DOUBLE TROUBLES – PRESENTING A SERIES OF DUAL PRIMARY MALIGNANCIES.

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CASE1

- 46 year old female -Right breast lump since 5 months with history of easy fatiguability and backache.
- Examination of Right breast lump -upper outer quadrant lump 6x5 cm with single palpable axillary node -**cT3N1** lesion**.**
- Trucut biopsy breast lump- Invasive ductal carcinoma, NOS, triple negative breast cancer(TNBC), grade 3.
- Urinary Bence Jones proteins – positive

- PET- CT suggestive of Right breast lesion was 6x 5 cm with right axillary lymph node 2 x 2cm with diffuse FDG uptake involving axial and appendicular skeleton noted.
- Bone marrow biopsy -80% plasma cells with M band, 9.2 g/dL IgG Kappa, Serum B2 microglobulin – 10.6 mg/L.
- Multiple myeloma (MM)- stage RISS/ISS III
- Started on bortezomib + lenalidomide + dexamethasone -8 cycles.
- NACT 4 cycles – Adriamycin + Cyclophosphamide -for carcinoma breast.

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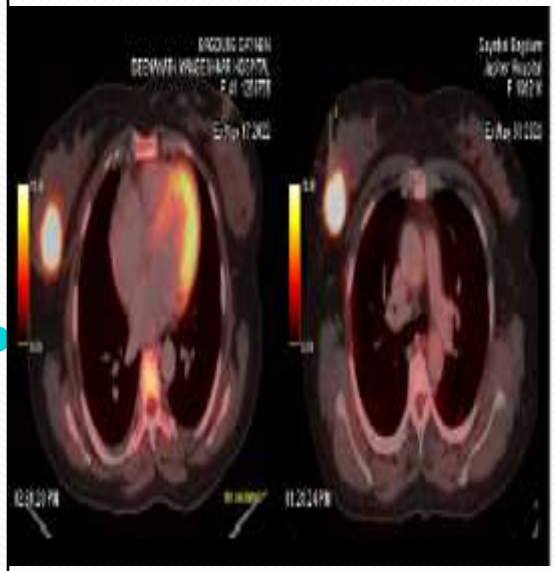

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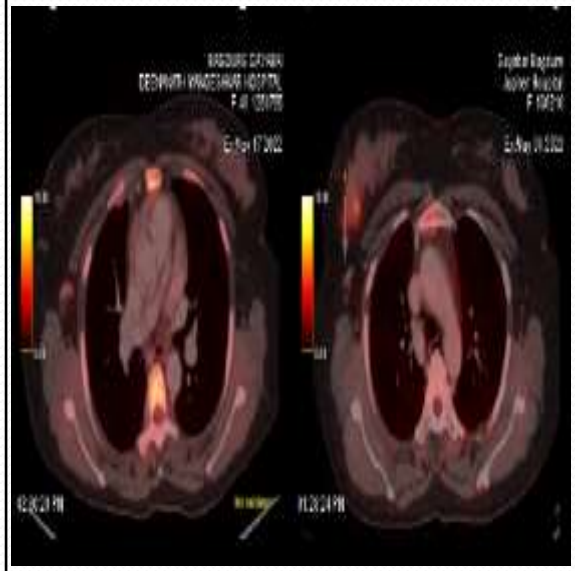

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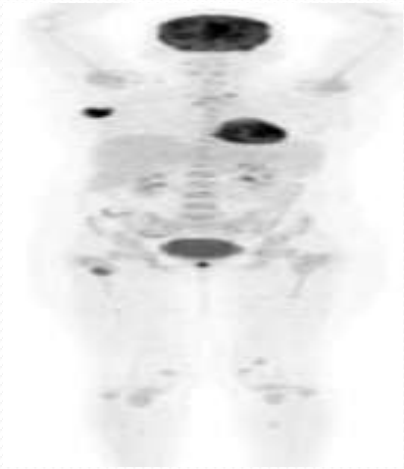

