CASE OF THE MONTH FEBRUARY 2019

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ATTENDING CONSULTANT

PATHOLOGY

RGCIRC

CASE PRESENTATION

- A 60 year old lady, an operated case of endometrial tumor, post TAH+BSO WITH RPLND presented after 2 months with right sided scapular and costal region pain which got aggravated with movement.
- There was no history of trauma/ prolonged fever.
- There was no history of previous radiation/ chemotherapy.
- The patient was a diabetic since 10 years and suffering from hypothyroidism for 6-7 years

EXAMINATION

- At presentation, she was conscious, oriented with normal cranial examination.
- Motor examination revealed mild weakness in left lower limb(power- 4-/5) with normal power in all other limbs.
- There was graded sensory loss to touch and pain below D6 level.

INVESTIGATION

- **MRI Spine** revealed a large enhancing solid lesion (54 x 33 x 40mm) involving the right posterior elements, spinous process and extending to the posterolateral aspect of the vertebral bodies of D5 & D6 vertebra.

- The lesion was involving the right 5th costovertebral junction, posterior paravertebral soft tissues and extending to the right posterolateral epidural space of the dorsal spine canal, compressing and displacing the dorsal cord to the left lateral aspect of the spinal canal.

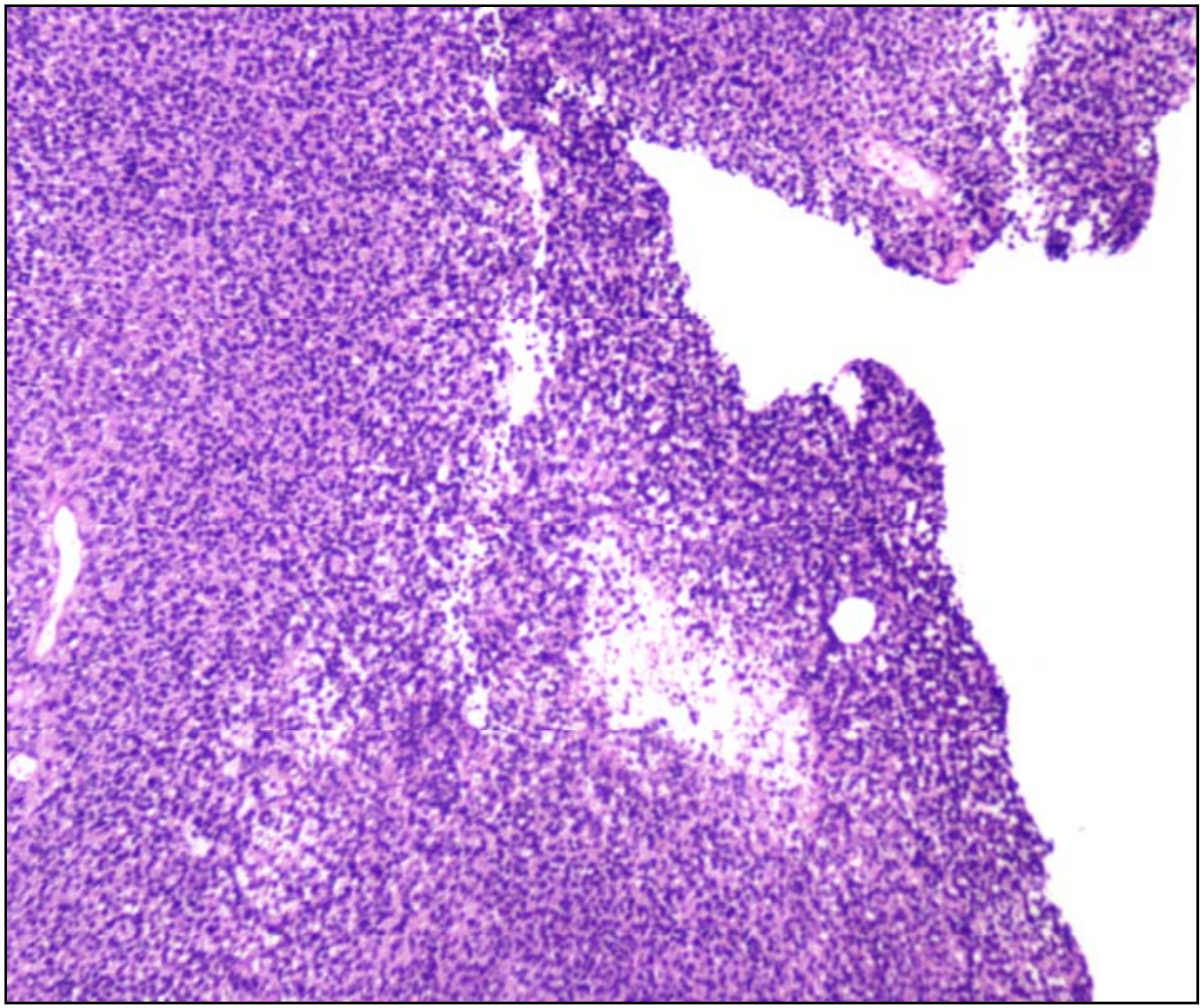
INVESTIGATION

- **Whole Body PET CT** revealed :
- Metabolically active metastatic peritoneal deposits in left paracolic gutter and right pelvic regions.
- Metabolically active irregular enhancing hypodense lesion in segment IV of liver.
- Metabolically inactive few retroperitoneal lymphnodes
- Hypermetabolic destructive lytic lesion with associated soft tissue component and interspinal extension involving D5 and D6 vertebra

