

# CASE PRESENTATION: Cervical Cancer with rare/ unusual histology



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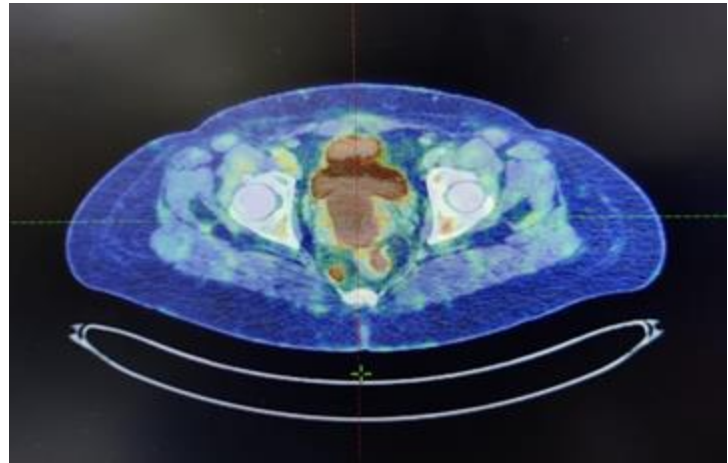
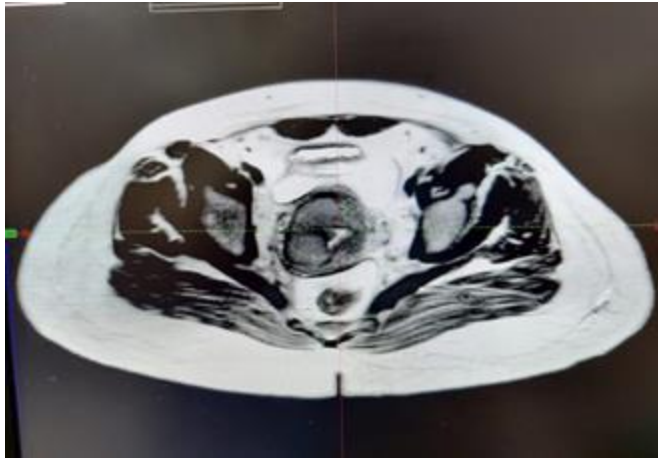
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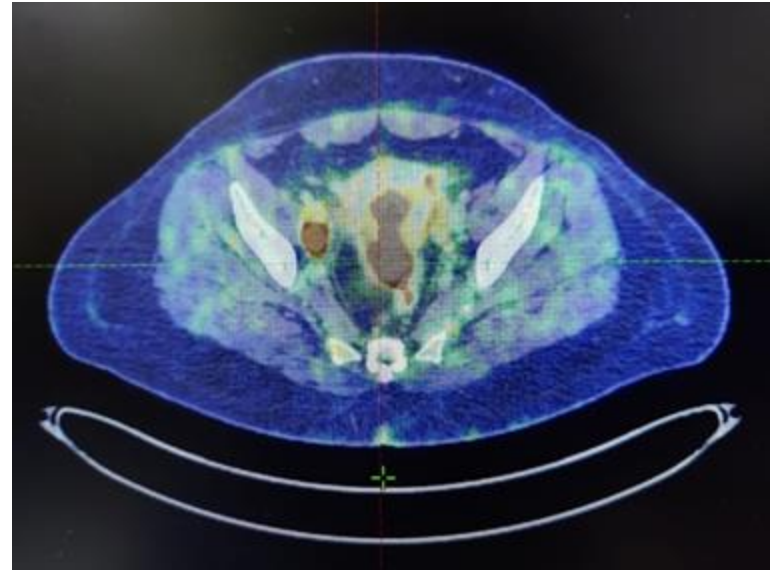
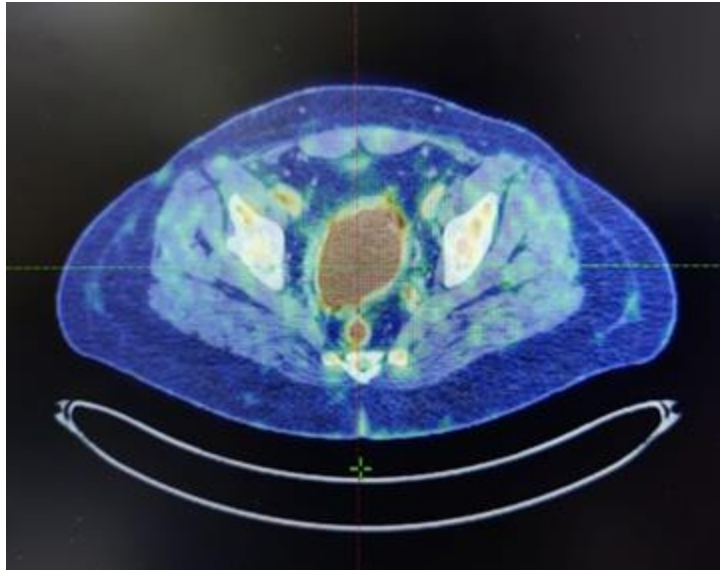