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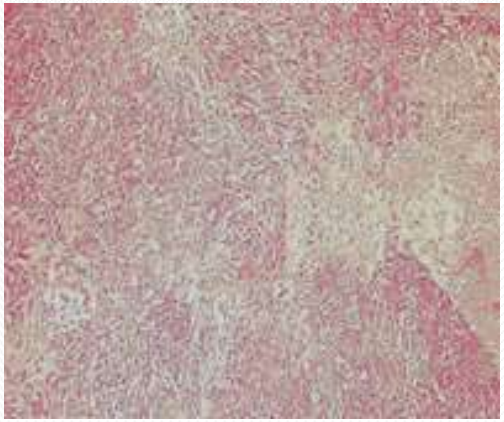

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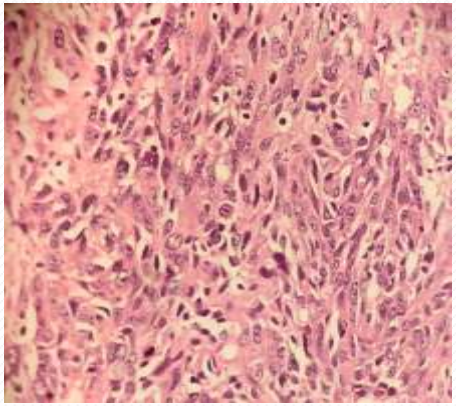
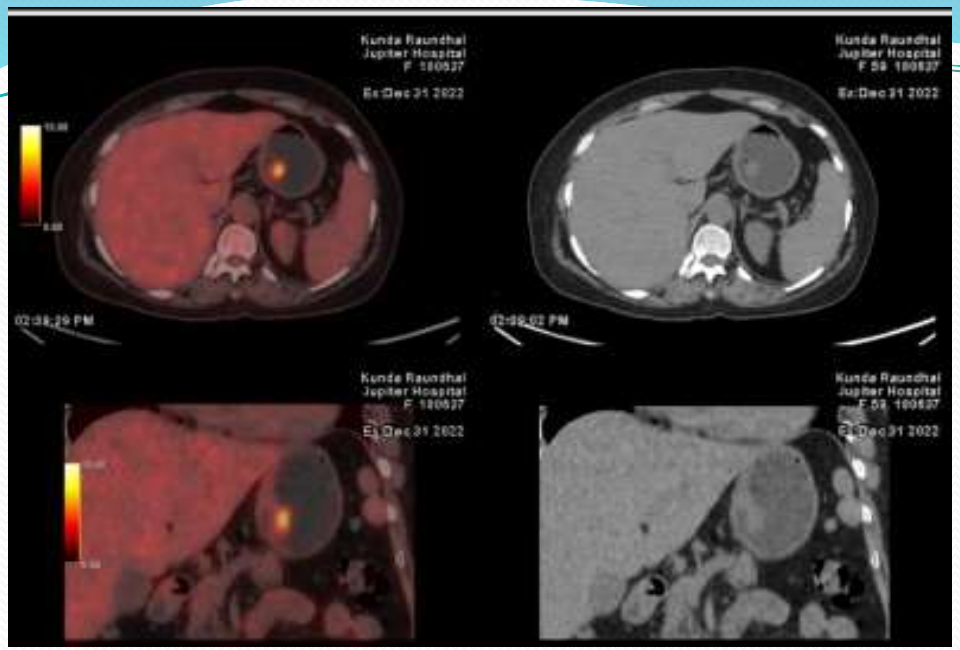


- PETCT- post NACT suggestive of right breast lump- 3.5 x 3.1cm (SUVm 42.2 -> 19.7) and right axillary Lymph node- 1.4 x 0.5cm (SUVm 2.4 -> 2.5).
- Decrease in size of breast lesion and metabolic activity of skeletal lesions were noted.
- Patient underwent right sided modified radical mastectomy(MRM)
- Post operatively – 4 cycles of adjuvant paclitaxel chemotherapy,
- Weekly bortezomib and dexamethasone for multiple myeloma and is on follow up with no recurrent disease.

CASE2

- 53 year old female presented with polypoidal growth in the left nasal cavity.
- HPE of biopsy from polypoidal lesion is s/o undifferentiated carcinoma .
- Wide local excision WLE (left cheek+ ala+vestible) with nasolabial flap with modified neck dissection (MND)Type II was done.

