification,
  - invading the renal sinus
  - large necrotic tumors.



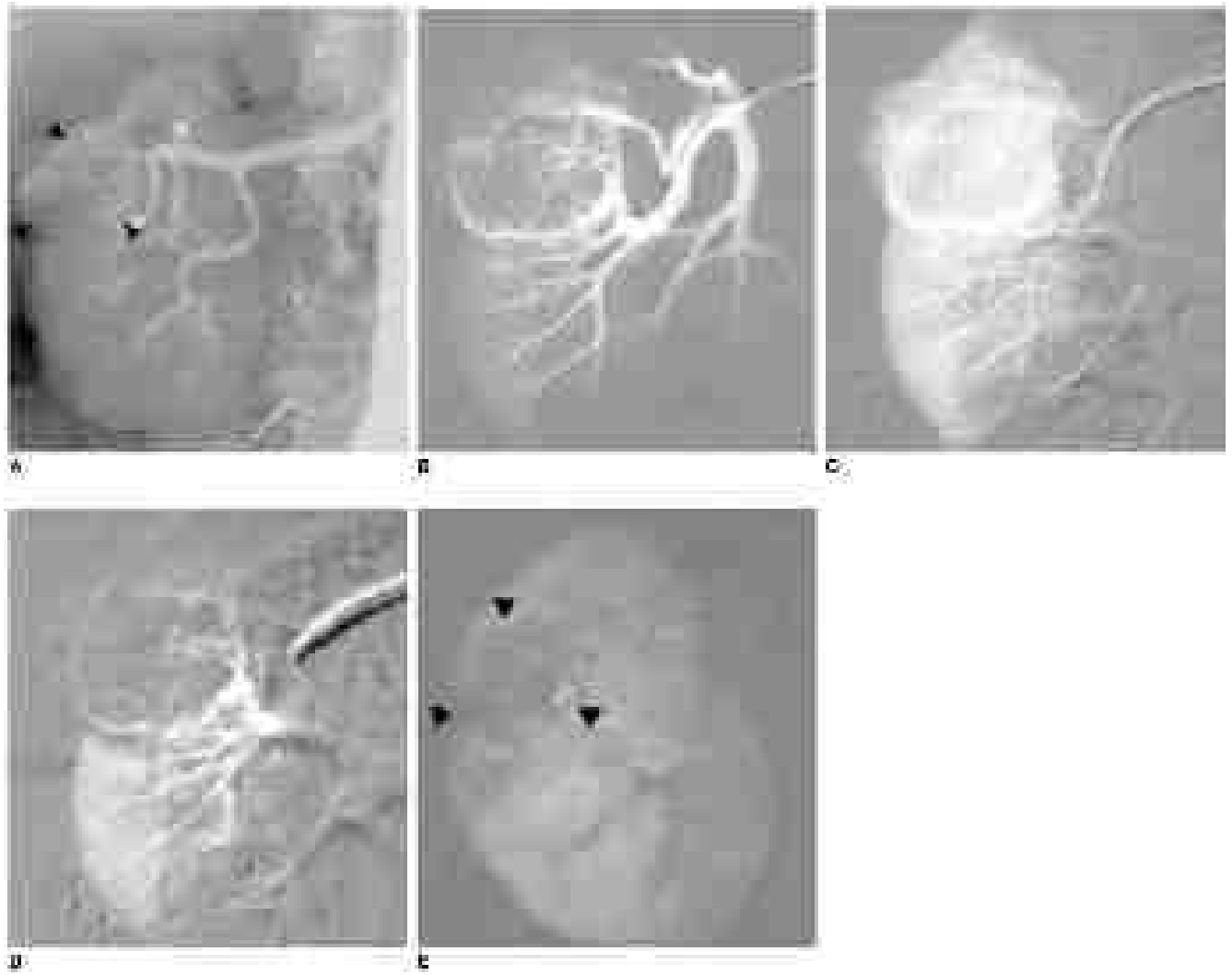
- Retroperitoneal liposarcoma
  - presence of a large vessel extending into the renal cortex suggestive of AML
  - liposarcoma is hypovascular
  - May show specks of calcifiactions.



- Oncocytoma- central stellate scar – showing delayed enhancement on post contrast imaging and delayed washout.

Interventional Radiology

- DSA followed by embolization
- Larger AMLs, or those that have been symptomatic
- Lesions presenting with acute retroperitoneal hemorrhage



ANGIOMYOLIPOMA

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Jr Pathology
DrRG Wiseman Pinto
Professor and Head of department of pathologyGMC
ExDean Goa University
Ex Dean GMC
President Asian Society of Cytopathology
Chairman international Affairs Committee of IAC
India's Representative to International Academy of cytology and EFCS (European Federation of cytology societies)

CASE

- 19 year old female
- Presented with C/O **Hematuria** and **left renal lump**

- On evaluation **MRI**: left complex cystic lesion in interpolar cortex with parapelvic extension (5.4x5.2x5 cm).
- Perinephric fat extension +
- Enhancing nodular soft tissue component- 2x1.2cm (BOSNAIK IV cyst)
- Associated with large exophytic mass arising from upper pole and interpolar region- predominant fat content

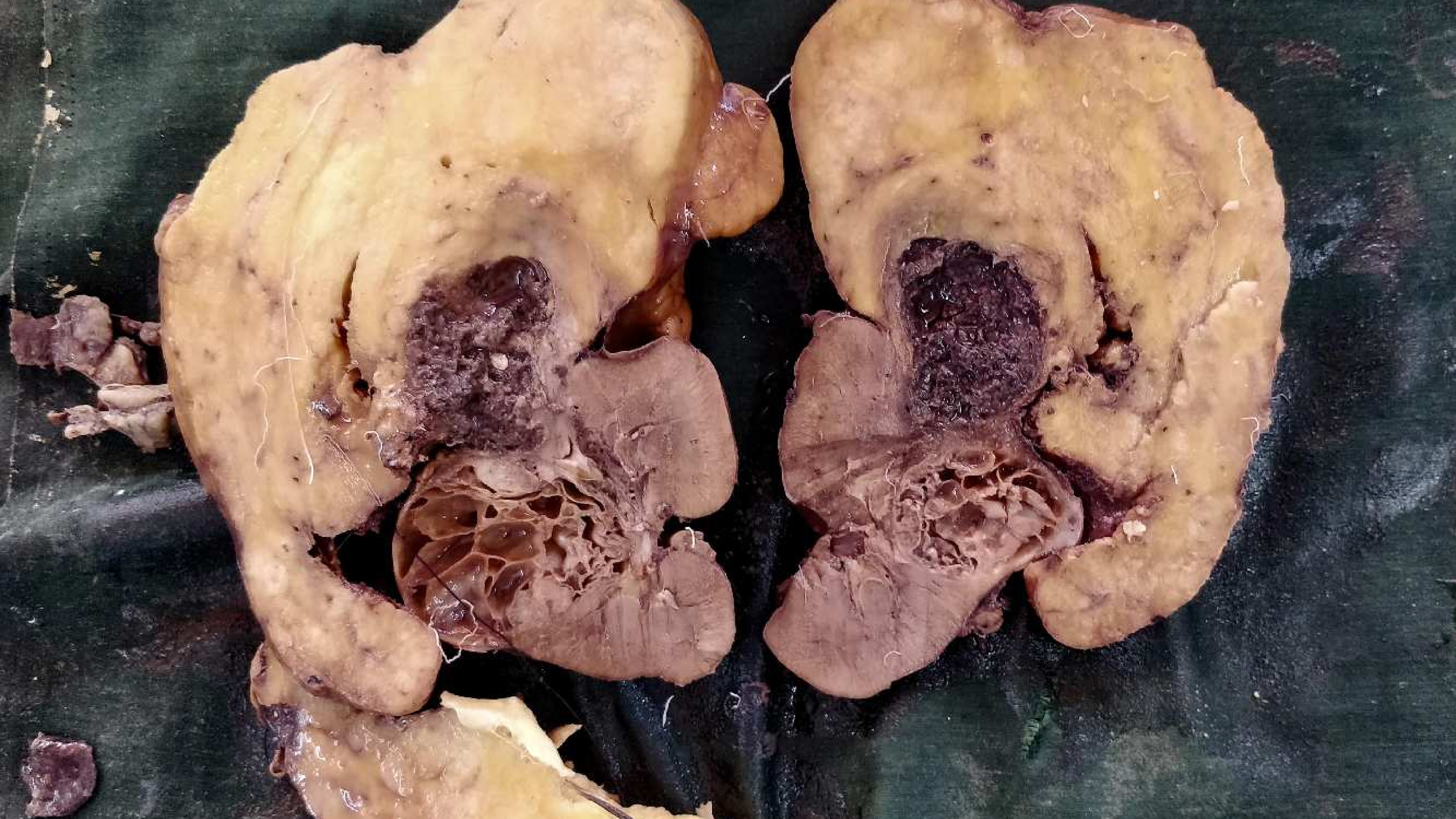
Gross

- Specimen of left radical nephrectomy, entirely measures~ 17x16x7cm. Left kidney measures ~ 9x8x5 cm and shows a **brownish-yellow mass** arising from upper and interpolar region measures ~ 17x15x7 cm , appears breaking through the cortex into perinephric fat

- **Cut section:** multiloculated cystic lesion arising in middle pole of kidney measures ~ 5x4x4 cm, filled with serous fluid and solid component measures ~ 2x1 cm.