# Clinical History

- 49 years old active lady with no comorbidities.
- c/o bleeding per vaginum since 1 month
- USG TVS (08/09/20) : bulky uterus with fibroid. Bulky cervix with well defined isoechoic lesion along posterior wall with increased vascularity.

**Whole body PET-CT (Sep 2020)** showed large 5.2 x 5.2 x 8.1 cm FDG avid fairly marginated heterogeneously enhancing mass in cervix, extending into vaginal vault and bilateral parametrium. A 3.4 x 4.5 cm nodal mass was also noted in right adnexa with multiple other bilateral external iliac and perirectal nodes and mildly avid aortocaval nodes.





# Histology.....

- Hysteroscopic biopsy (14/09/20): poorly differentiated carcinoma with a solid and trabecular architecture.
- Immunohistochemistry showed.....

# Diagnosis

High grade Neuroendocrine carcinoma  
(Large cell neuroendocrine carcinoma)

Focal squamous differentiation

# Incidence, classification & differentiation

- NECC accounts for 0.5 to 1.4% of all cervical cancers
- The terminology for NETs of the uterine cervix was presented in 1997 and was considered similar to that used for pulmonary NETs
- Small cell NEC is the most common type, followed by large Cell NEC
- Well-differentiated NETs, typical & atypical carcinoid are very rare at this location
- Immunohistochemical p16 expression may suggest a cervical origin of NEC
- High-risk HPV DNA has been detected in the majority of small cell & large cell NECC (85 & 88%)
- In high-grade NEC, p53 expression ranging between 40 and 86% and P53 mutations from 27 to 59%
- Large cell NECC may be positive for p63, a marker strongly expressed in squamous cell carcinomas.
- Isolated neuroendocrine cells may occur in squamous cell carcinomas & adenocarcinomas; however they should not be interpreted as NECs if they lack the morphological features of NECs
- Mixed neuroendocrine–non neuroendocrine neoplasms (MiNENs)

# Survival & prognosis

- NECC is highly aggressive tumor & is more likely to invade the lymph vascular space.
- Local and distant relapses occur more often in NECC.
- Five year overall survival is significantly poorer with around 20-30% compared to > 65% for squamous cell carcinoma and adenocarcinoma of the cervix

## References:

- Tempfer et al. BMC Cancer (2018) 18:530
- Wang HL, Lu DW. Am J Surg Pathol. 2004;28:901–8.
- Brambilla E et al. Am J Pathol 1996;149:1941–1952.
- William Travis, Modern Pathology (2012) 25, S18–S30



# Tumour board discussion

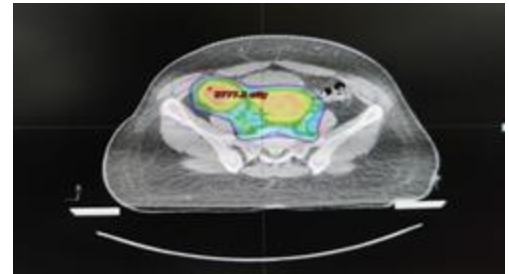
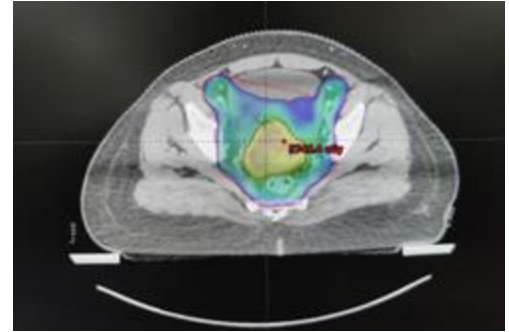
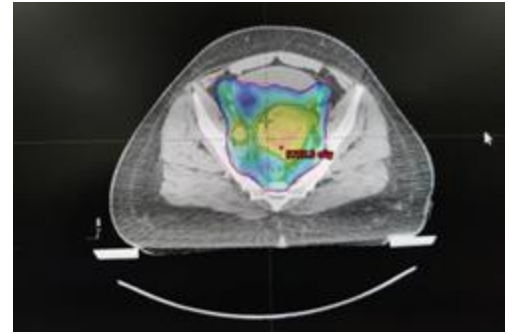
- Neuroendocrine cancers comprise 0.5-1.1% of all cervical cancers with large cell neuroendocrine cancers being even rarer and very aggressive.
- Only 70 cases reported thus far, majority succumb within 1-1.5 years
- Due to its rarity, no consensus exists on the optimal treatment plan, and most treatment methods are mainly adapted from treatments used for neuroendocrine carcinomas of the lung.
- So far, chemotherapy has become the mainstream of management, especially considering LCNEC's aggressive, early metastatic behavior.
- Decision: Concurrent chemoradiation with VMAT/RapidArc and cisplatin + etoposide followed by adjuvant chemotherapy.