- HPE of excised specimen is suggestive of **invasive malignant melanoma pT4bN2a ,** with margins negative, 2/32 nodes positive for tumor, perineural invasion present .IHC is positive for HMB 45.
- Adjuvant immunotherapy was advised but due to financial constraints patient deferred the treatment.
- There is doubtful benefit of adjuvant chemotherapy and radiotherapy and patient was kept under surveillance.



- PET CT scan done after 2 months of follow up was suggestive of FDG avid intraluminal nodular lesion in proximal part of stomach.
- UGI endoscopy revealed polypoidal lesion with ulcerated mucosa in proximal stomach below GEJ.
- Biopsy stomach lesion- Adenomatous polyp with Grade II Adenocarcinoma.

- As performance status of patient was good, Proximal partial gastrectomy was done.

- HPE was suggestive of **adenocarcinoma microinvasive** – pT1a- moderately differentiated, invades muscularis mucosa, all margins free , no lymphovascular invasion, no perineural invasion, no lymphnodes positive for tumor.

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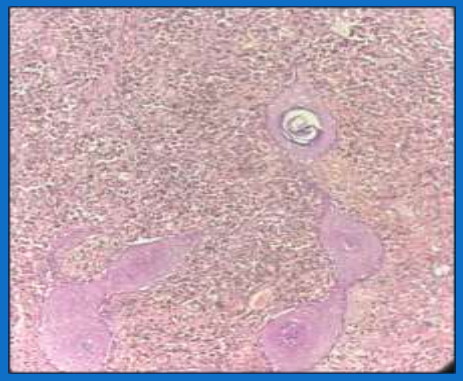

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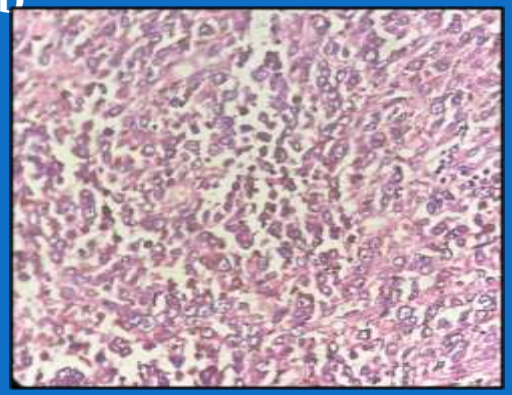

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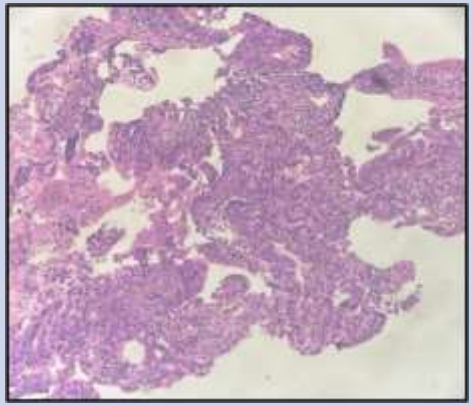

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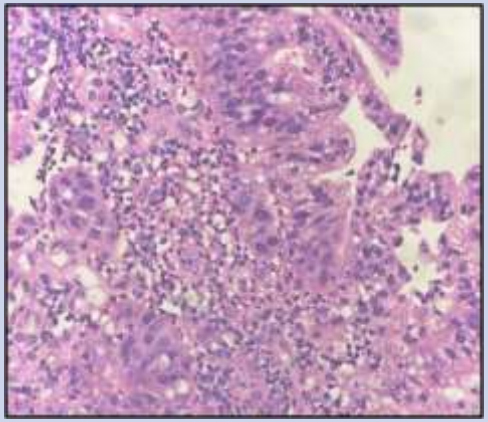


- No Adjuvant treatment was required for Ca stomach. Patient is in follow up with no recurrent disease.

CASE 3

- 60 year old gentleman presented with abdominal pain, decreased appetite , weight loss, bleeding PR since 2 months.

