Endometrial cancer following cervical cancer radiotherapy Or synchronous endometrial – cervical cancer missed?

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INTRODUCTION

- A 69 year old patient presented with abdominal distension and pressure symptoms.
- Per abdomen – 22 weeks size cystic to firm non tender mass

  Per Vaginal- stenosed cervix flushed with vagina
- On ultrasound- intrauterine homogenous fluid collection noted
- Past history of cancer cervix treated with radical radiotherapy
- Drained per vaginally under ultrasound guidance and fluid sent for histology and cytology and CT scan was arranged

DIAGNOSIS?????

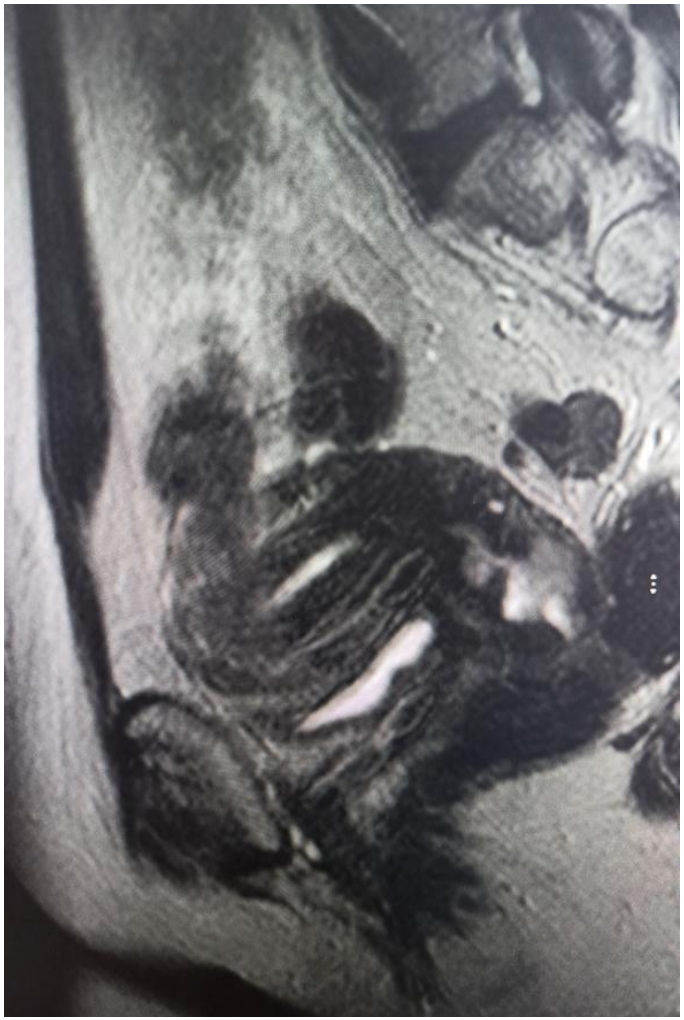
Journey of the Patient

2011

- Mrs X 61 yr old, PS 0 , BMI 23,presented with postmenopausal bleeding and underwent pipelle & cervical biopsy.
- Reported as Complex atypical endometrial hyperplasia & cervical biopsy with well-differentiated endometriod carcinoma+CGIN
- O/E- Cervical tumour with parametrial involvement. Clinically stage 2B
- MRI- endometrium unremarkable, Endocervical mass of 23mm with early parametrial involvement. Fibroid of 3 cm.

- Weekly Cisplatin and external beam radiotherapy followed by HDR brachytherapy, completed March 2012