# Chemotherapy

- Patient was started on most accepted chemotherapy schedule for neuroendocrine carcinomas of cisplatin and etoposide.
- However, patient developed severe side-effects and could not tolerate the chemotherapy.
- Hence, chemotherapy was discontinued and patient was continued on external beam radiotherapy after discussion with the patient and her family.

# External Beam Radiotherapy

- A **VMAT/Rapid Arc** plan using TrueBeam STx machine with a dose of 50.4 Gy in 28 fractions to the target volume with a simultaneous integrated boost upto 56 Gy to the bulky cervical disease (Sept 2020-Oct 2020)
- Followed by **Stereotactic Body Radiotherapy (SBRT)** boost of 4 Gy in single fraction to the lymph nodal mass was administered to the patient.
- She further received 3 sessions of **intracavitary brachytherapy** using Gammamed Plus HDR unit ( $\text{Ir}^{192}$ ) to a dose of 21 Gy in 3 fractions weekly after the completion of external beam radiotherapy.



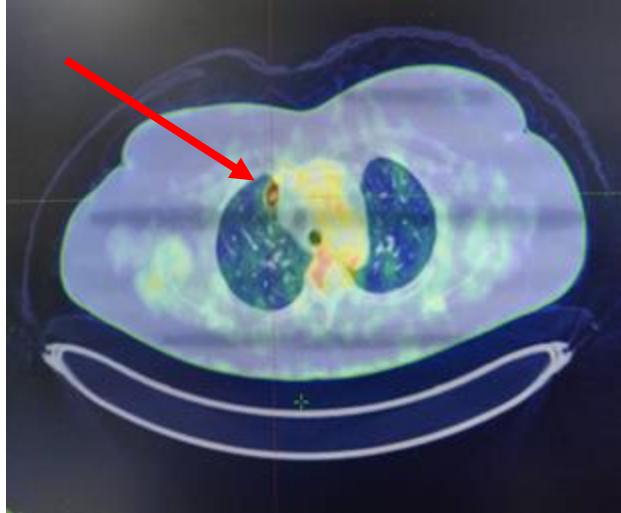
# Response to treatment

**PET-CT (17.11.2020):** showed complete response in Cervix disease and abdominal nodes.

## Follow Up scans: Oligo-recurrence

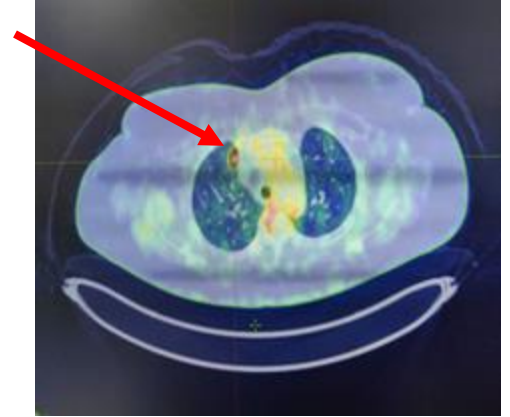
**PET-CT (08/03/21):** showed complete response in Cervix disease and abdominal nodes.

However, a subpleural nodule was noted in the apical segment of the right upper lobe as a new finding.



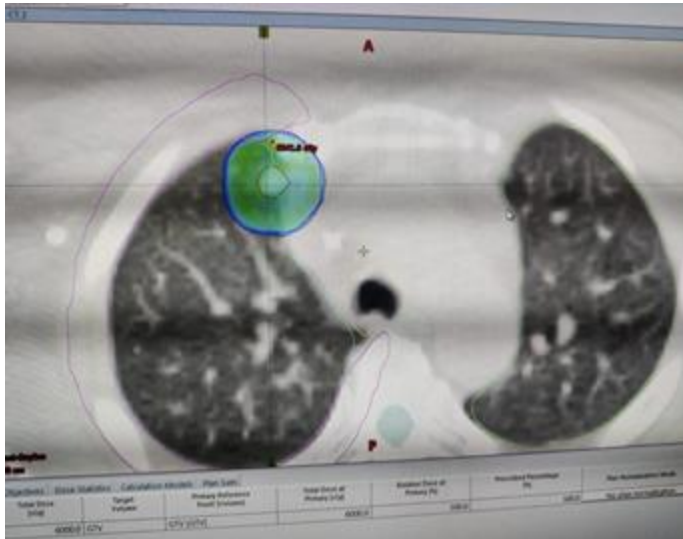
# Oligorecurrence: Further treatment Dilemmas