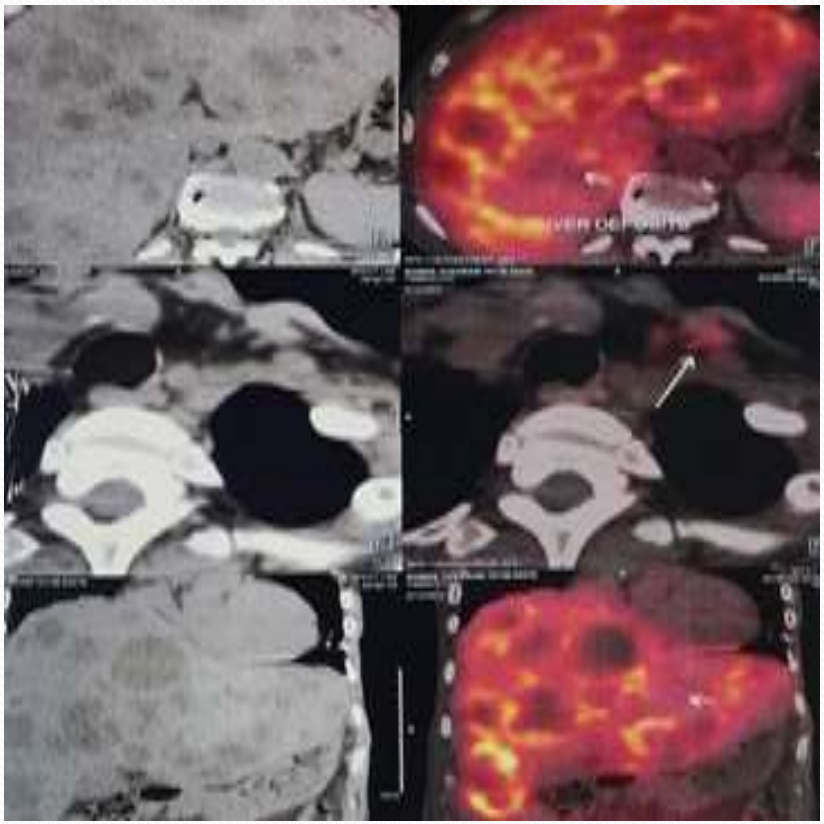
- On examination- liver is enlarged with hard, irregular liver border. Per rectal examination revealed grade 2 prostate, hard in consistency.

- CECT abdomen and pelvis suggestive of Multiple liver metastasis with enlarged prostate.

- Serum prostate specific antigen (PSA) -100 ng/ml, carcino embryonic antigen (CEA)- 64 ng/ml.

- TRUS- Prostate Biopsy diagnosed with adenocarcinoma with gleasons score 4+5- CA prostate with neuroendocrine differentiation.

- PSMA PET scan suggestive of - PSMA ligand uptake in prostate, inguinal -pelvic abdominal nodes, liver, skeletal deposits



PSMA PET scan suggestive of - PSMA ligand uptake in prostate, inguinal -pelvic abdominal nodes, liver, skeletal deposits.

- Colonoscopy suggestive of 2 small sessile polyp in rectum
- Biopsy- Rectal polyp- s/o poorly differentiated adeno carcinoma .
- IHC Rectal biopsy- CDX2 positive.

- IHC of liver biopsy- CK 7 ,CK20,CDX2 Negative, PSA strongly positive, CEA positive in few cells, suggestive of metastasis from **prostatic adenocarcinoma**

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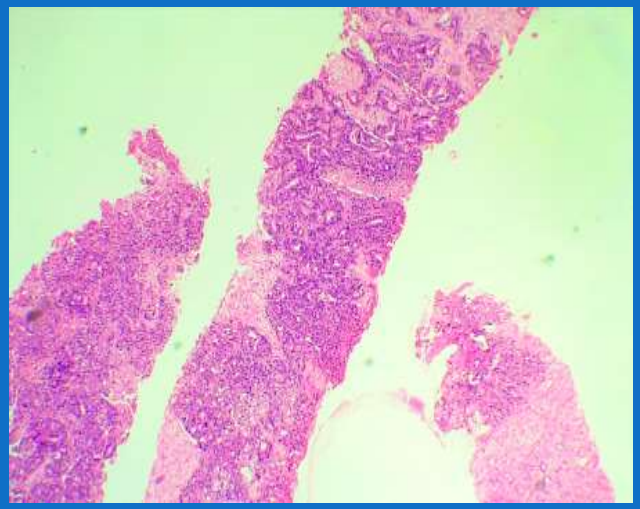