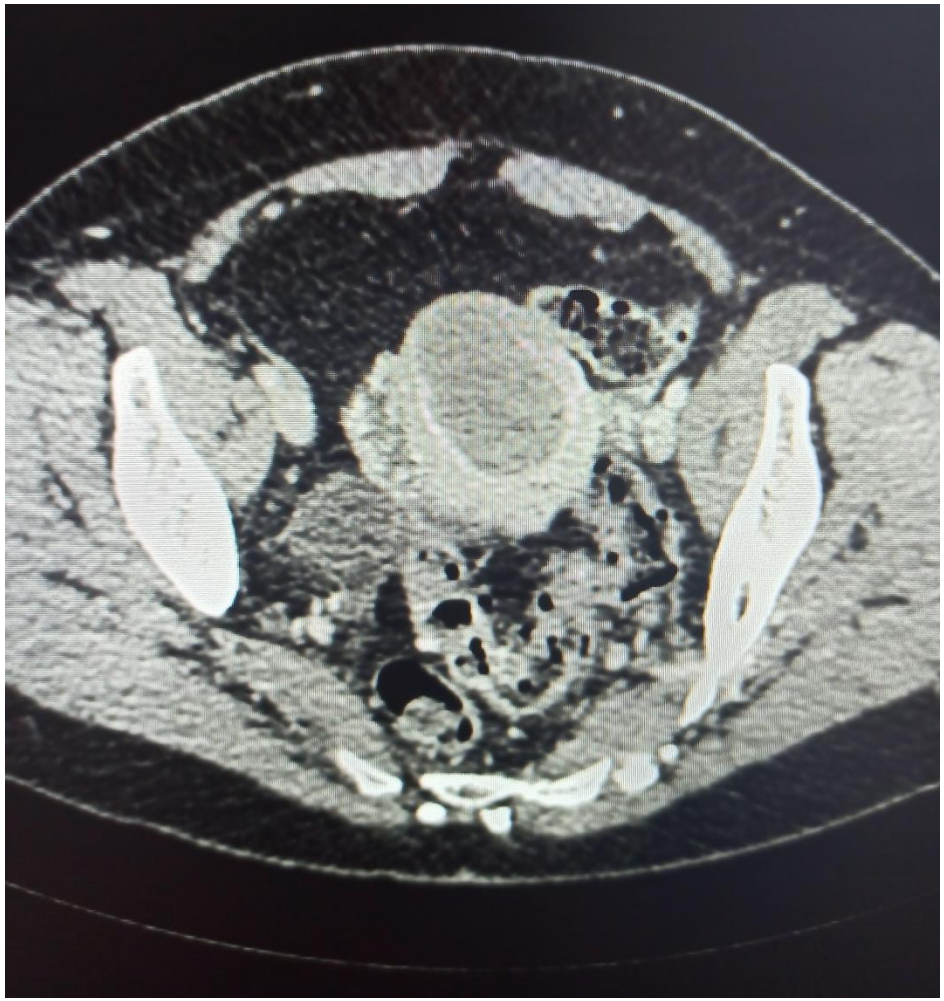
- She was under regular 6 monthly follow up with oncologists and stayed asymptomatic.



2015

- Developed left sided lower abdominal pain.
- CT scan showed complex heterogeneous mass with cystic areas involving the uterine fundus suggestive of cystic degeneration of fibroid. Not suspicious of malignancy.
- She was discussed in the **MDT** and on TVS concluded to be cystic degeneration of fibroid with normal endometrial lining
- Repeat ultrasound in 2 months time which revealed similar findings.
- Continued her follow ups with oncologists till 2017 (5 years) when she was discharged to GP care