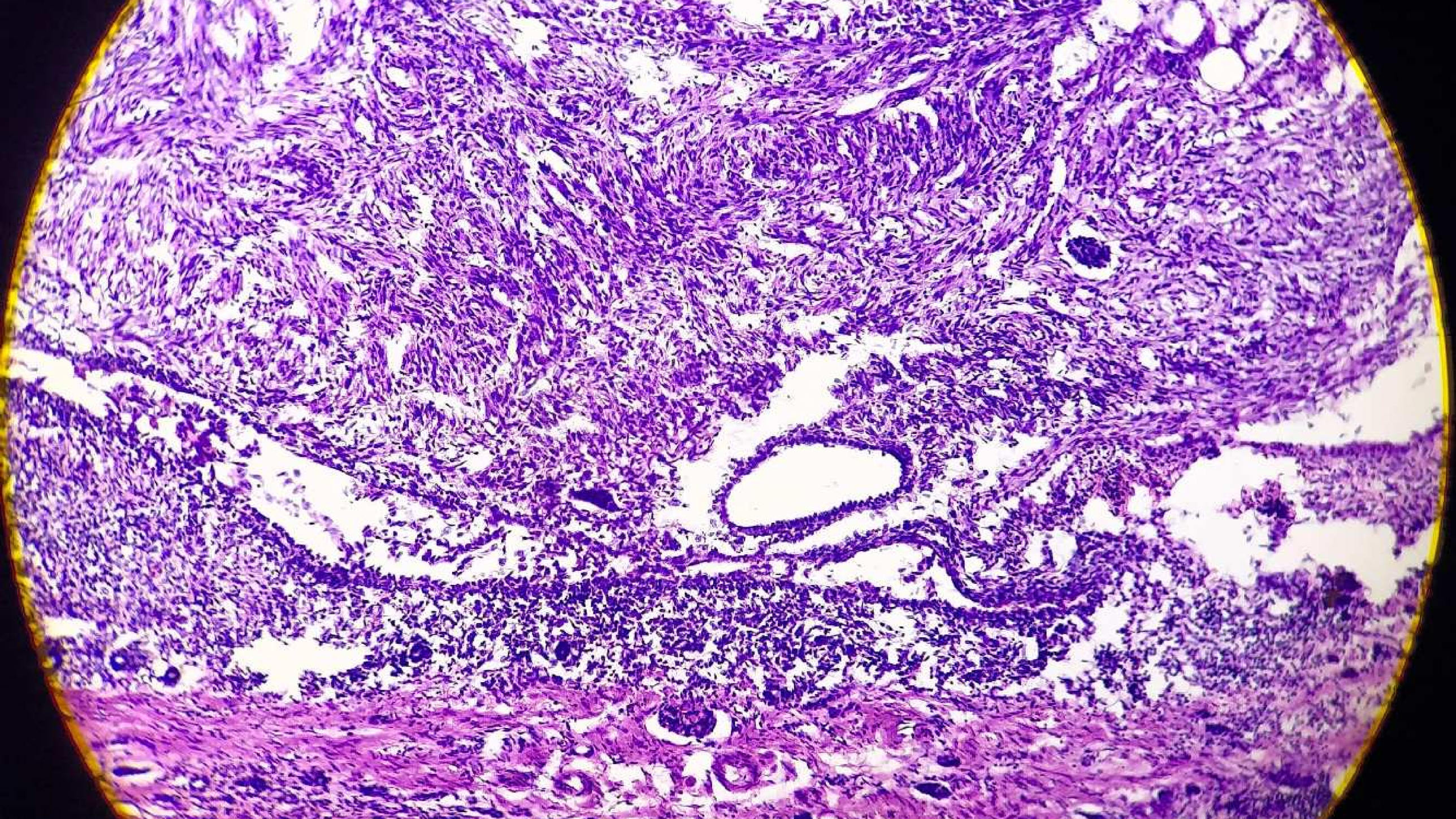
- Another hemorrhagic cystic areas above multiloculated cystic lesion arising between upper and middle pole measures ~ 4x2.5x2.5 cm

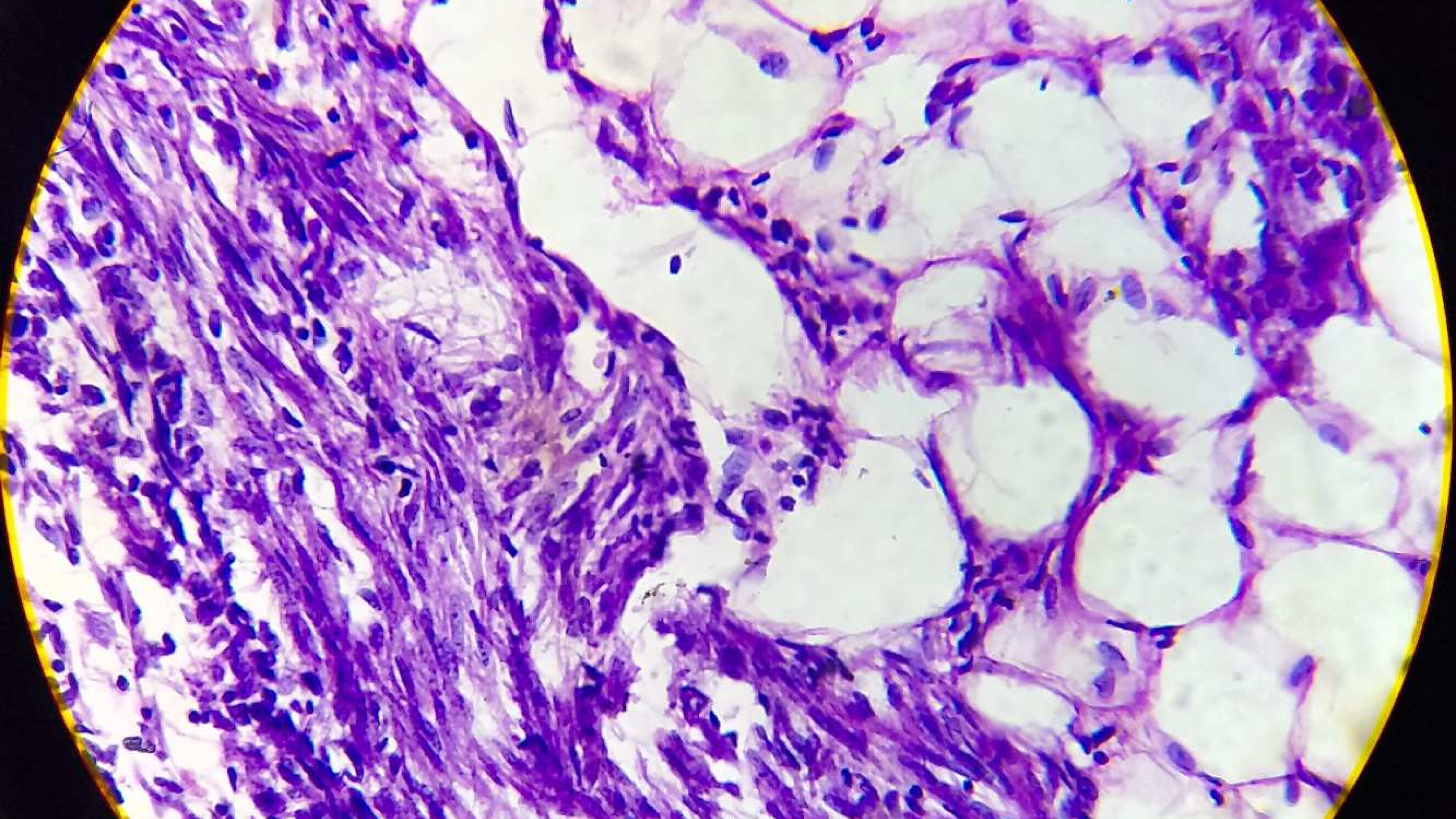
- **<u>Cut section of larger mass:</u>**
- Brownish yellow and shows few whitish nodular areas measures ~ 2.5x2.5 cm
- Bottle also encloses brownish yellow specimen with part of ribs attached measures ~ 6x3x2 cm. Cut section is brownish yellow . No lymph nodes isolated.