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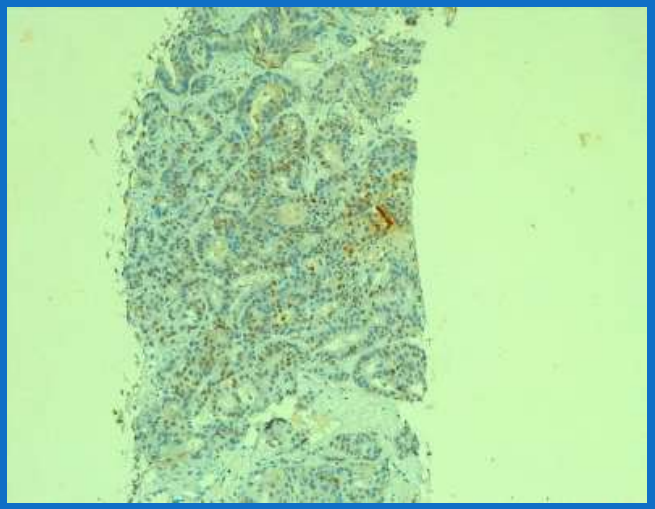

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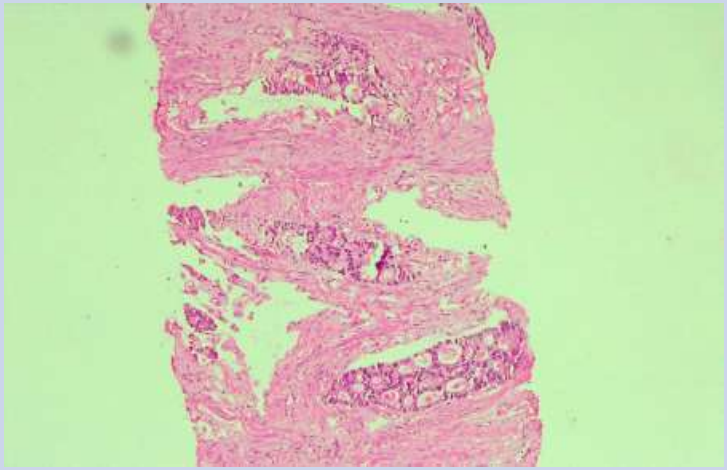

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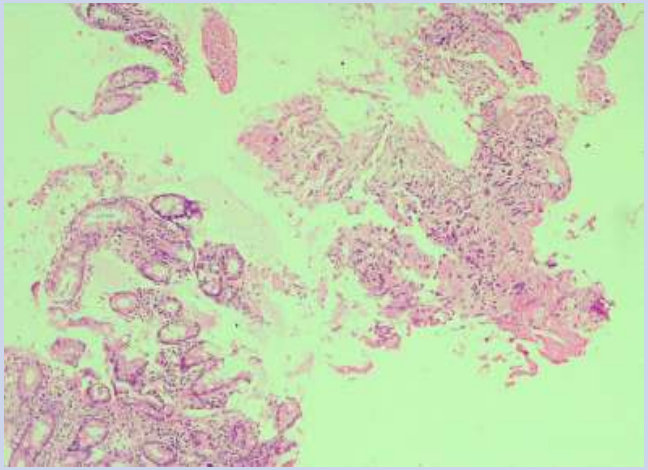

- Bilateral Orchidectomy was done and bicalutamide was started .

- Patient did not follow up subsequently and died of liver disease.

CASE 4

- A 55 year old female presented with abdominal distention since 6 months with no h/o respiratory distress.
- USG abdomen and pelvis is suggestive of **22x19cm** cystic mass lesion arising from right ovary with multiple septae (pelvis till epigastrium).
- Serum (beta HCG)- 2.9 mIU/ml, serum (AFP)-2.8 ng/ml, CA-19.9-2.1 u/ml, **CA 125 -137.9** U/ml-, CEA- 3.8 ng/ml.