Fibroid degeneration CT scan

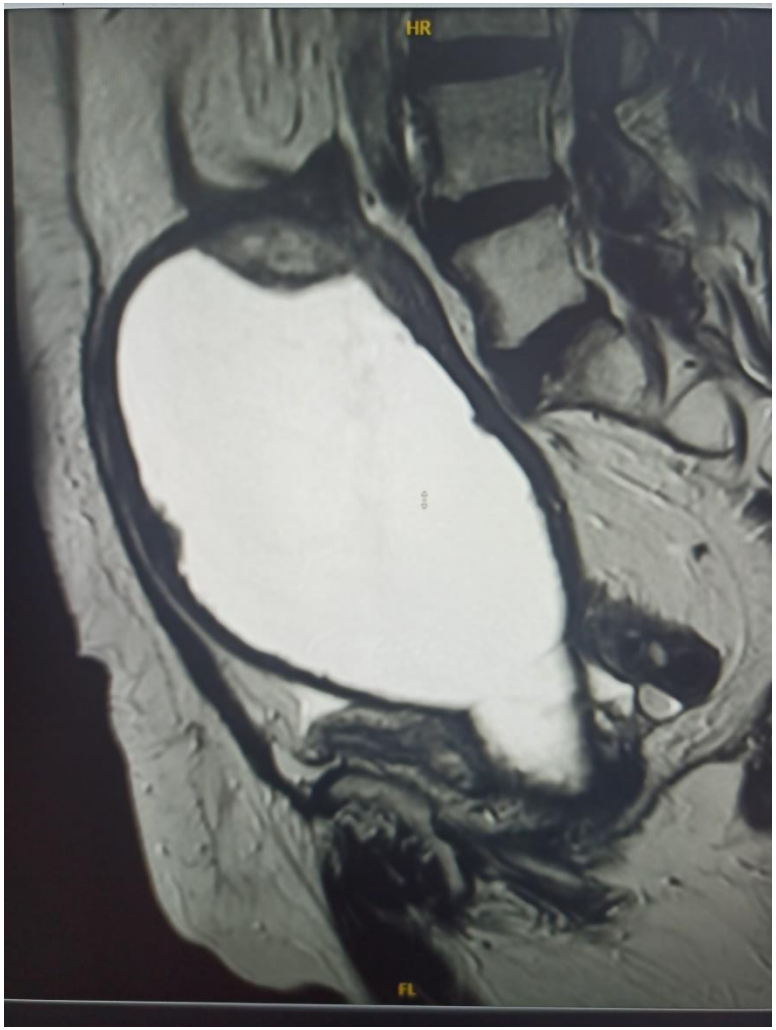


2020

- Intrauterine fluid histology – degenerative and inflammatory cells
- CT scan and MRI concluded solid papillary projections into the fluid filled cavity suspicious of malignancy in view of repeated fluid collection, right pelvicalyceal dilatation.

- Underwent GA Hysteroscopy but failed due to radiotherapy changes.
- Discussed in MDT and planned for laparotomy and TAH BSO