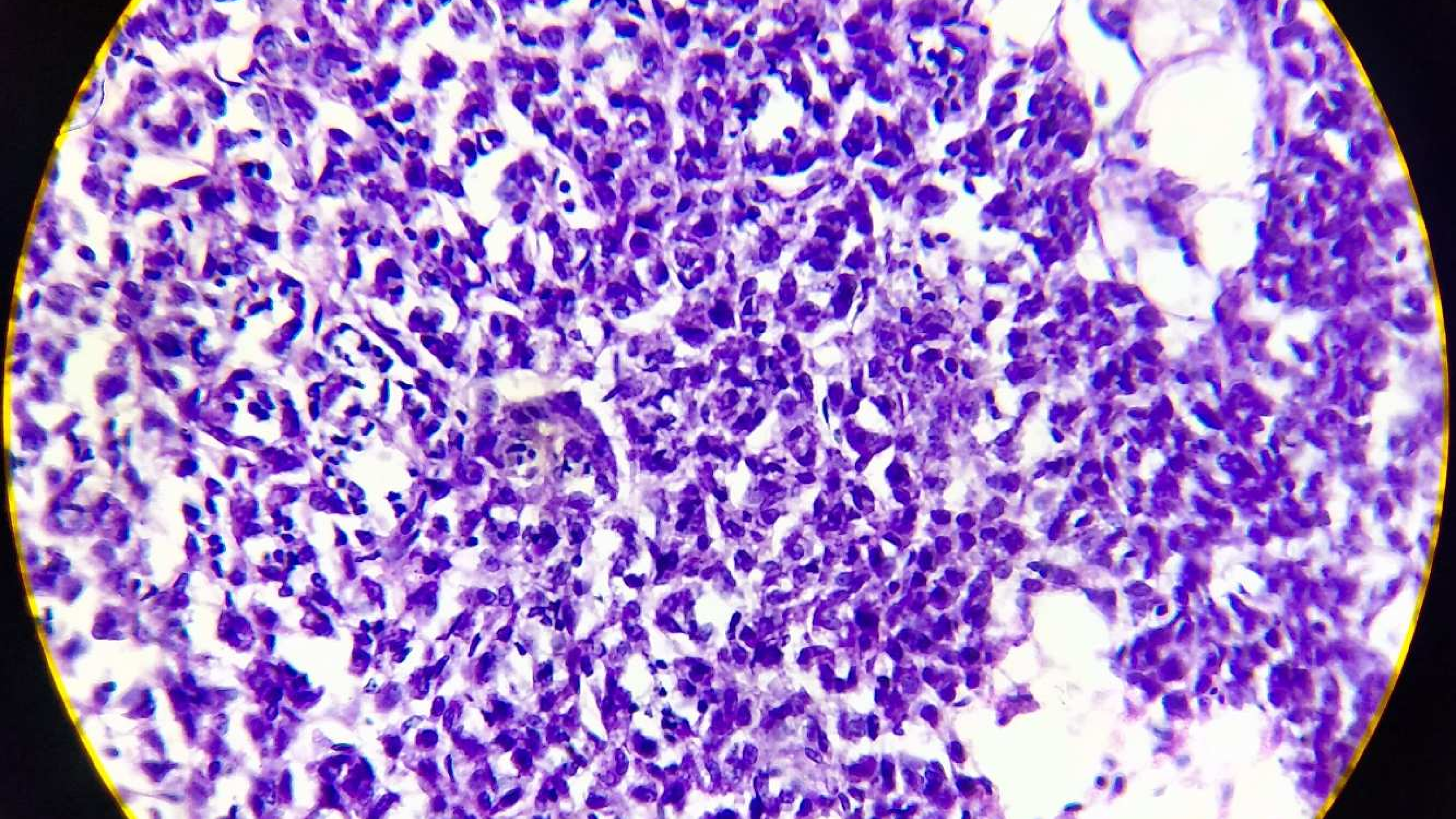


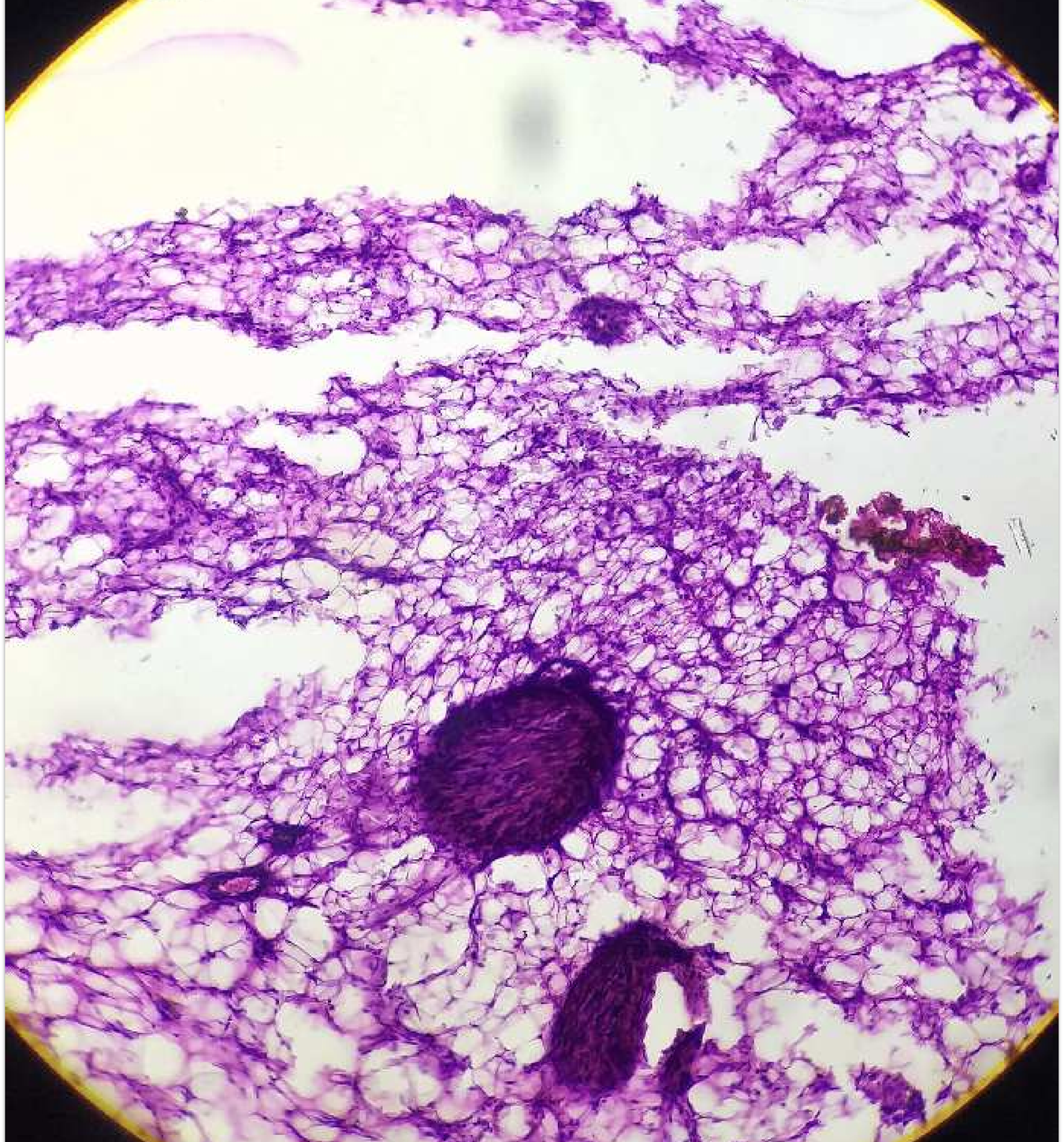
MICROSCOPY

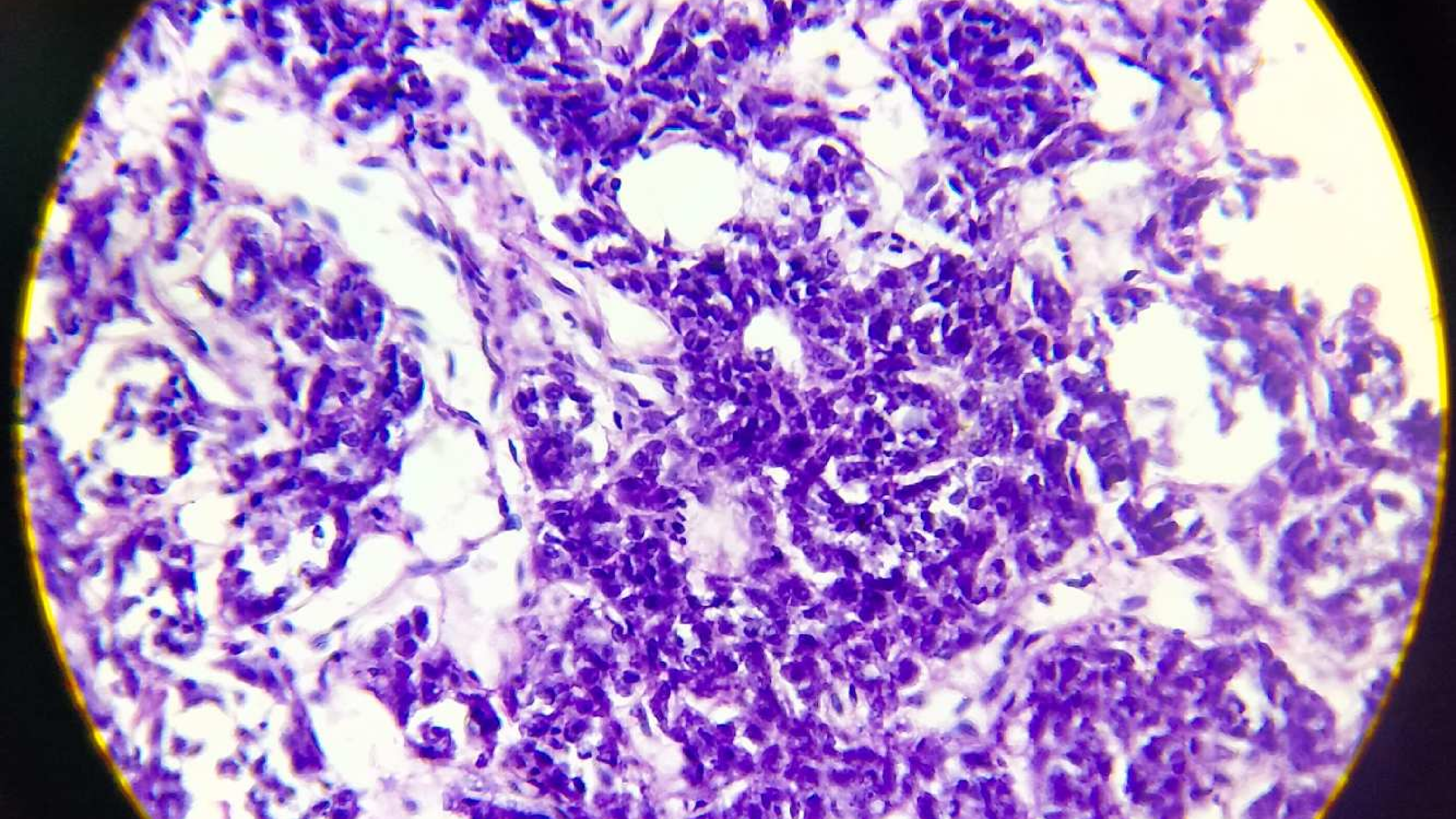
- Multiple sections from the left renal mass shows angiomyolipoma with epithelial cysts.