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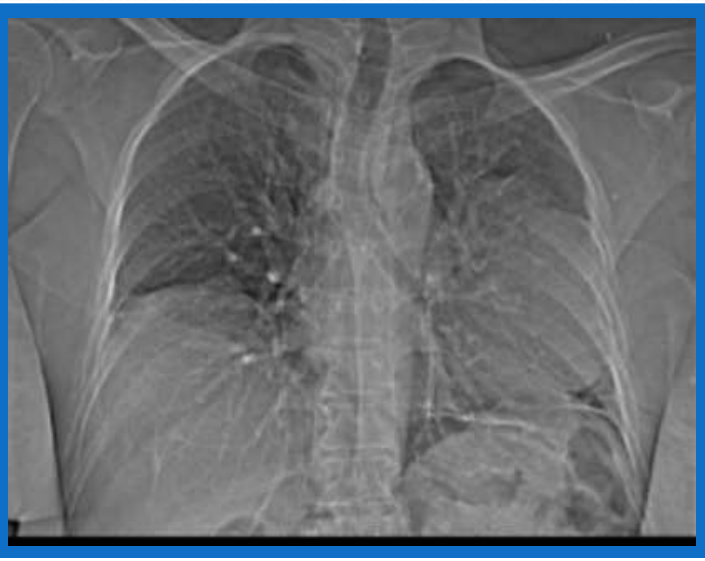

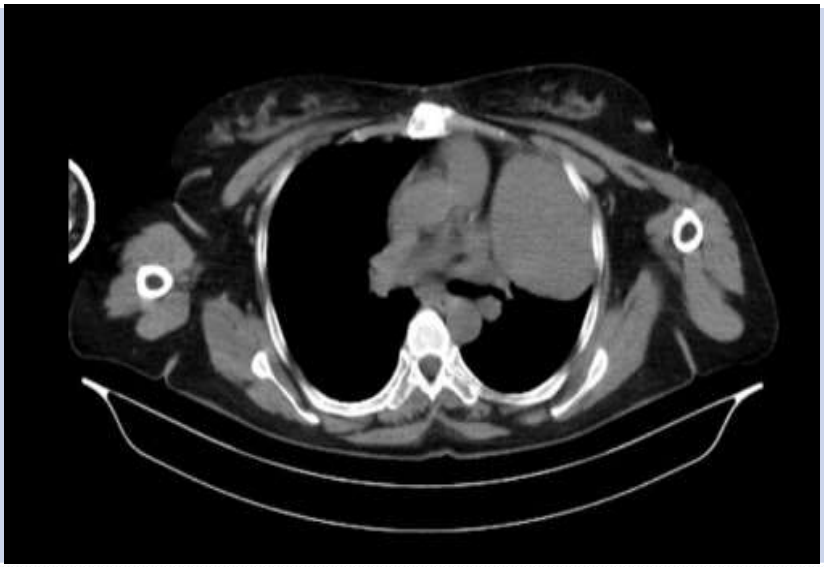

- Chest X ray – homogenous opacity in left upper lobe of lung.
- HRCT chest suggestive of 8.6x7.7x6.6cm solid soft tissue density lesion in left upper lobe showing heterogenous enhancement.
- CECT abdomen/pelvis suggestive of large cystic lesion from right ovary (32.5x18x28.5cm) with few areas of solid mural nodules and internal septae from the pelvis.

- Total abdominal hysterectomy and bilateral salphigo-oophorectomy (TAH + BSO) was done for huge ovarian mass.

- HPE s/o borderline mucinous cyst papillary tumor of ovary, outer surface free of tumor, with no vascular or stromal invasion

- Lung mass trucut biopsy HPE- plasmacytoma or inflammatory myofibroblastic tumor. IHC- CD138- Positive in plasma cells. Serum Immunoglobulin (IgG4) -normal.

- On fibreoptic bronchoscopy left middle lobe revealed- walls friable and bleed on touch.