SURGERY

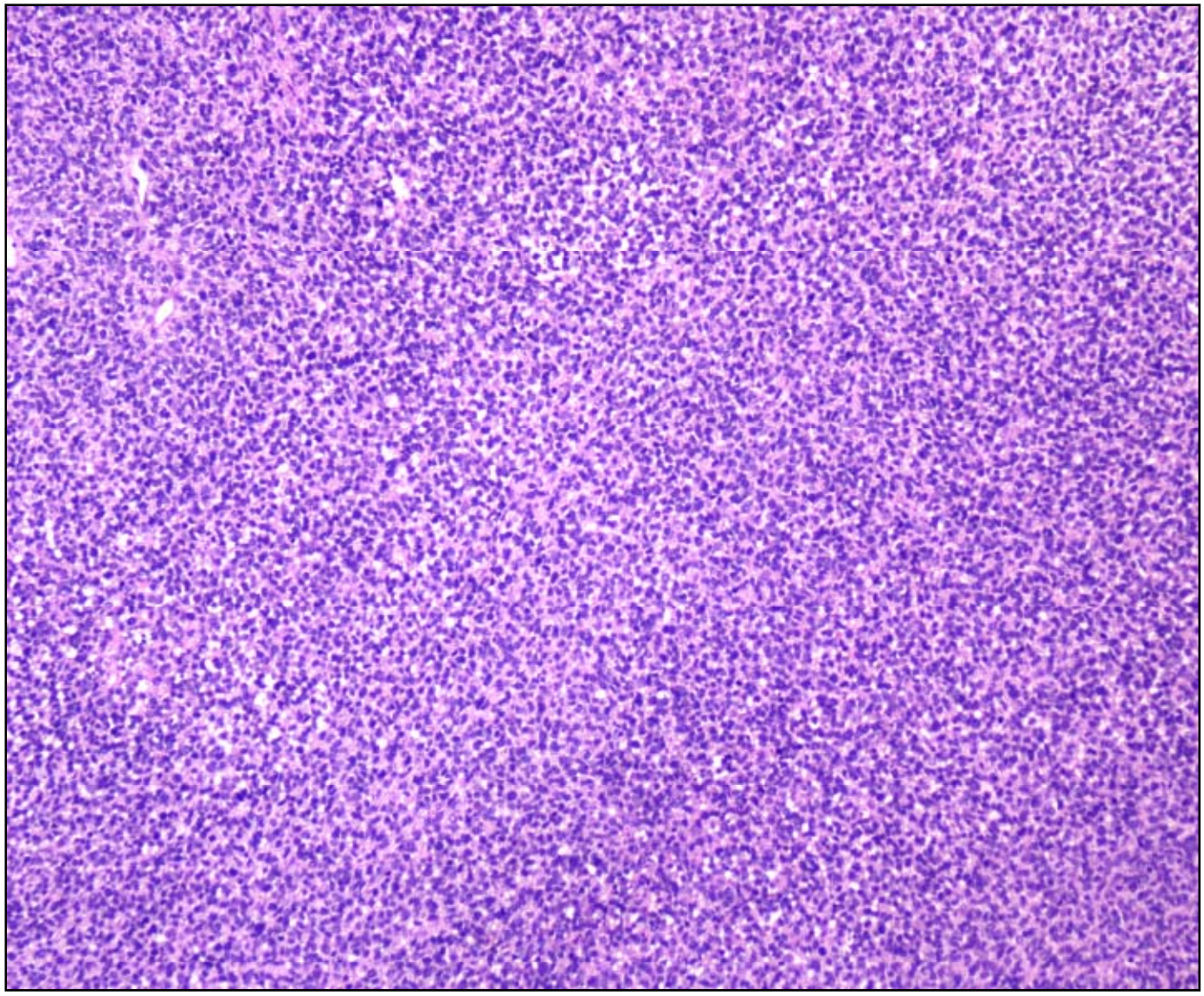
- D5 decompressive laminectomy + tumor removal was done and sent for histopathology