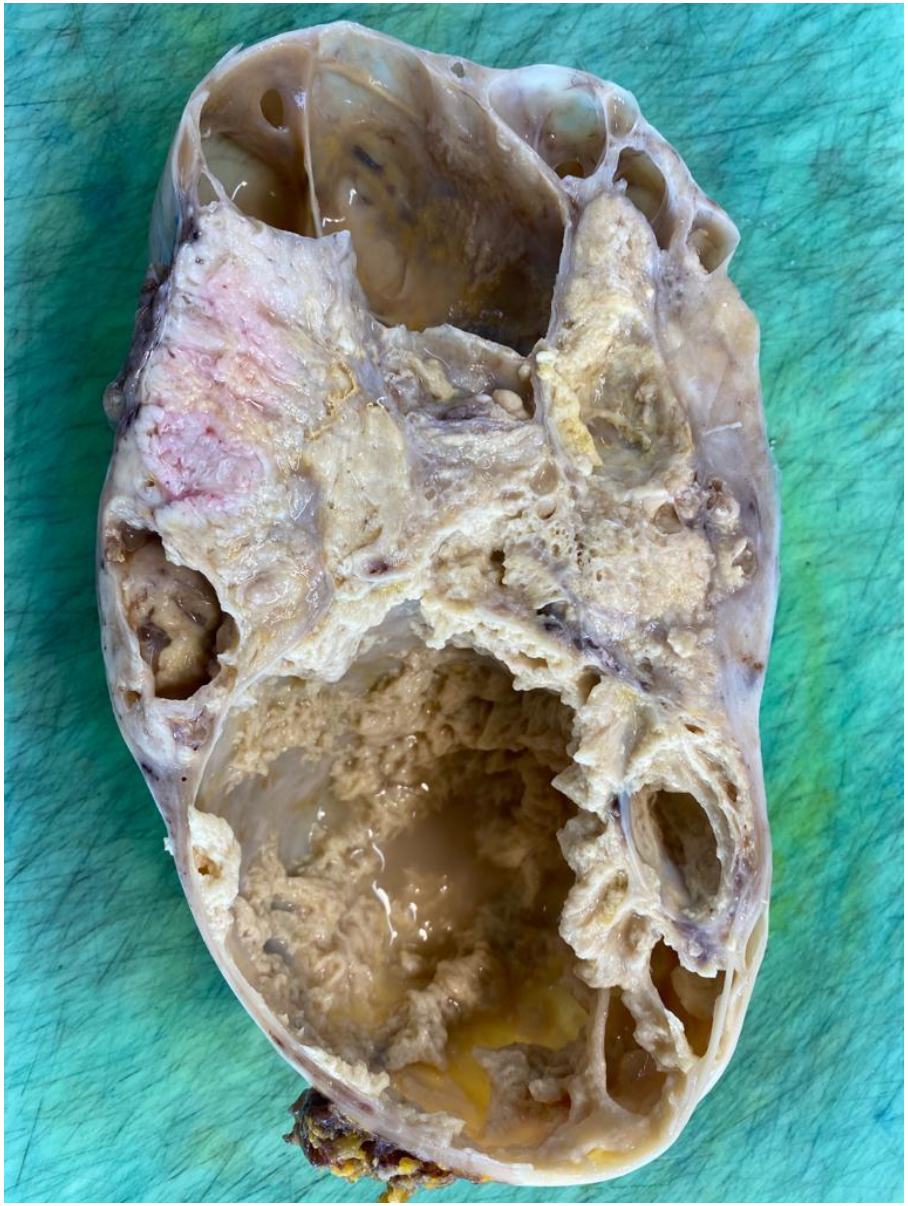
Intra uterine collection- MRI

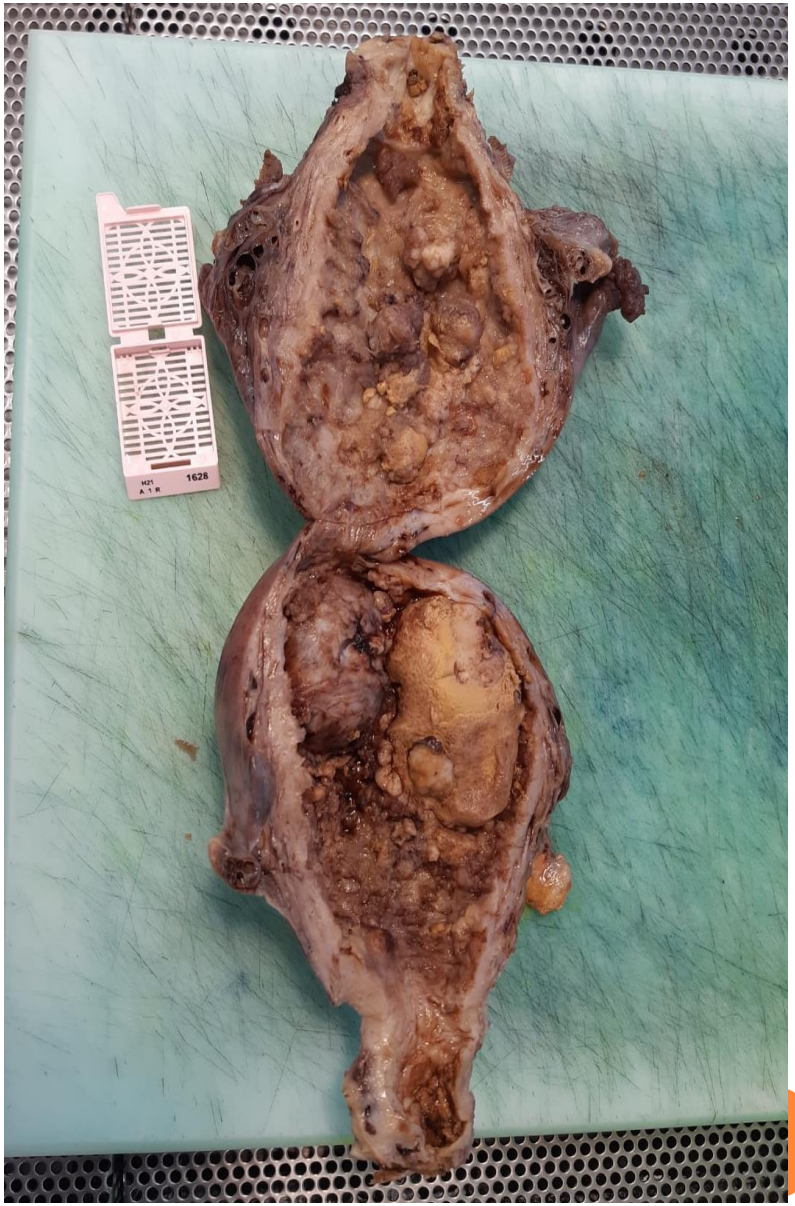


- Underwent a challenging surgery(due to fibrotic changes from radiotherapy) with plastered pelvic sidewalls & 22 week size uterus

- TAH BSO with bladder injury repair was done.

- Histology- CARCINOSARCOMA G3, SIEC, LVSI+ (extensive)Stage IA

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DISCUSSION

- Radiotherapy with MIRENA in situ – 2011
- Post radiotherapy hysterectomy in 2012
- Fibroid degeneration in post menopausal
- Pathogenesis of atypical endometrial hyperplasia to carcinosarcoma.
- Pelvic lymph node dissection in post radiotherapy patients (risks vs benefits)
- Treatment of carcinosarcoma without radiotherapy
- Further follow up

2011

- Synchronous primary malignancies of female genital tract although rare could be a possible explanation in our case

- Simple hysterectomy post radiotherapy in view of risk of endometrial cancer could have been an option.

- No significant data supporting MIRENA in situ along with brachytherapy found, however brachytherapy implants along with Mirena may not be feasible.