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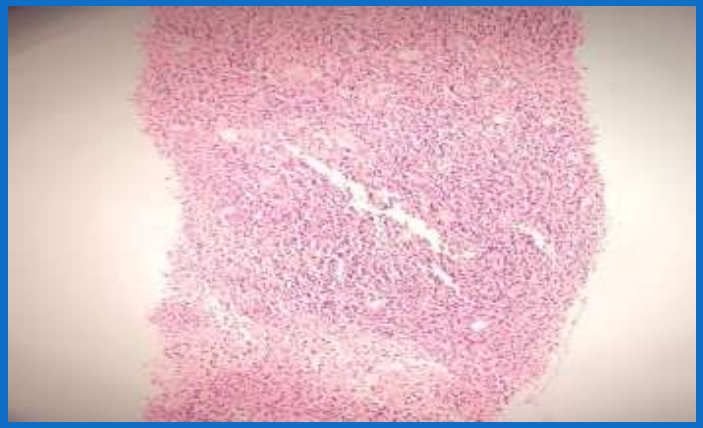

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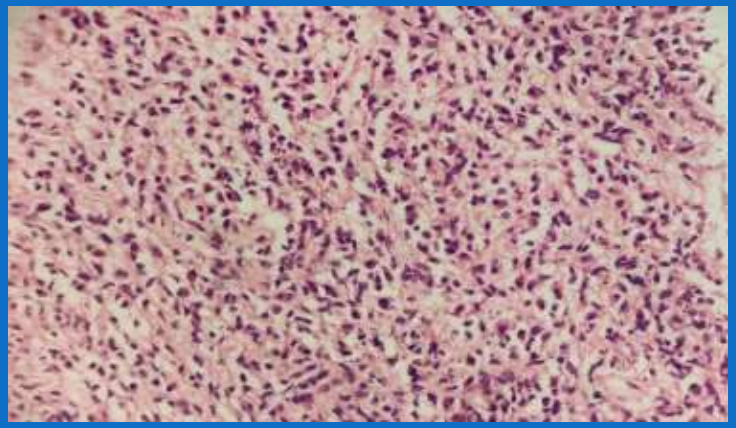

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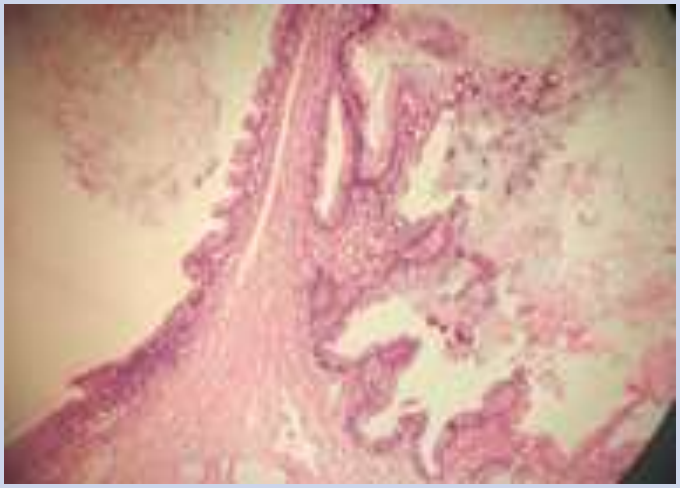

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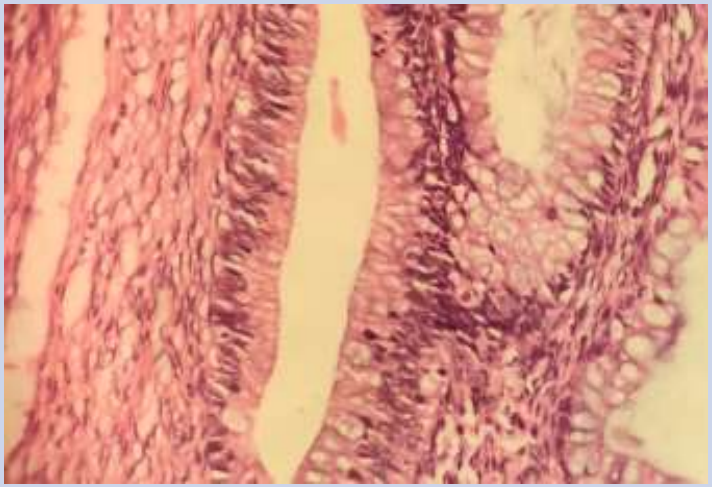

- In view of borderline mucinous cyst papillary tumor from ovary, no adjuvant chemotherapy was indicated.