HISTOPATHOLOGY



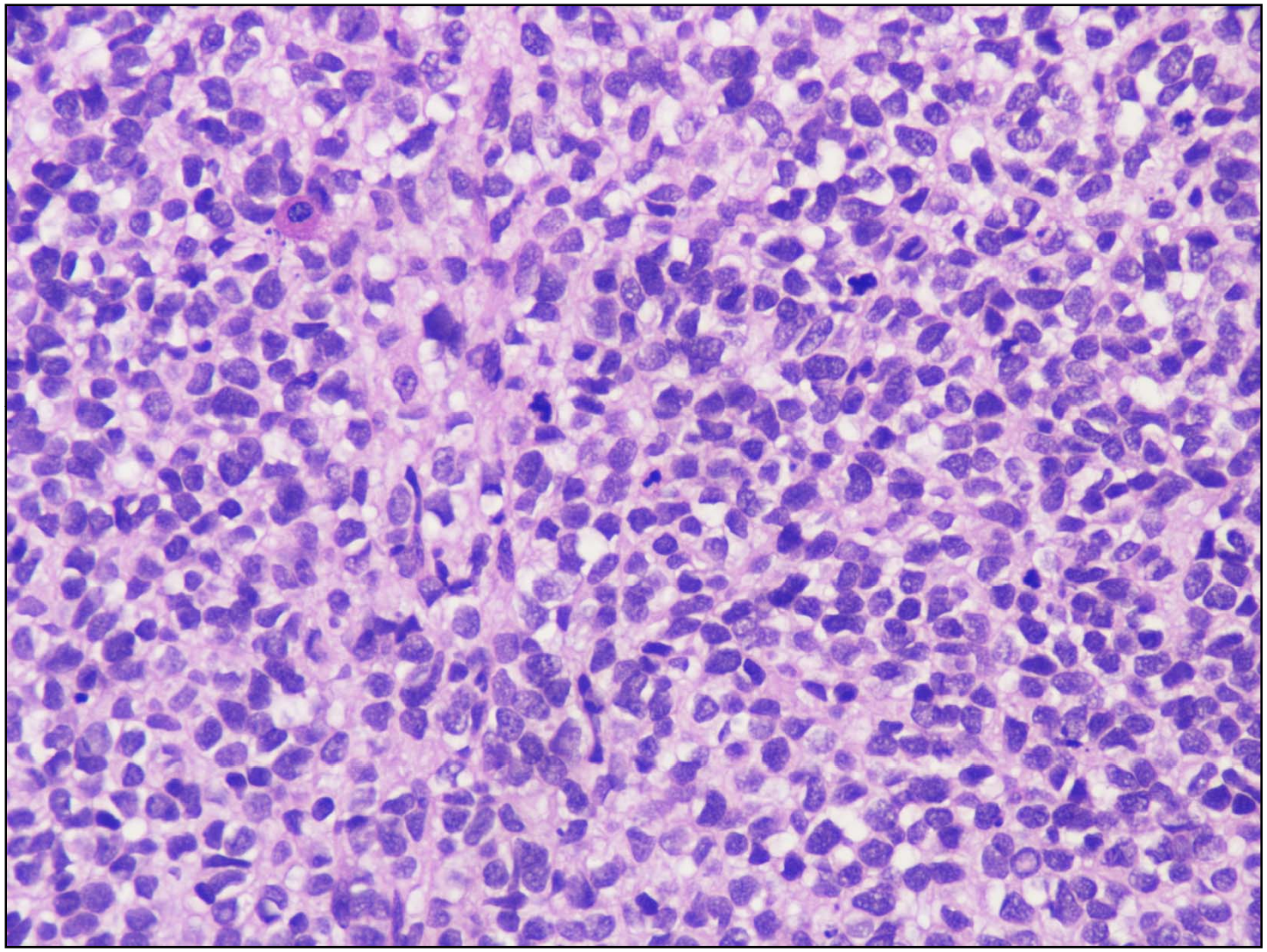
Sections show a cellular tumor arranged in solid sheets

(H & E, 40x)



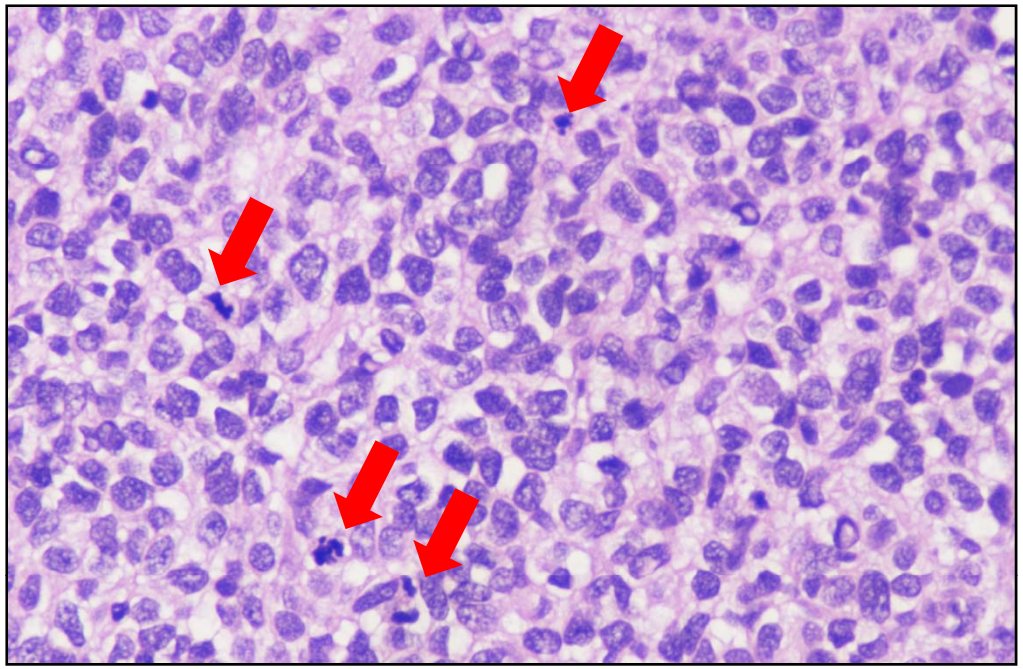
The cells have round to oval monomorphic appearance

(H & E, 40x)