- Diagnosis: Difficult Biopsy Vs To treat without biopsy
- Treatment Intent: Palliative Versus Curative
- Surgery : VATS Vs Open
- Stereotactic ablative body radiotherapy
- Re - initiation of chemotherapy Vs Local therapy followed by chemo



# SBRT to lung nodule

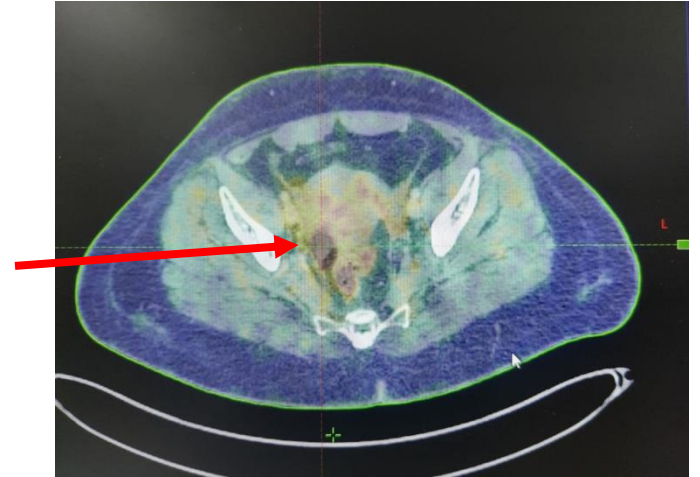
Underwent stereotactic ablative body radiotherapy to a dose of 60 Gy in 5 fractions to the lung nodule with 8 mm margins delivering a biologically equivalent dose of 132 Gy.



# Response to treatment

**PET CT scan after 5 months (28.08.21):** Lung Nodule : complete response

Another nodule in the right adnexa abutting peritoneal reflection in right lateral pelvic wall and adjacent rectouterine space was a new finding.

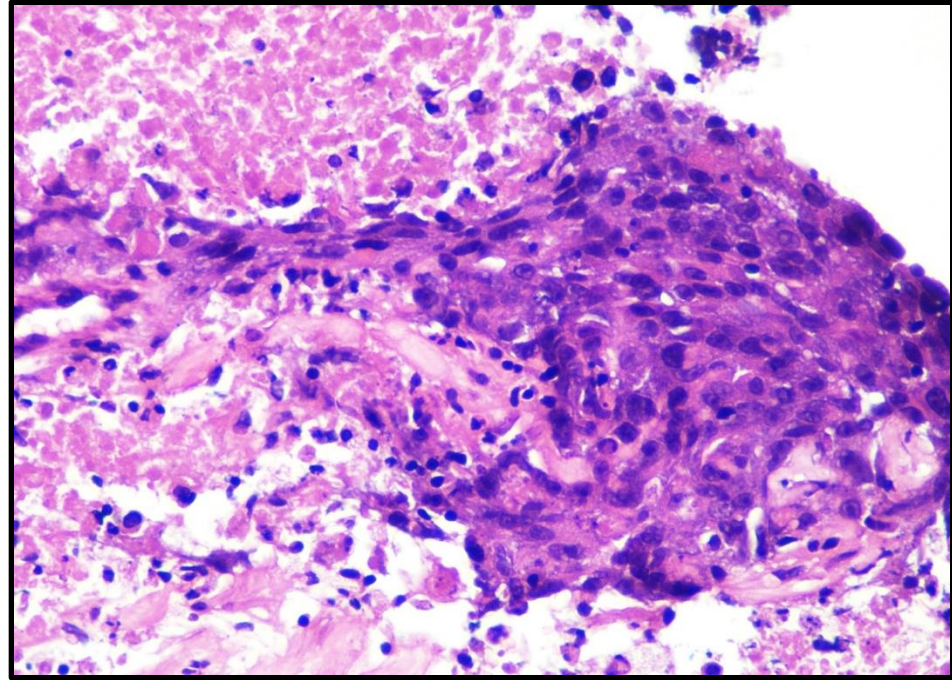
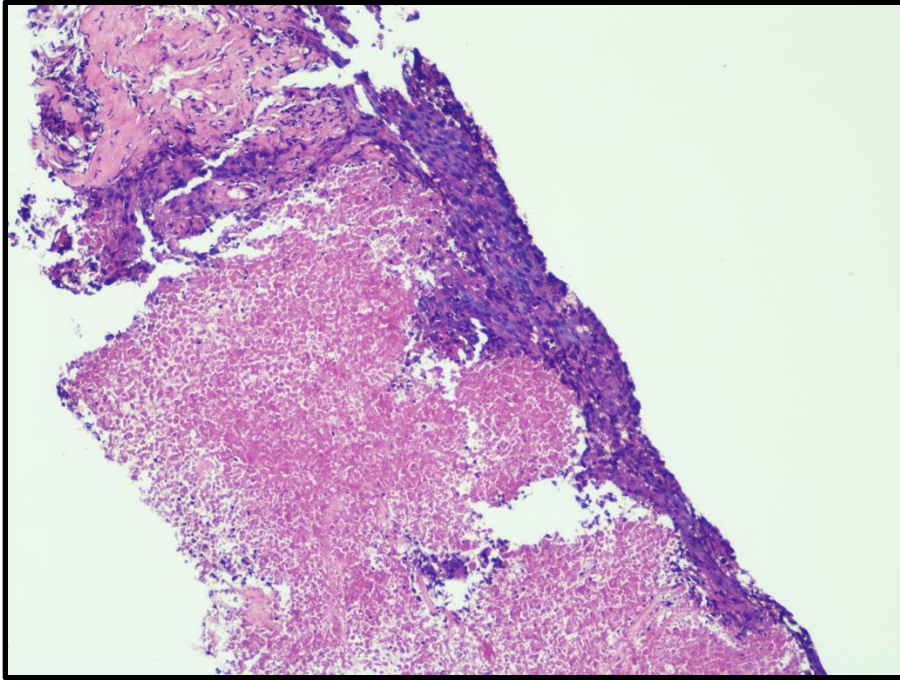