- For plasmacytoma patient underwent radiotherapy and improvement was seen after radiotherapy. Patient is on follow up with no new complaints.

Treatment and Outcome

Patient number	Cancer association	Treatment		Outcome
		First cancer	Second cancer	
1	Breast/ Multiple myeloma	Modified radical mastetcomy	Chemotherapy	Alive After 1 year after surgery
2	Nasal melanoma / Adenocarcinoma of stomach	WLE (left cheek+ ala+vestible) + nasolabial flap with + MND Type II	Proximal partial gastrectomy	Alive after 2 year of surgery
3	Prostate ca/ Rectal adenocarcinoma	B/L orchidectomy + hormonal therapy	-	Died of liver disease
4	Ovarian ca / Plasmacytoma	TAH+ BSO	Radiotherapy	Alive after 1 year of surgery

DISCUSSION

- Multiple primary malignant tumor(MPMT) - Two or more different primary malignant tumors that occur in patients at same time or at different time.

- The occurrence for second primary **0.734-11.7%.**

- The incidence at our institution - **1.03 %.**

- Warren and Gates -diagnostic criteria:

1) Each tumor must be distinct from each other;
2) Each tumor must present definite features of malignancy; and
3) The possibility that the one is a metastasis of another must be ruled out .

Risk factors

- Genetic susceptibility/ cancer syndromes predisposing to malignancy
- Intensive exposure to carcinogens including chemotherapy / radiotherapy used in the treatment of first primary case.
- Tumour specific characters.

- Weibo Y et al in china -radiation induced cancers account for 23% of repeat carcinomas.

- Ricceri et al found that multiple malignancies were on the rise post radiotherapy like connective tissue, thyroid, breast, bone.

- The incidence of second primary carcinoma of oral cavity associated with radiotherapy for nasopharyngeal carcinoma was upto 11% as shown by Song et al.

1.Weibo Y, Zihao Y, Guozhen X and Yimin H: Radiation Oncology. 4th Edition, Beijing: Chinese Union MedicalUniversity Press, Beijing, China,2008; pp 1374.

2.Ricceri F, Fasanelli F, Giraudo MT, et al. Risk of second primary malignancies in women with breast cancer: results from the European prospective investigation into cancer and nutrition (EPIC). Int J Cancer. 2015;137:940–8. https:// doi. org/ 10. 1002/ ijc. 29462

3..Song M, Zhuang SM, Chen SW, Zhang Q, Yang AK, Wang LP and Guo ZM: Survival study and treatment strategy for second primary tumors in the oral cavity in patients with nasopharyngeal carcinoma after definitive radiation. Head Neck 2012:34; 1551-1555.

- The choice of treatment should depend upon the location of tumor, curative surgical resection margins, chemotherapy and radiotherapy.

- If surgery is required it can be done so in a majority of cases with low rate of morbidity and mortality for both the tumors.

- The prognosis of these patients depends upon aggressive biology of the cancer and the stage presentation of each individual tumor and not merely the occurrence of two primary tumors.

- With the various therapeutic strategies that we have nowadays, given the stage presentation of the each individual cancers, successful management of these double primary tumors is possible.

- At present there is no specific treatment protocol of MPMN and many of the treating surgeons and physicians rely on cases reported.

RECOMMENDATIONS –

- Separate cancer registry for MPMN's / hereditary syndromes can be considered and followed up more frequently than the routine population.
- As there are variety of combinations of MPMN'S and treatment of both cancers with chemotherapy if needed can be challenging .

Conclusion

- It is mandatory that patients of MPMT's come for regular followup with adequate clinical and radiological imaging.
- When there is a diagnostic dilemma regarding primary and metastatic tumors, expert pathologist opinion, genetic analysis and IHC on both the tumors can provide the answer.
- Forming a cancer registry for MPMN's can be considered as there are variety of combinations of MPMN's.

THANK YOU