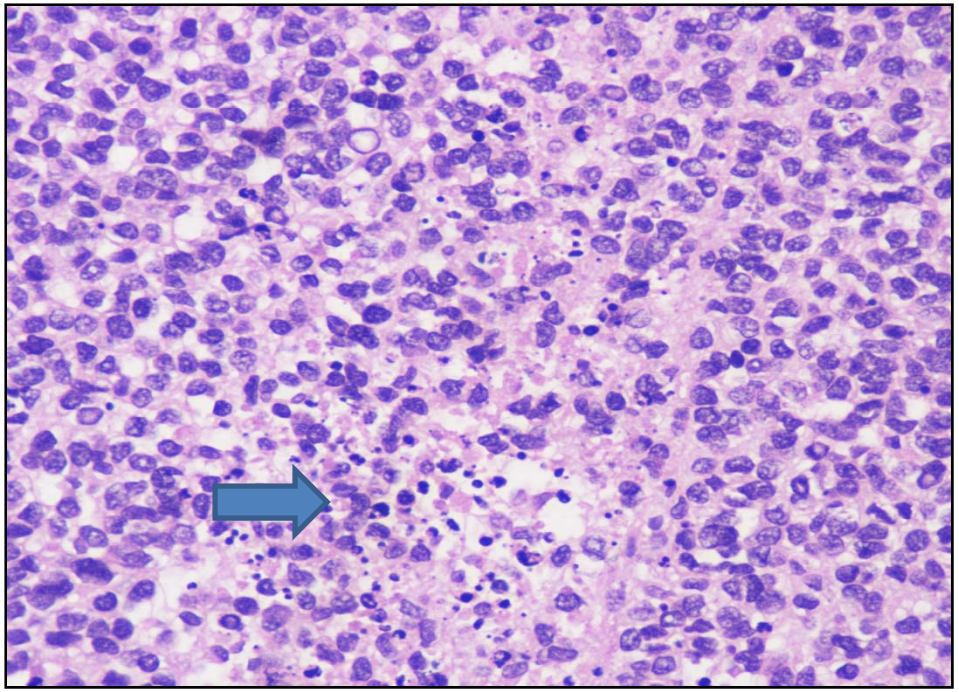
The cells have scant to moderate cytoplasm, fine granular chromatin and inconspicuous nucleoli

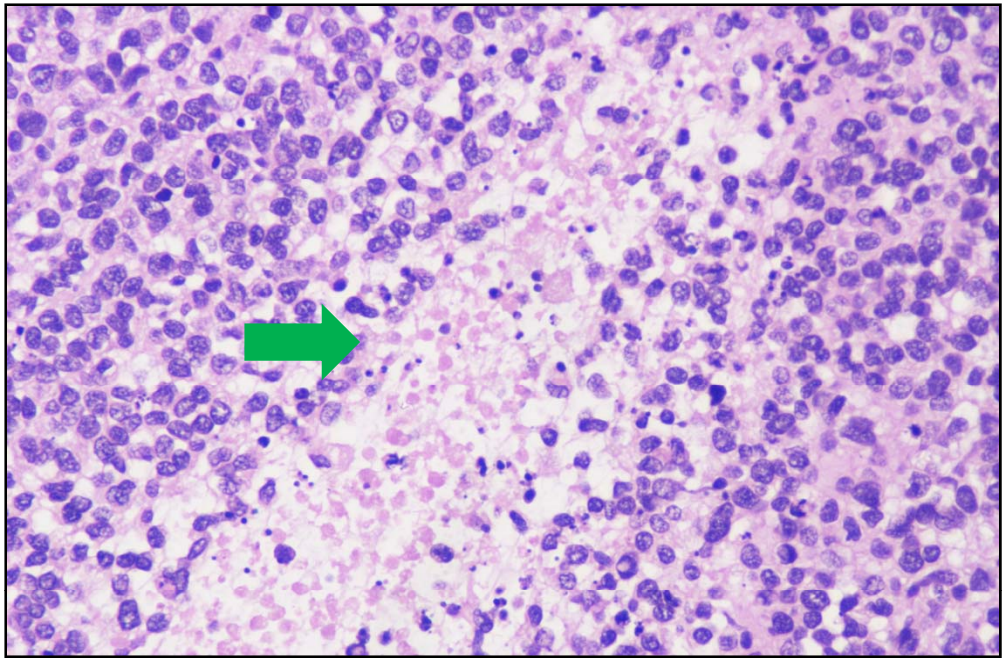
(H & E, 400x)



Brisk mitosis(>10/10HPF) noted.(red arrows)

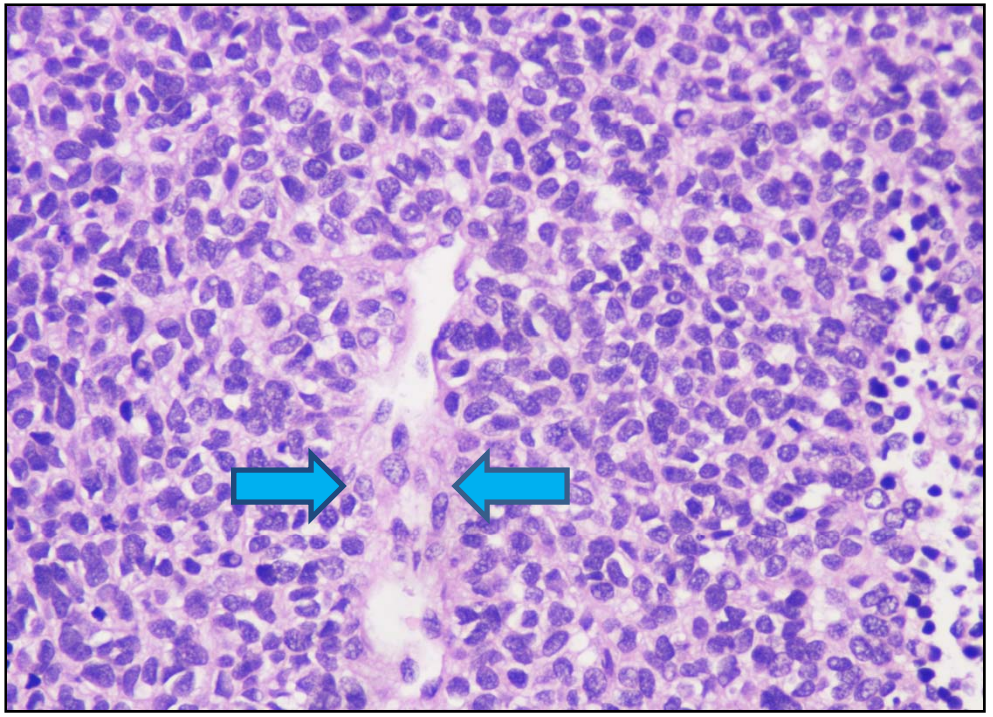
Apoptosis readily noted(blue arrow)