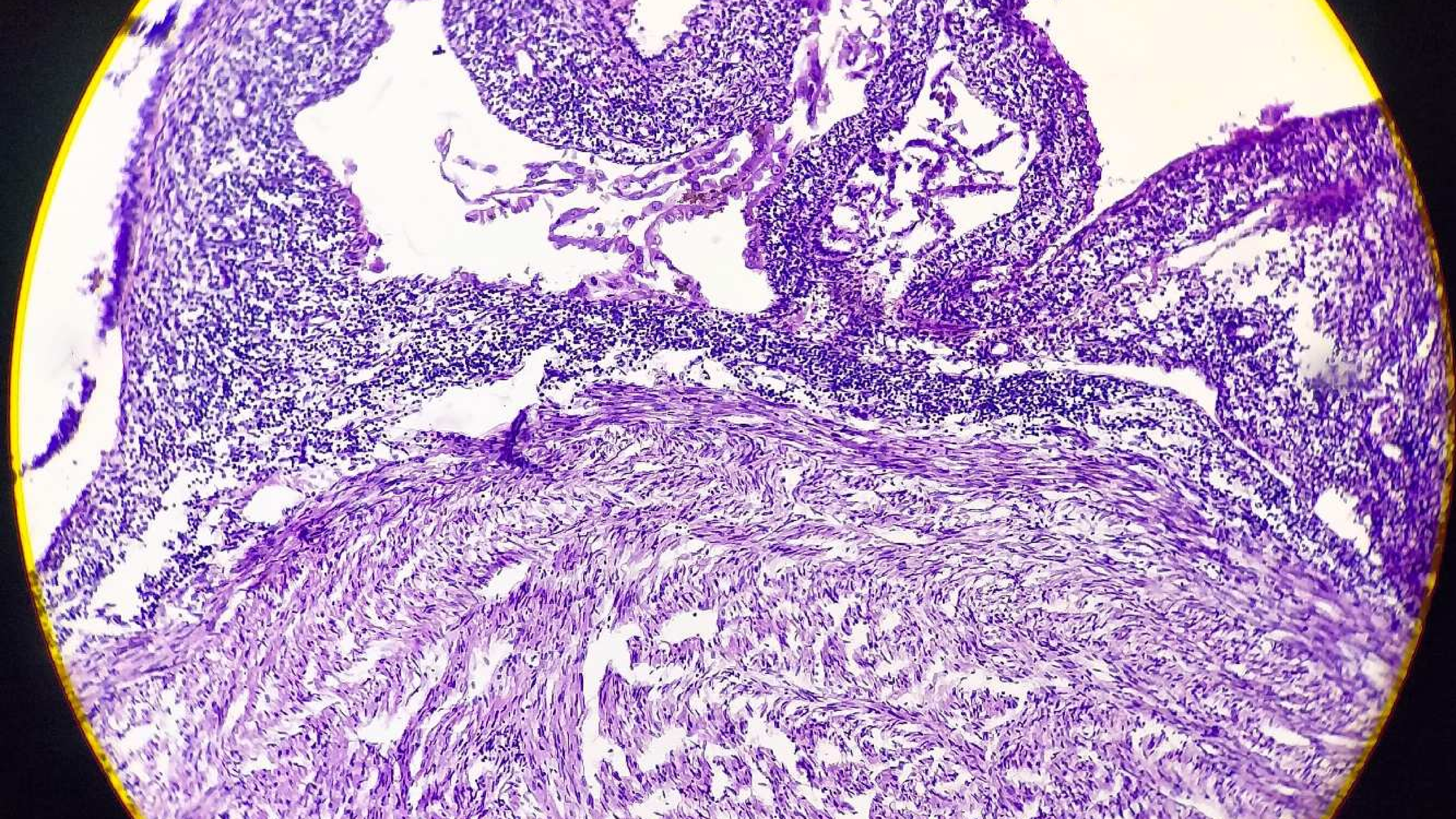


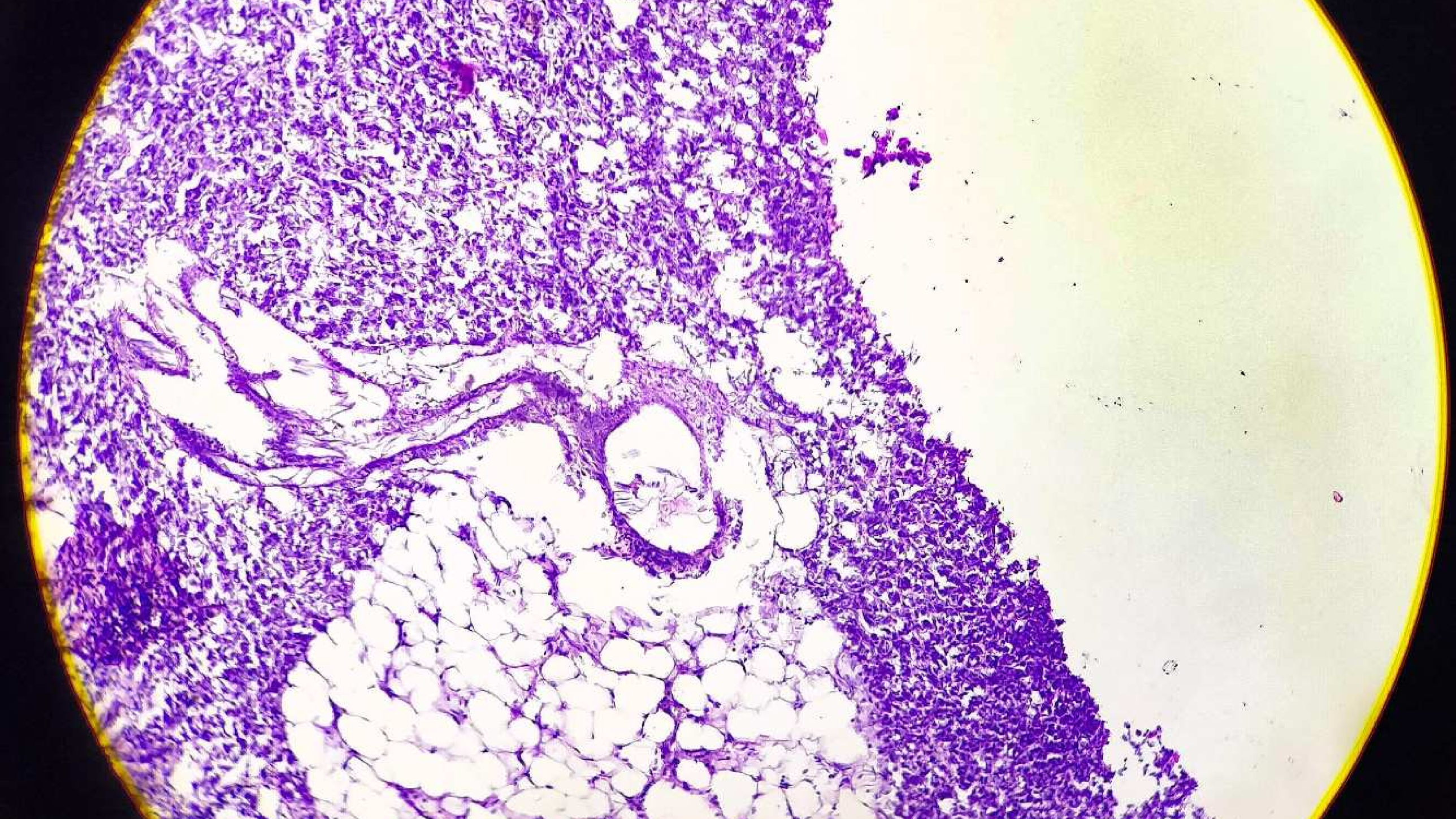


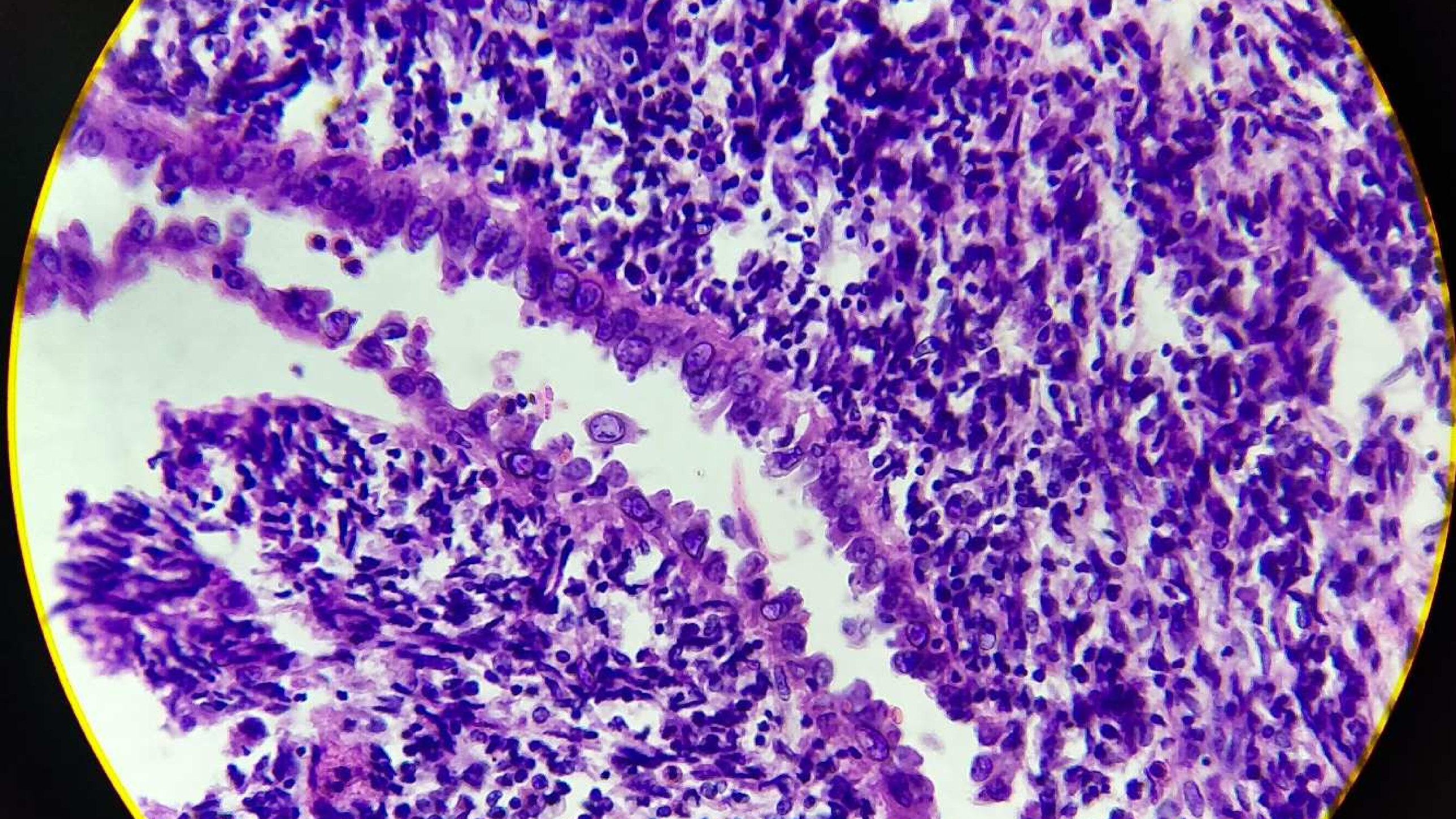


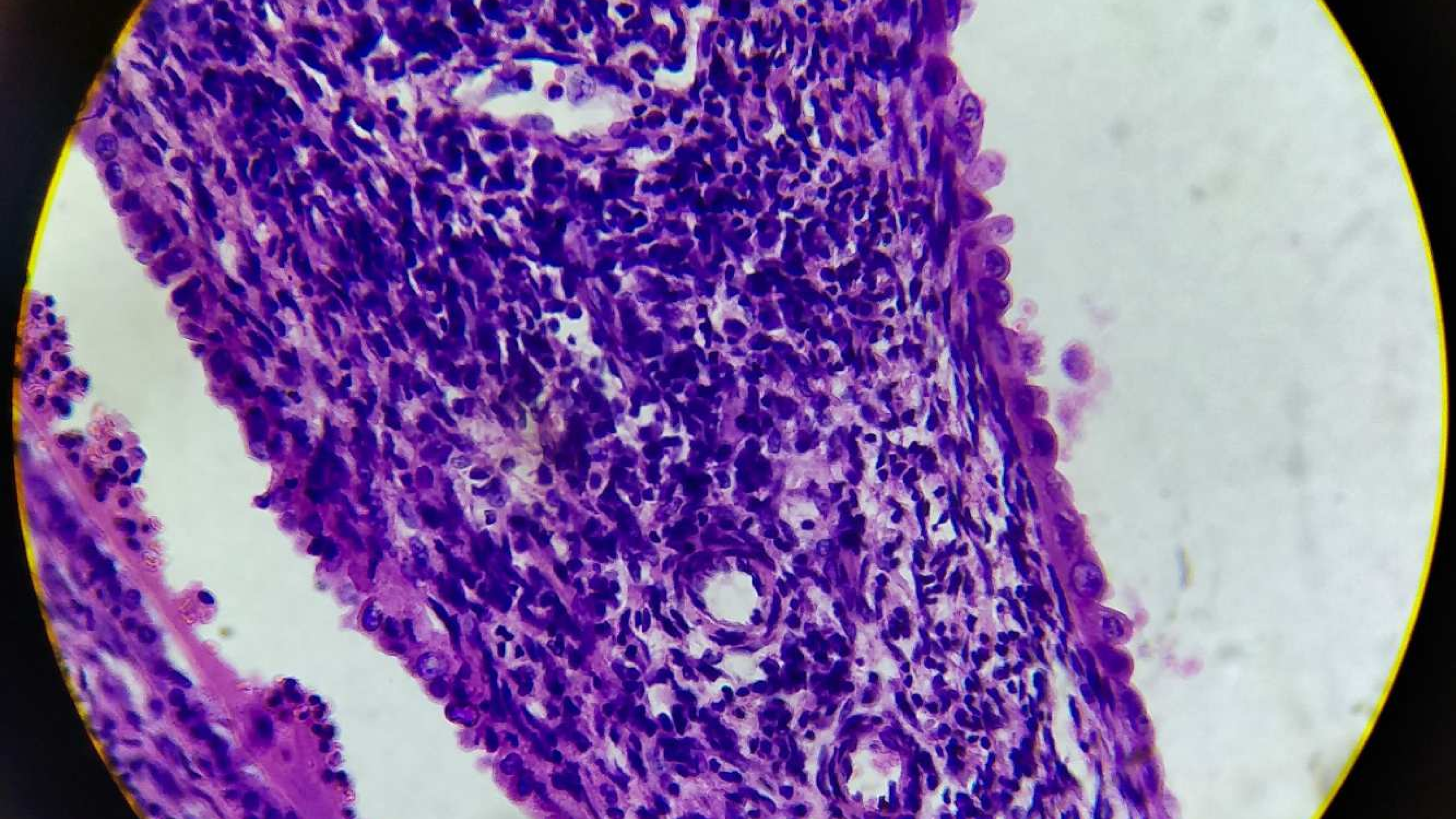


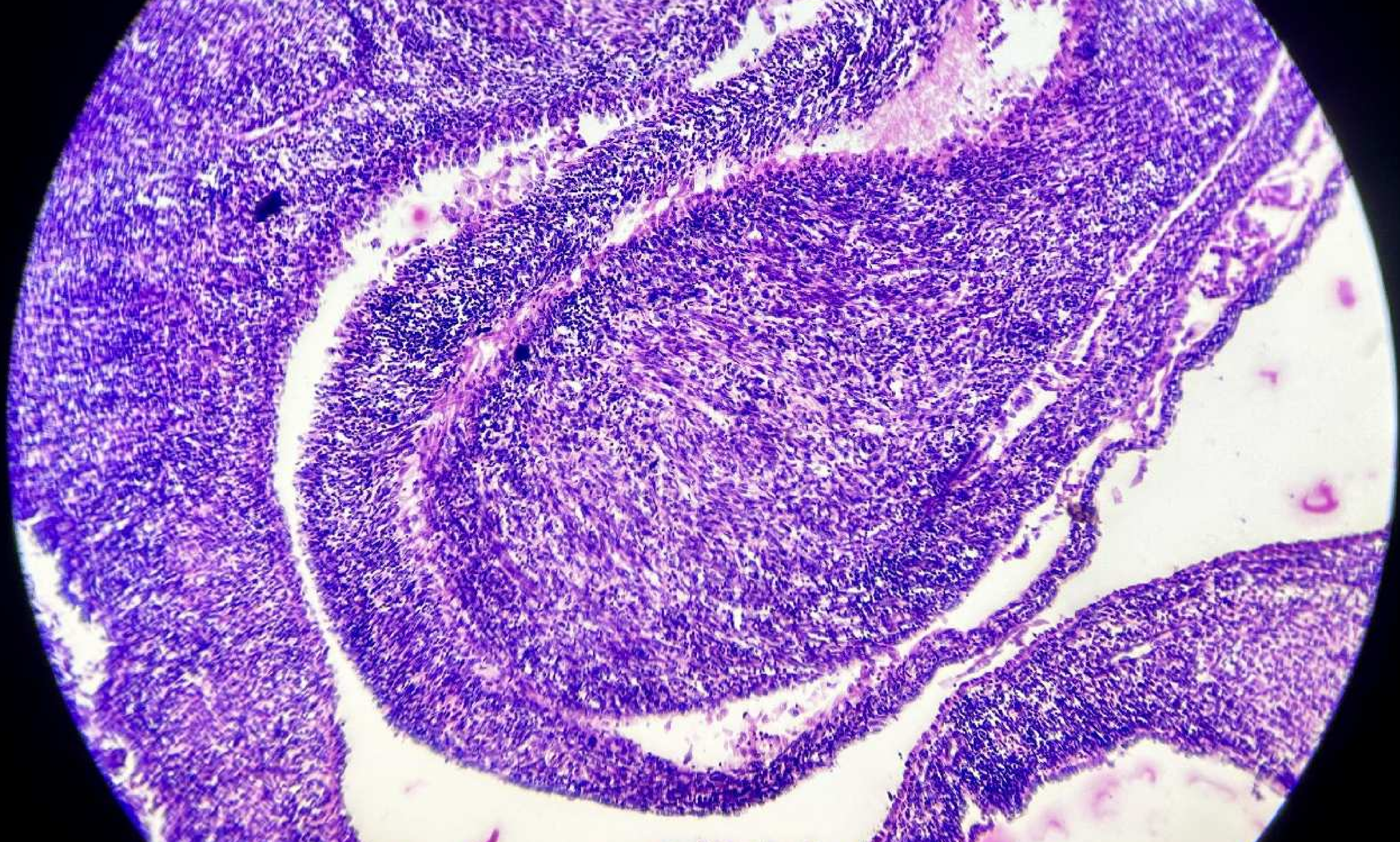


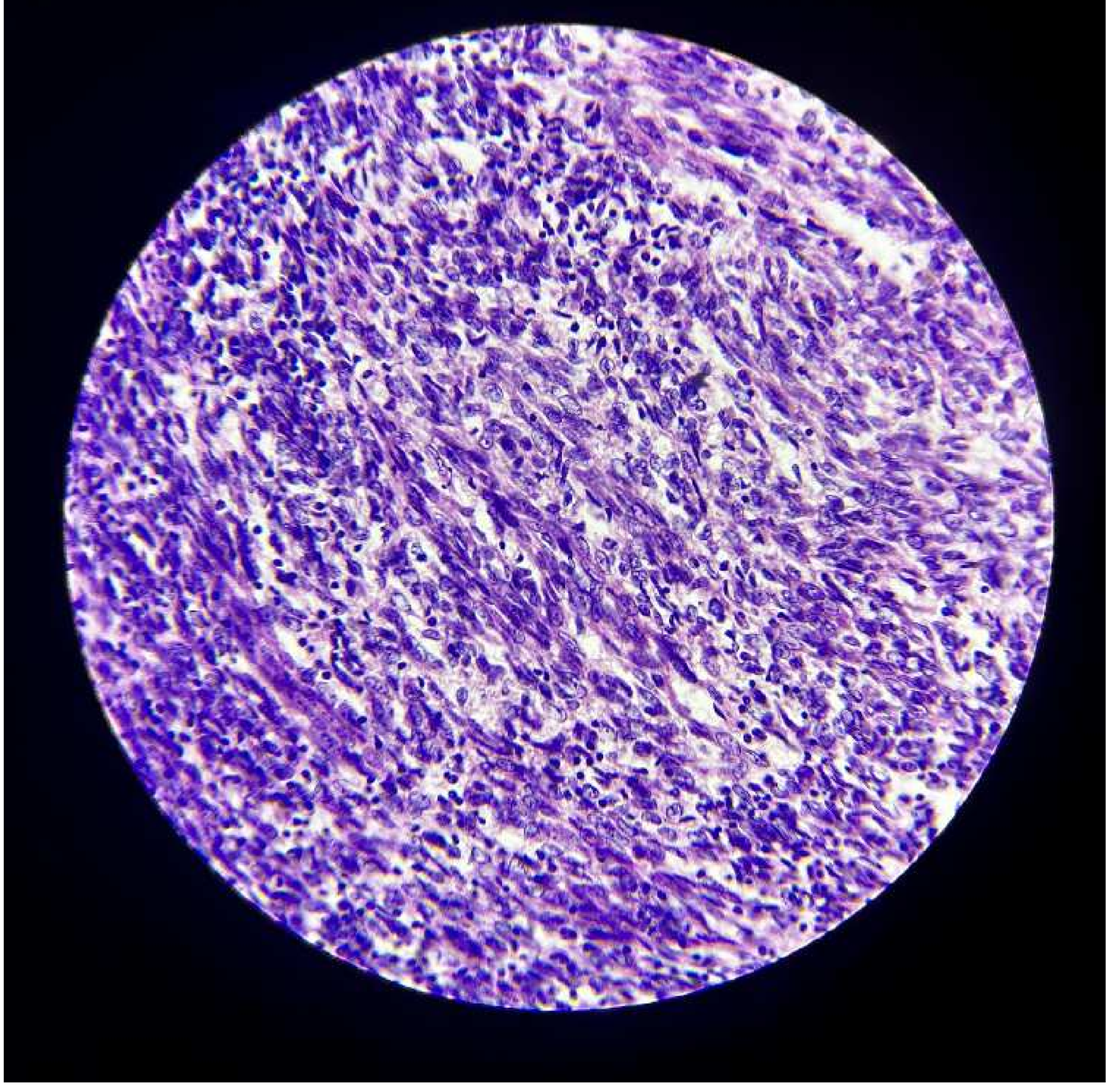












DISCUSSION

- Member of ***perivascular epithelioid cell (PEC) tumour*** family
- ***Benign*** tumour associated with renal angiomyolipoma
- Classic variant is a benign ***mesenchymal*** neoplasm composed of admixture of ***thick dysmorphic blood vessels, smooth muscle and adipose tissue.***
- Rarely nodal involvement of renal angiomyolipoma likely due to multicentric tumour rather than metastasis.

- Amount of each component is variable
- Some cases show significant sclerosis
- ***Epithelioid variant has potential to metastasise***
- Angiomyolipoma can occur in extrarenal sites

SITES

- Kidney
- Retroperitoneal and periaortic lymph nodes draining the involved kidney
- Liver , ovary

EPIDEMIOLOGY

- Reported in ***0.13-2.2%*** of asymptomatic adults