# Recurrence?

1. Biopsy: .....

# TRUS guided - Rectal biopsy done in end of August 2021

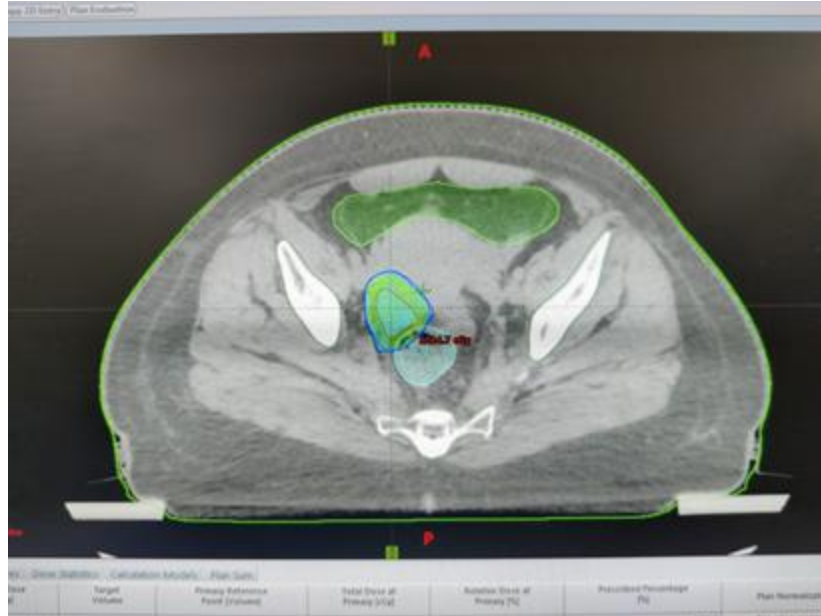


# Further treatment?

1. Palliative chemotherapy?
2. Surgery?
3. Stereotactic ablative body radiotherapy: Re –Radiation after 11 months?

# SBRT to pelvic node

The patient underwent SBRT to the pelvic lesion to a dose of 30 Gy in 5 fractions from 07/09/2021 to 11/09/2021.



## Current Status

The patient recently underwent whole body PET-CTs on 28/01/2022, 20.04.22, 07.07.2022 AND 20.07.2024: No evidence of disease anywhere in the body.

## TAKE HOME POINTS:

- Oligo-recurrence & Oligometastatic cases should be offered curative treatment options and should be treated differently than a widely metastatic disease
- SBRT is effective and shows equivalent results in lung lesions c.f Surgery
- Re-Radiation with SBRT is feasible and effective to provide local control