Areas of necrosis seen(green arrow)

Few small capillaries noted



SUMMARY OF HISTOPATHOLOGY

- Sections show a cellular tumor arranged in solid sheets with cells having round to oval monomorphic appearance with fine granular chromatin and inconspicuous nucleoli with few small capillaries.
- Brisk mitosis(>10/10HPF) and apoptosis noted.
- Areas of necrosis seen.

HISTOMORPHOLOGICAL DIFFERENTIAL DIAGNOSIS

- High grade endometrial stromal sarcoma
- Metastatic poorly differentiated carcinoma
- Ewing’s sarcoma
- Malignant mixed mullerian tumor

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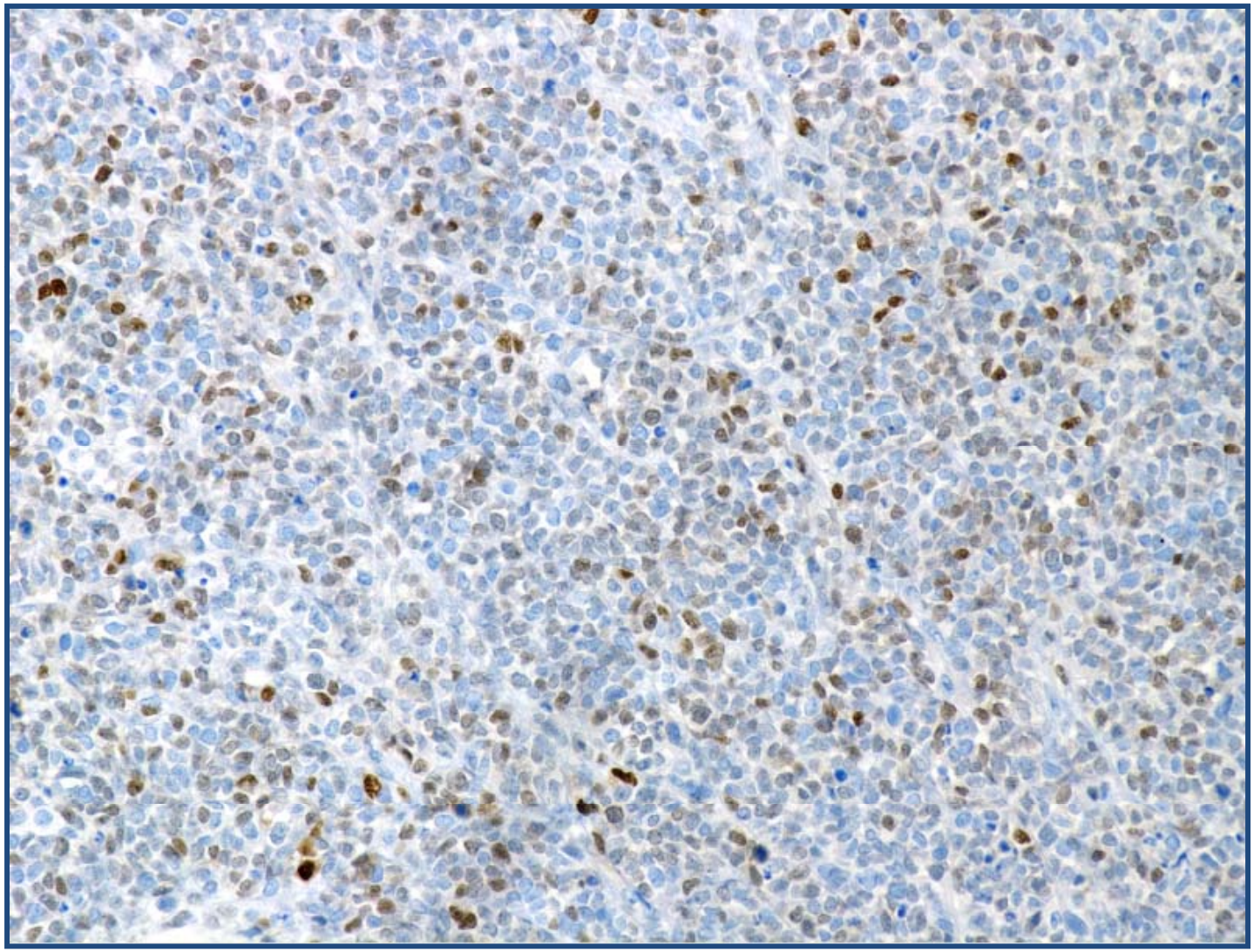
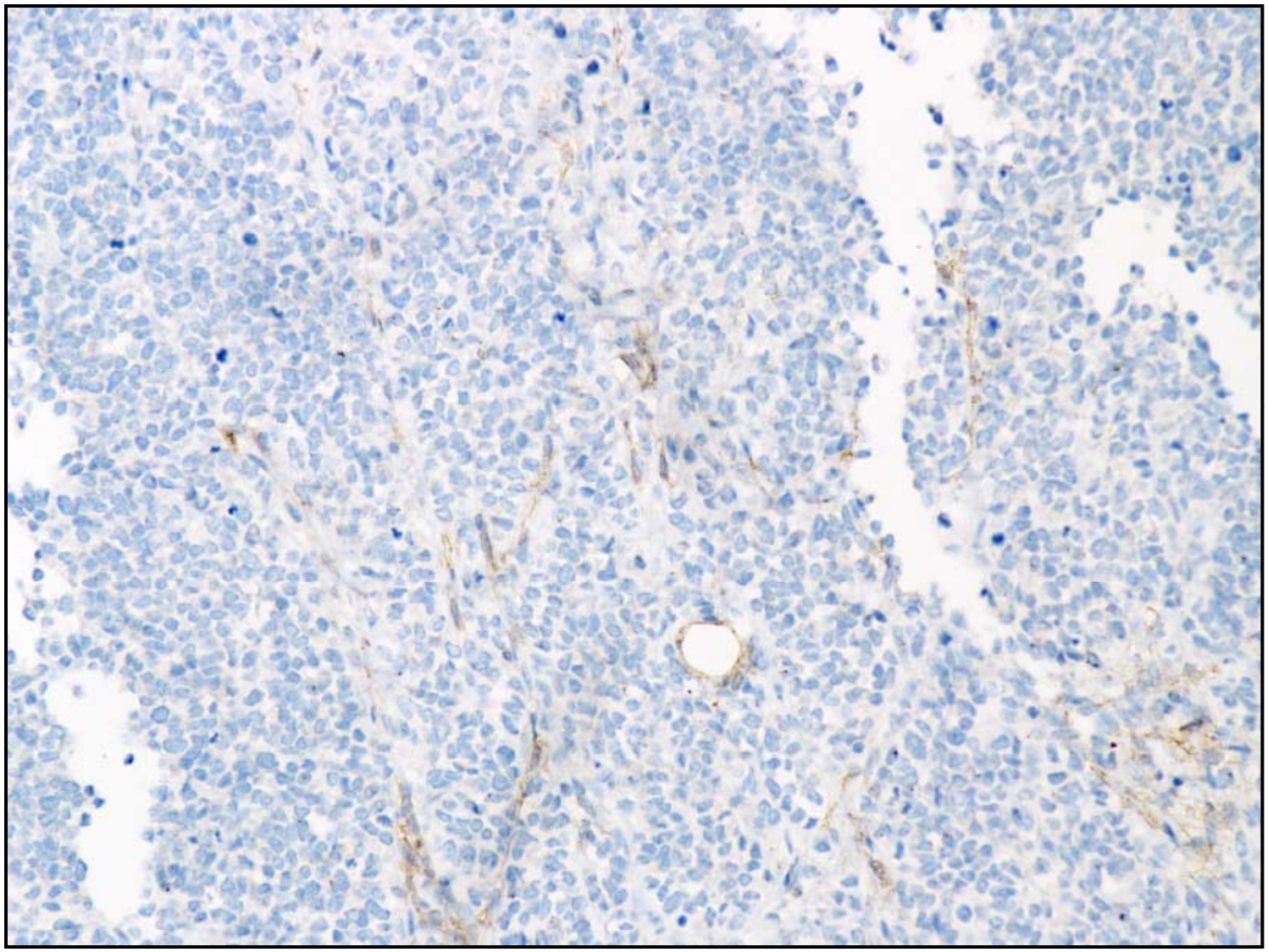
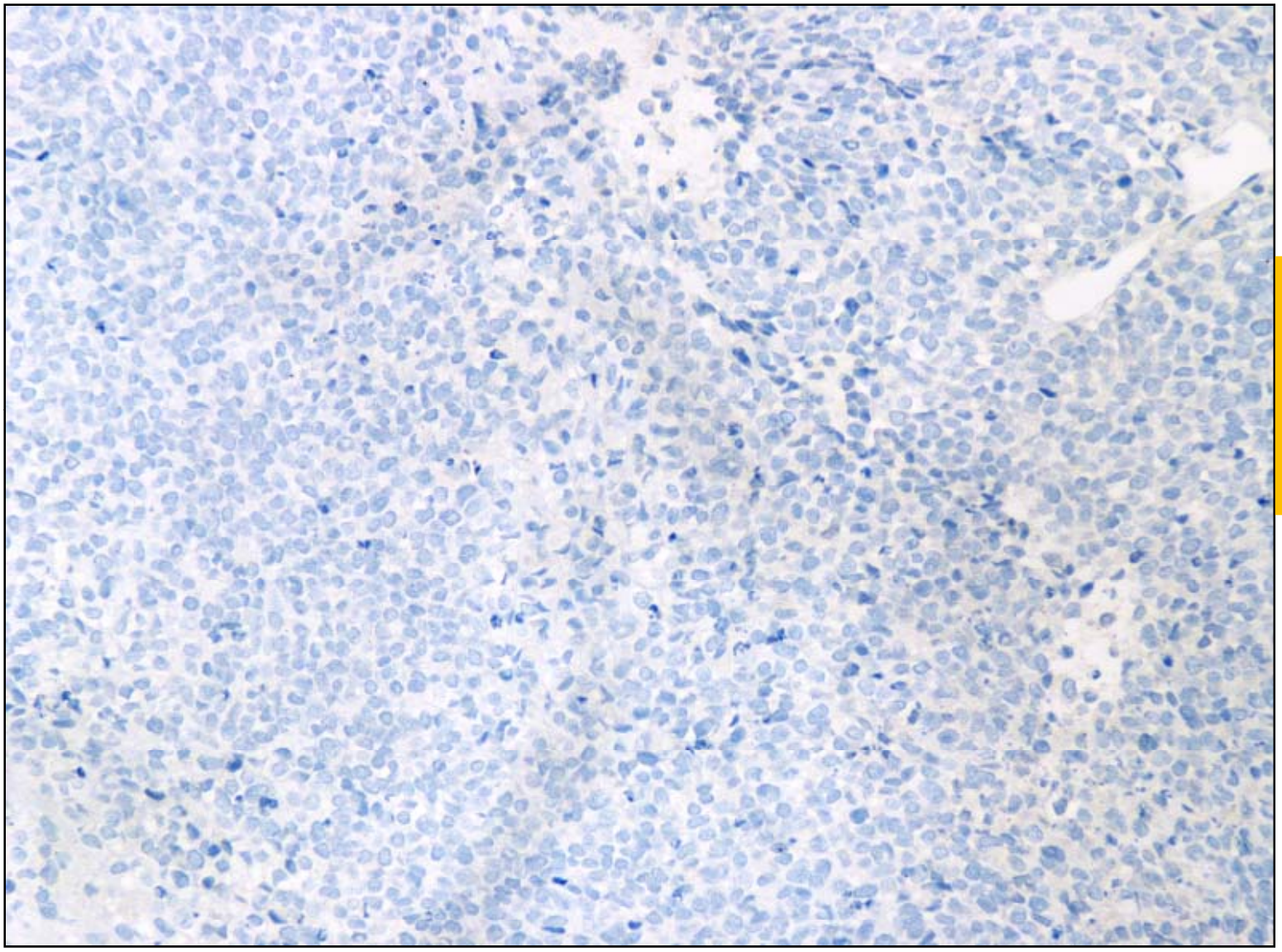