- Occurs sporadically or in patients with ***tuberous sclerosis***
- Majority are sporadic cases (80%) and usually diagnosed in middle aged adults (F>M)
- Tuberous sclerosis cases occur in young patients and have no sex predilection
- Constitutes ~1% of all resected renal tumours

TYPES

- Classical
- Epithelioid
- AML with oncocytic
- AML with spindle cell
- Liposarcoma
- AMLEC (Angiomyolipoma with epithelial cysts)

PATHOPHYSIOLOGY

- ***Arises from perivascular epithelioid cells***

CLINICAL FEATURES

- Usually ***asymptomatic*** in screened tuberous sclerosis patients due to smaller size when discovered
- May coexist with renal cell carcinoma in non-tuberous sclerosis patients, particularly clear cell carcinoma
- Large, multifocal and can extend into the renal vein or vena cava
- Classic variant is benign but may be complicated by haemorrhage if the tumour is large

DIAGNOSIS

- Imaging is often sufficient to give diagnosis for classic angiomyolipoma
- Definitive diagnosis by light microscopic examination of tissue
- Fat poor and epithelioid variants may additionally require immunohistochemistry .

PROGNOSTIC FACTORS

- Benign course in angiomyolipoma, classic variant
- Tumours with epithelioid and pleomorphic features can have a more aggressive course
- Sarcomatous transformation with distant metastasis is extremely rare
- Retroperitoneal haemorrhage is an important complication

- Patients with bilateral disease can have renal failure
- Death can occur due to involvement of contiguous organs particularly blood vessels

TREATMENT

- Tumours may be embolized or undergo surgical excision
- ***mTOR inhibitors: everolimus*** can be used if large or extending into the vena cava.

GROSS

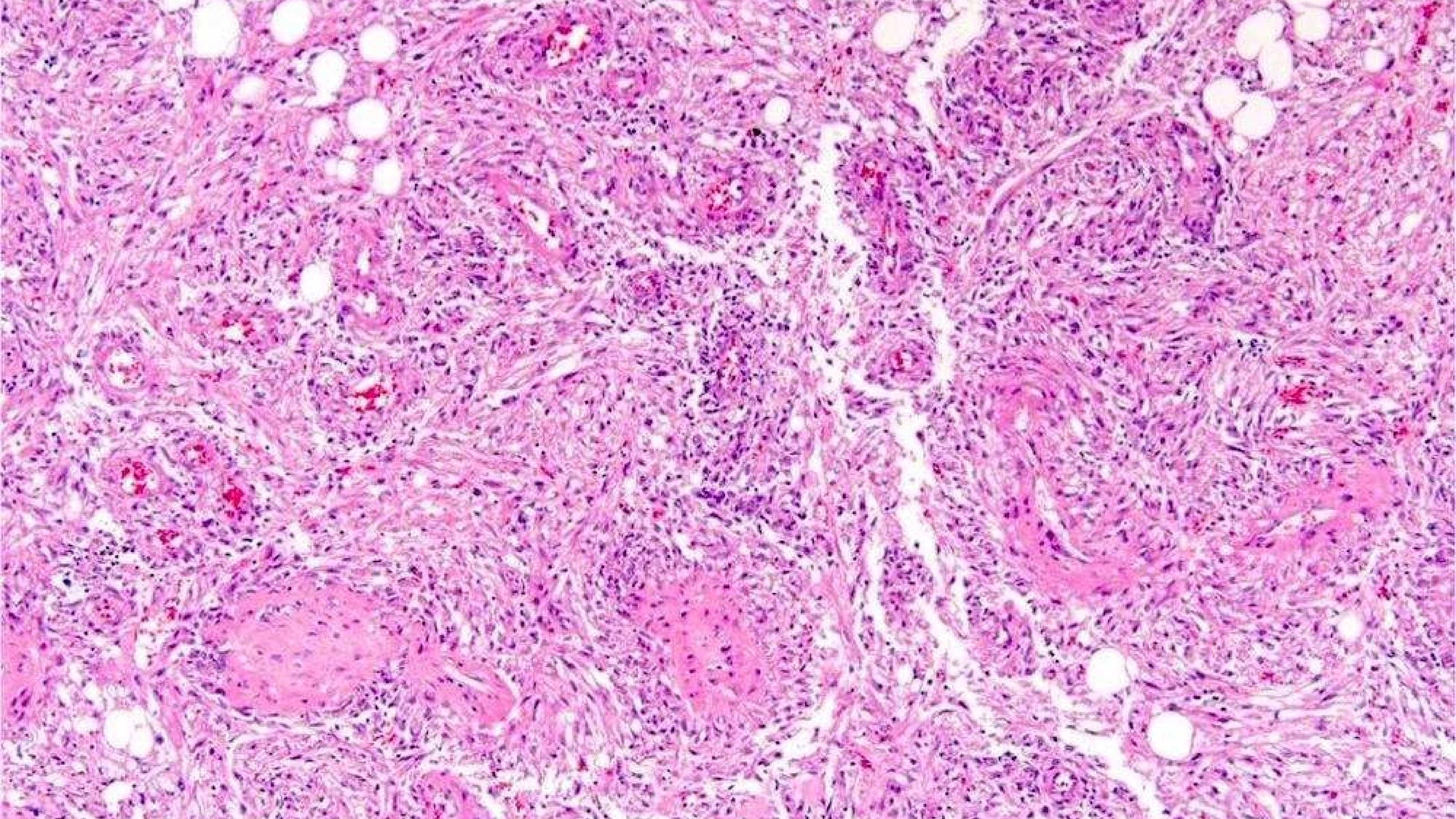
- Tumour ranges from 0.5 to 25 cm
- Circumscribed, not encapsulated with pushing border
- Cut surface: can have red (vascular component), grey-white (smooth muscle component) or yellow (adipose component) appearance
- May involve the intrarenal venous system , the renal vein or the vena cava despite being benign
- Tumours rarely have cystic component

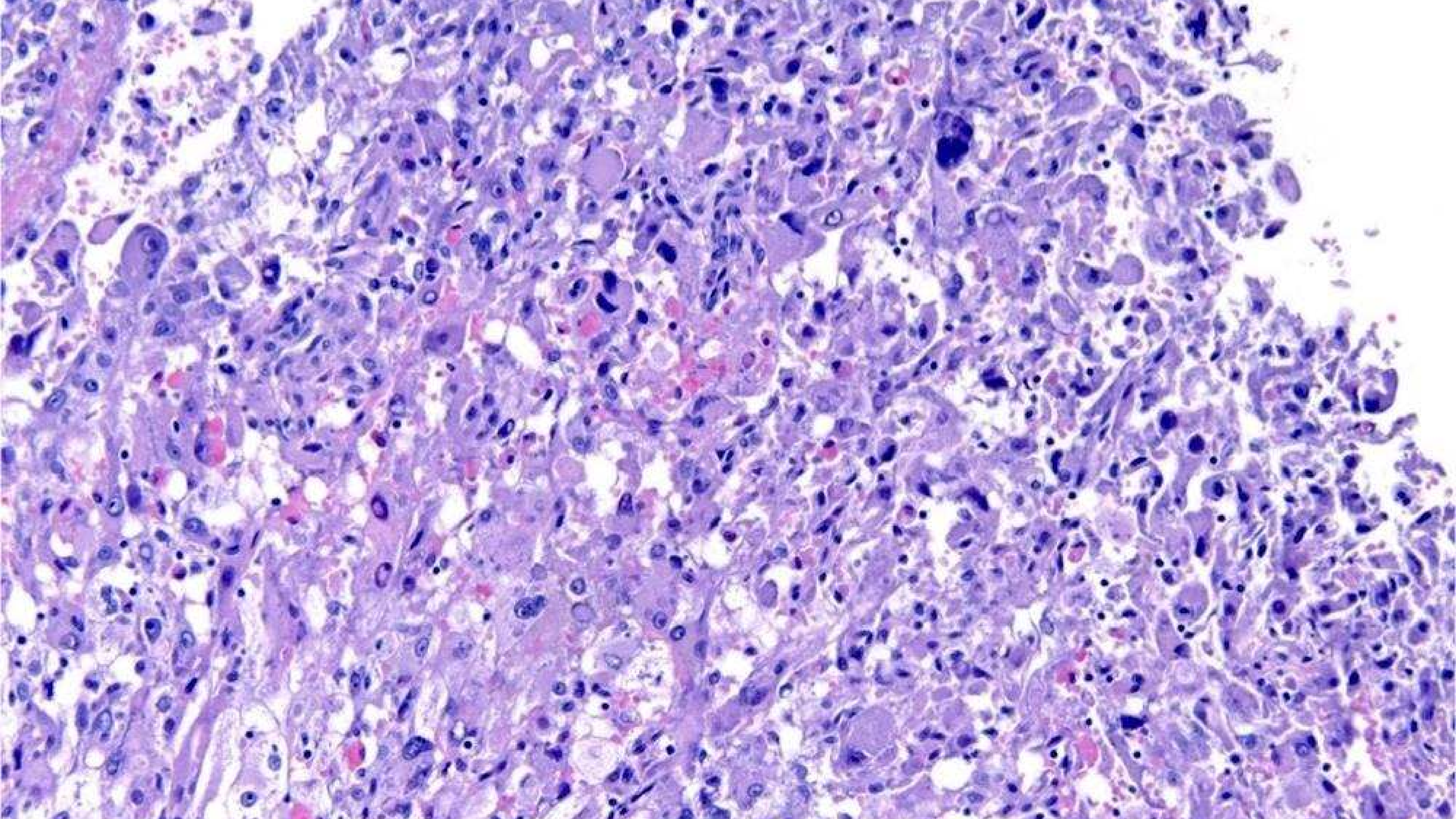
- Tumours are usually unilateral and unifocal
- Multiple (~33%) or bilateral(15%) tumours suggest underlying tuberous sclerosis

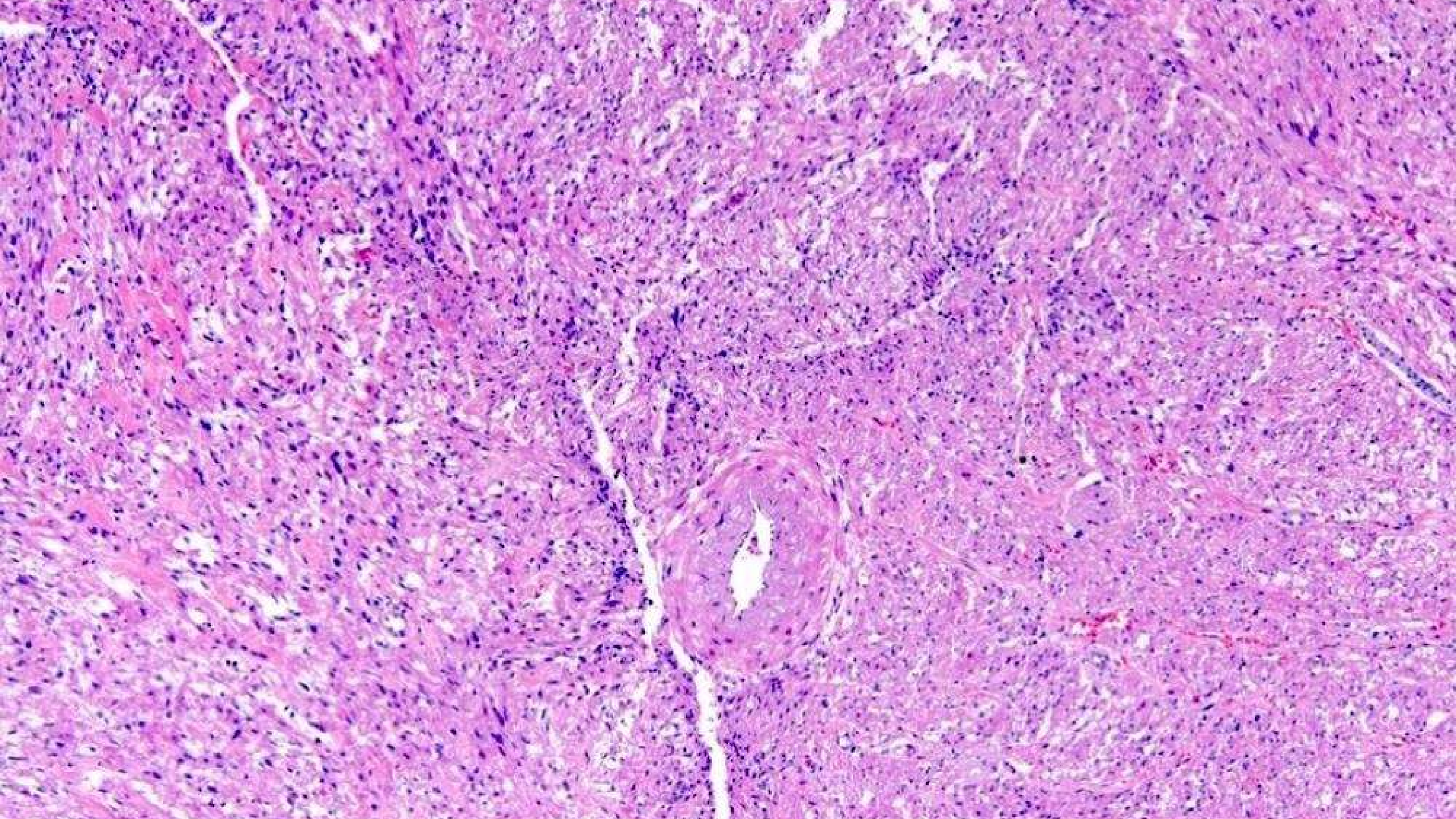
MICROSCOPY

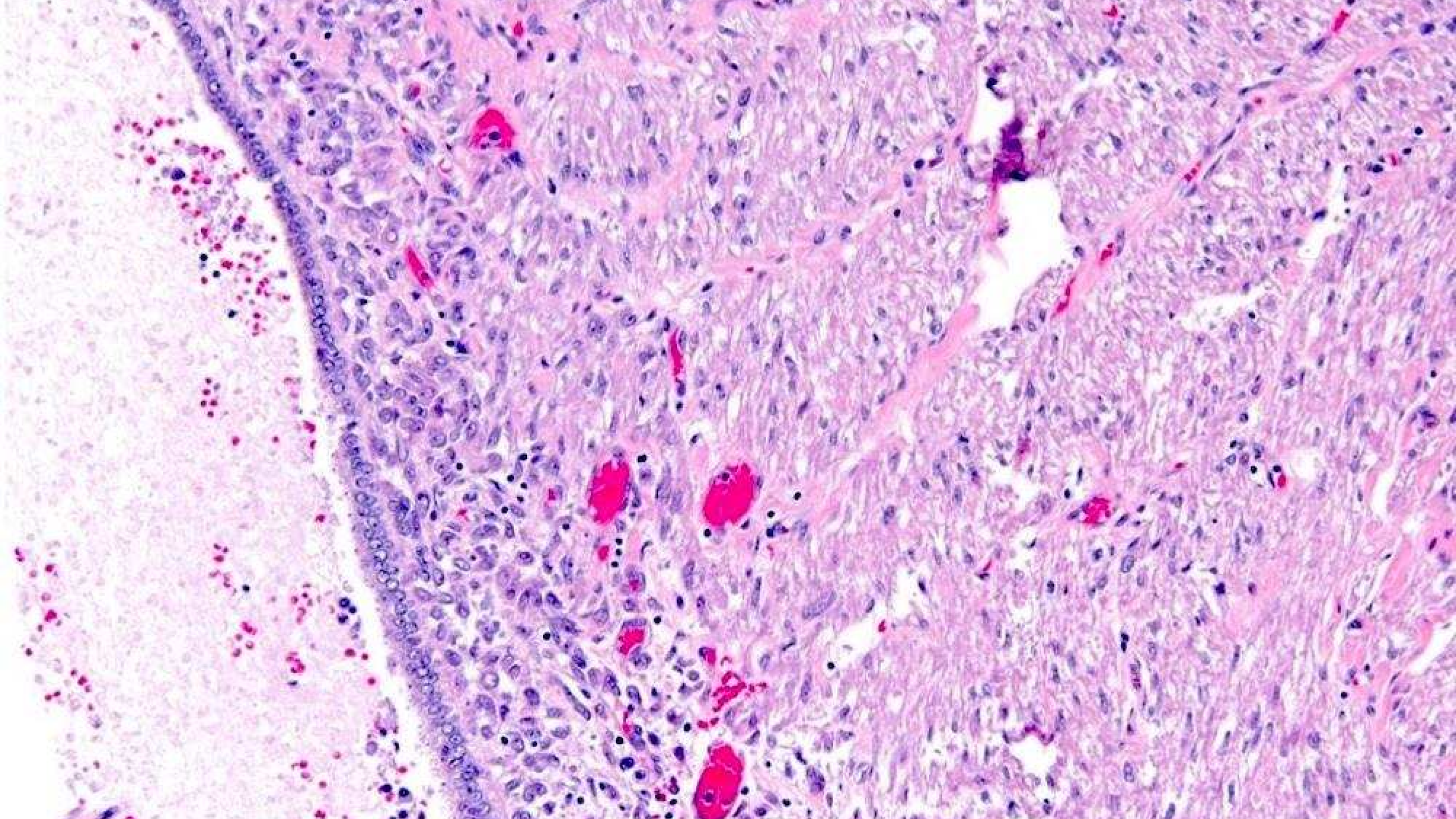
- Classic triphasic with Myoid spindle cells, mature adipose tissue and dysmorphic thick walled blood vessels without elastic lamina
- Smooth muscle component appears to originate from vessel walls and may be hyper cellular, atypical, pleomorphic or epithelioid
- Vascular component is in the form of thick walled hyalinized vessels
- Fat component is in the form of mature adipose tissue and is seen in more than 90% of tumours