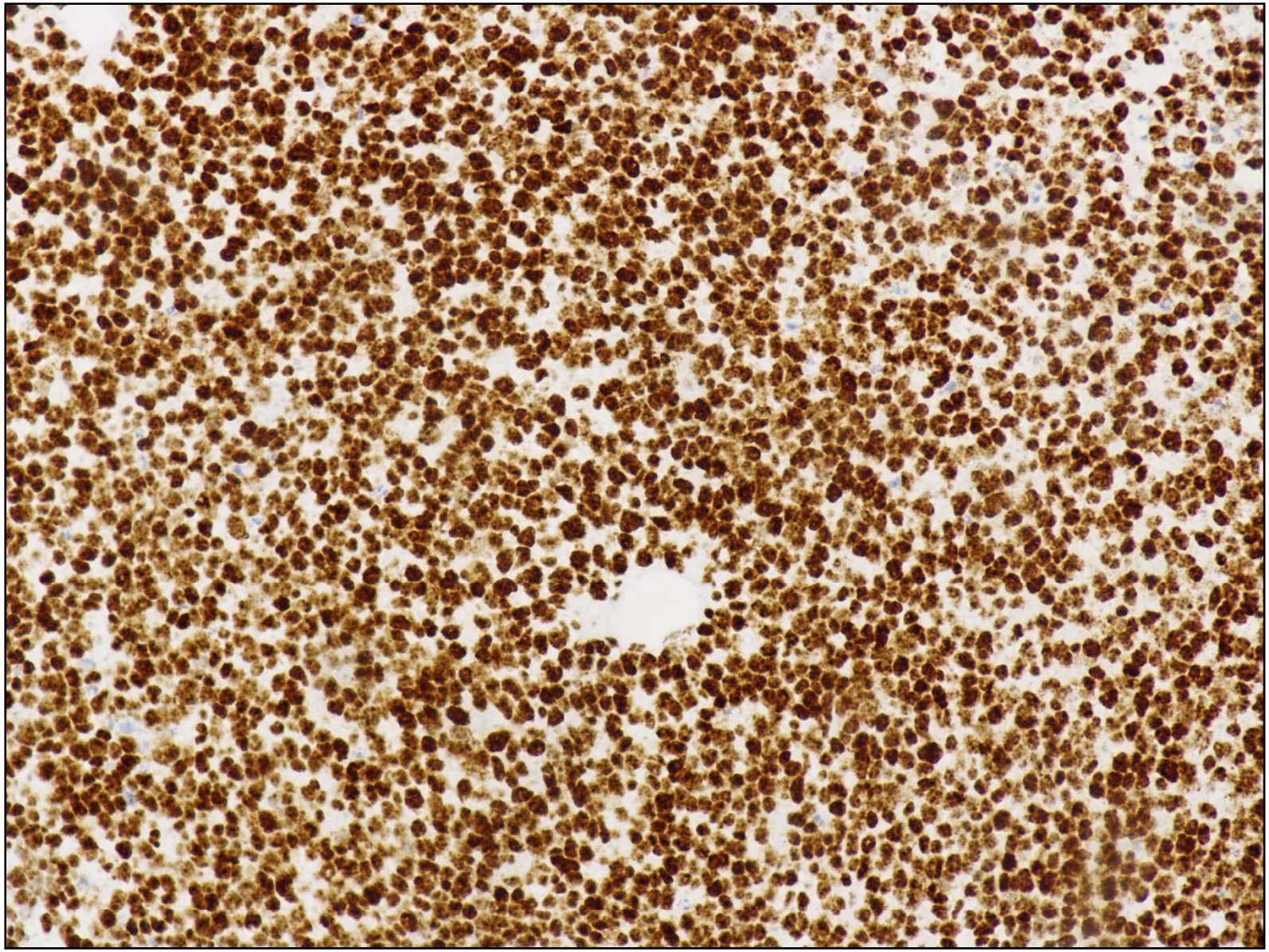
CYCLIN D1
POSITIVE



CD10
NEGATIVE



CK,P16,
CD10,SMA,
ER,PAX8,
NKX2.2
NEGATIVE



MSH6,
MSH2,
MLH1
PMS2
INTACT

SUMMARY OF IHC

POSITIVE	NEGATIVE
CYCLIN D1	CK,P16,CD10,SMA,ER,PAX8, NKX2.2.

- There was retained expression of MSH6,MSH2,MLH1 AND PMS2

FINAL DIAGNOSIS

- **OVERALL FEATURES ARE SUGGESTIVE OF METASTASIS OF HIGH GRADE ENDOMETRIAL STROMAL SARCOMA**

MOLECULAR STUDIES

- Next generation sequencing and tumor mutation burden analysis were done
- **Mutation load**:0.83 Mutations/Mb(not significant)

NGS

Clinically Significant Biomarkers

Indicated Contraindicated

Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
BRAF p.(G469R) c.1405G>A B-Raf proto-oncogene, serine/threonine kinase	None	vemurafenib	0

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
BRAF	p.(G469R)	c.1405G>A	COSM457	chr7:140481403	32.25%	NM_004333.4	missense(pathogenic)
JAK1	p.(=)	c.2199A>G	.	chr1:65310489	48.79%	NM_002227.3	synonymous
ALK	p.(I1461V)	c.4381A>G	.	chr2:29416572	99.65%	NM_004304.4	missense (benign)
IDH1	p.(=)	c.315C>T	.	chr2:209113192	99.00%	NM_005896.3	synonymous
FGFR3	p.(=)	c.1953G>A	.	chr4:1807894	99.90%	NM_000142.4	synonymous
PDGFRA	p.(=)	c.1701A>G	.	chr4:55141055	99.65%	NM_006206.5	synonymous
KIT	p.(M541L)	c.1621A>C	.	chr4:55593464	49.45%	NM_000222.2	missense
FGFR4	p.(=)	c.483A>G	.	chr5:176517985	48.13%	NM_213647.2	synonymous
EGFR	p.(=)	c.2361G>A	.	chr7:55249063	52.66%	NM_005228.4	synonymous
RET	p.(=)	c.2307G>T	.	chr10:43613843	99.95%	NM_020975.4	synonymous
RET	p.(=)	c.2712C>G	.	chr10:43615633	50.50%	NM_020975.4	synonymous
MAP2K2	p.(=)	c.192C>T	.	chr19:4117528	47.05%	NM_030662.3	synonymous

YWHAE-FAM22 genetic fusion usually found in high grade ESS was not included in the panel for NGS as it is not a targetable molecular event

SUBSEQUENT MANAGEMENT

- She was maintained on regular physiotherapy.