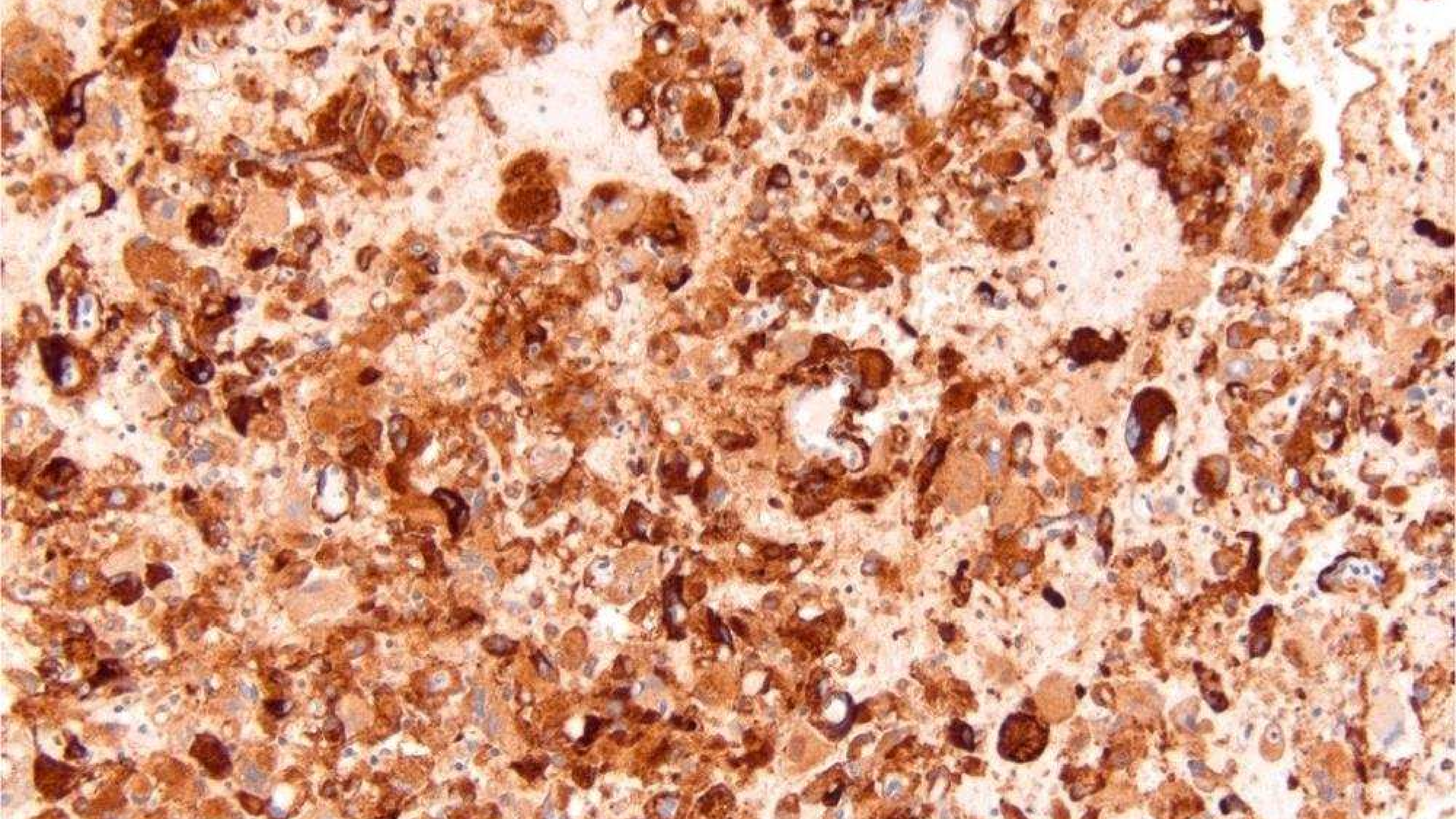
- ***Epithelioid variant:***
- Pure or pre-dominant population of polygonal cells with clear or densely eosinophilic cytoplasm, large, hyper chromatic, bizarre nuclei
- Multilobated nuclei and multinucleation is common
- Haemorrhage, mitotic figures and necrosis are common
- ***Angiomyolipoma with epithelial cysts (AMLEC)*** represents a morphologic spectrum of the tumours that is characterised by ***cysts lined by cuboidal or hobnail epithelial cells reminiscent of renal tubular epithelium***

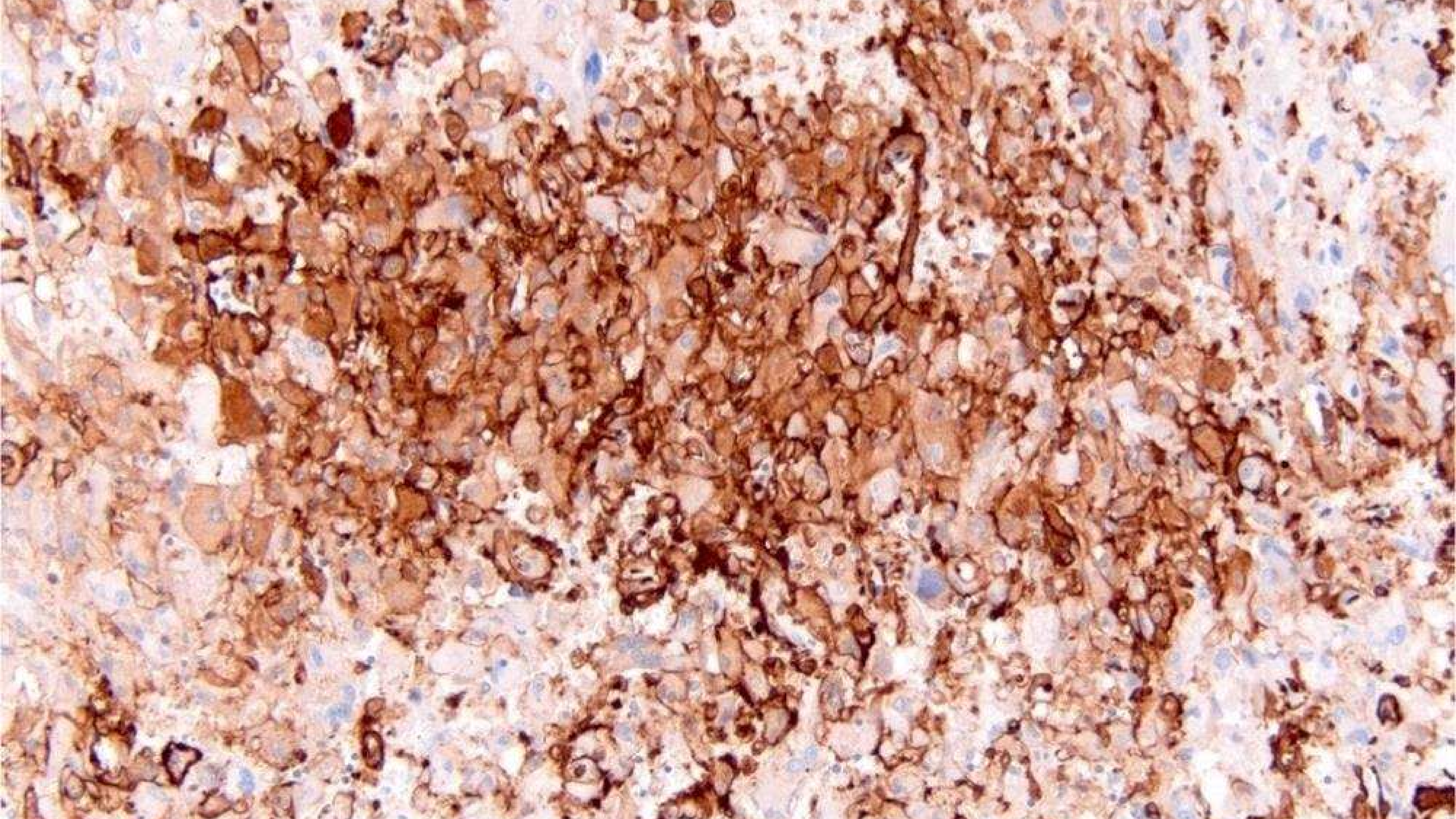












POSITIVE STAINS

- HMB45(melanocytic marker)
- MART1/ MelanA
- SMA(smooth muscle marker), calponin

NEGATIVE STAINS

- Cytokeratin
- PAX8
- CAIX
- GATA3
- Inhibin
- CD117

MOLECULAR/CYTOGENETIC

- TSC2 > TSC1 mutations in sporadic angiomyolipoma
- P53 mutation in epithelioid angiomyolipoma

DIFFERENTIAL DIAGNOSIS

- ***Renal cell carcinoma , clear cell type:***
- Tumours with sarcomatoid differentiation or fat invasion can mimick
- Positive for AE1/ AE3, PAX8
- Negative for SMA and melanocytic markers
- ***Well differentiated liposarcoma***:
- No vascular or adipose component , negative for melanocytic markers

✳ ***Leiomyoma:***

- No vascular or adipose component
- Negative for melanocytic markers

✳ ***Leiomyosarcoma:***

- Prominent atypia , infiltrative, usually no vascular or adipose component
- Negative for melanocytic markers

- ***Pleomorphic rhabdomyosarcoma:***
- Smooth muscle component is markedly atypical, tumour is infiltrative, no vascular or adipose component
- Negative for melanocytic markers
- ***Melanoma:***
- Marked atypia, no adipose or vascular component
- Negative for SMA

- **Oncocytoma:**
- No adipose or vascular component; oncocytes seen
- Negative for melanocytic markers and SMA
- ***Mixed epithelial and stromal tumour of the kidney (MEST):***
- Ovarian stroma like spindle cells of the solid MEST component are positive for SMA, desmin , ER, PR and FOXL2 and negative for melanocytic markers
- Epithelial component of MEST is similar to AMLEC and is positive for PAX8.