- She was referred for Palliative External Beam Radiotherapy.
- **She received** 20Gy/5# given 5 days a week
- She was being discharged in stable condition.

DISCUSSION

- This case has been presented because of the rarity of the metastatic presentation at this site (spine).
- Endometrial Stromal Sarcoma (ESS) is a rare tumour (less than 10% of uterine sarcomas and 0.25% of all malignant uterine tumours), affecting women with an average age of 45 years.
- The most common metastatic sites of endometrial stromal sarcoma include GIT, pelvis and lung.
- Bone metastases are rare and the few cases were reported in axial skeleton (dorsal and lumbar vertebrae, sacrum, and iliac bones).

- Most ESSs are clinically indolent, histologically classified as low-grade, with a 5-year survival rate of 65%.
- In contrast, high-grade or undifferentiated ESS cases are more aggressive with less than a 25% 5-year survival.
- The microscopic diagnosis of ESS at this site may be challenging and requires a comprehensive IHC panel for the accurate diagnosis.
- The previous history of a primary uterine tumor aided in the diagnosis as in our case.

HIGH GRADE ENDOMETRIAL STROMAL SARCOMA

- A malignant tumor of endometrial stromal derivation with high grade round cell morphology sometimes associated with a low grade spindle cell component.

- Age group:28-67(mean 50)

- Clinical features:

✓ Abnormal vaginal bleeding

✓ Pelvic mass

- Histopathology :

✓ Confluent, permeative and destructive growth

✓ Close juxtaposition of high grade round cells and low grade spindle cells

✓ Mitotic activity >10/10hpf

✓ Necrosis usually present

- IHC:

  Usually Cyclin D1 positive

  CD10,ER,PR negative(unlike low grade ESS)

- Genetic profile:YWHAE-FAM22 genetic fusion as a result of t(10;17)(q22;p13)
- Prognosis: earlier and more frequent recurrences compared to low grade ESS