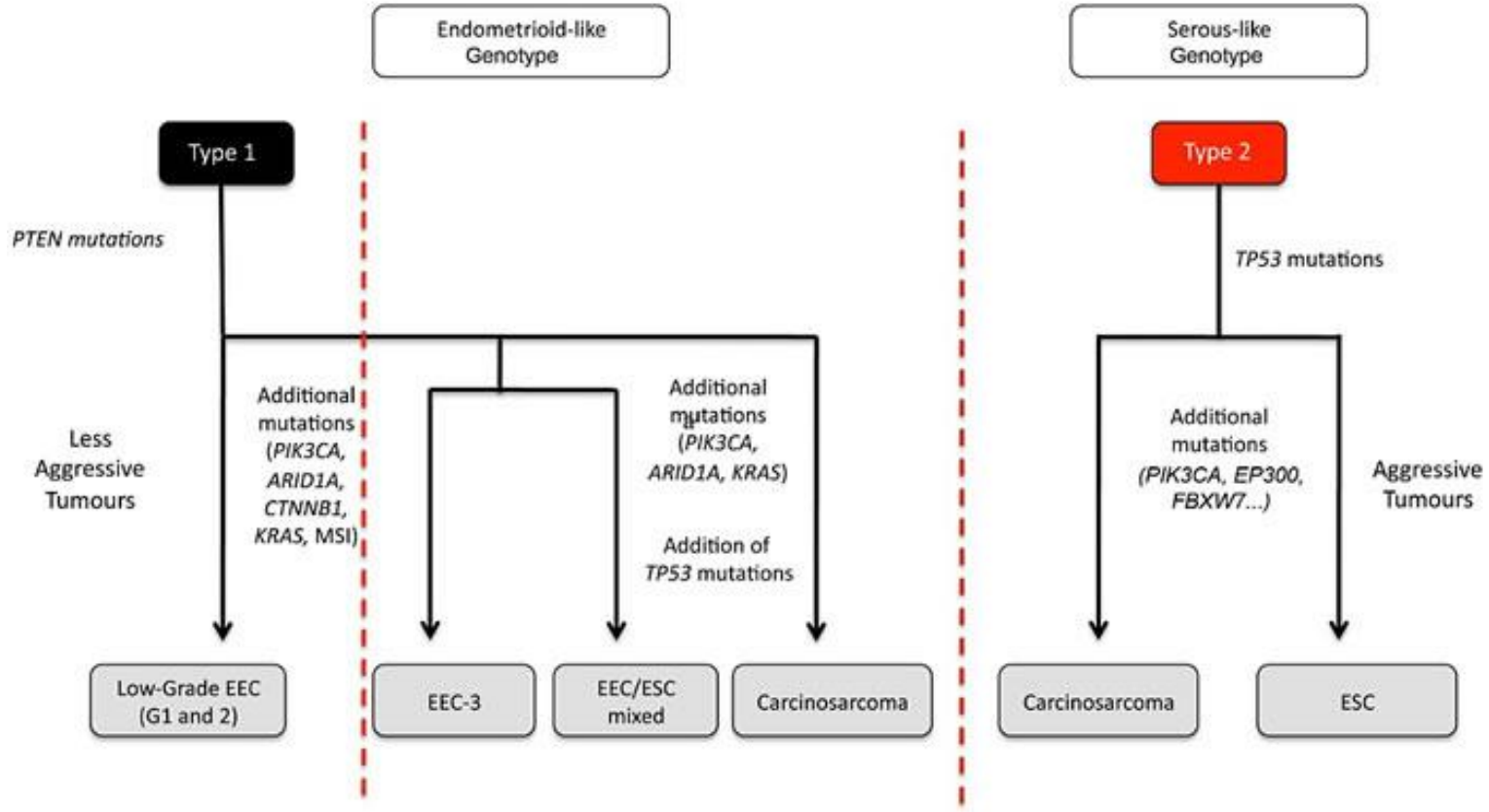
2015 -FIBROID DEGENERATION

- Pathogenesis for degeneration of fibroids in postmenopausal women remains unclear

- Excessive production of growth factors (epidermal or insulin-like) from the fibroid
- Uterine leiomyosarcoma- with rapid enlargement of the fibroid

- Follow up in 2-3 months with no changes, ruled out the possibility of leiomyosarcoma in our case.

UTERINE CARCINOSARCOMAS ARISE THROUGH TRANS-DIFFERENTIATION OF UTERINE CARCINOMA INTO SARCOMA,(ENDOMETRIOID CARCINOMA-LIKE OR SEROUS CARCINOMA-LIKE)



- Radiation is a possible etiological factor but the exact etiology is not known yet. However, tamoxifen may induce carcinogenesis in some patients.

(Singh R. Review literature on uterine carcinosarcoma. J Cancer Res Ther. 2014 Jul-Sep;10(3):461-8. doi: 10.4103/0973-1482.138197. PMID: 25313723.)

Ideal treatment may not be applicable in all cases

- Considering the aggressive nature of carcinosarcoma(five year survival of 50% for SI/II) , surgery with lymphadenectomy followed by chemo radiotherapy is the ideal treatment in literature.

- Role of further lymphadenectomy (post radiotherapy patient) as the histological diagnosis is made, now is controversial.

- Seagle BL, Kanis M, Kocherginsky M, Strauss JB, Shahabi S. Stage I uterine carcinosarcoma: Matched cohort analyses for lymphadenectomy, chemotherapy, and brachytherapy. Gynecol Oncol. 2017 Apr;145(1):71-77. doi: 10.1016/j.ygyno.2017.01.010. Epub 2017 Mar 15. PMID: 28317560.(Lymphadenectomy to at least 15-20 removed nodes is associated with increased survival of women with node-negative uterine carcinosarcoma. Adjuvant "cuff and chemo" with vaginal brachytherapy and multiagent chemotherapy is associated with increased survival)

What next?

- Overall survival is comparable in both adjuvant radiotherapy or chemotherapy arms.
- Radiotherapy
  - local vault recurrence reduced
  - increased toxicity
- Chemotherapy
  - reduced toxicity
  - reduced overall recurrence

- European Organization for Research and Treatment of Cancer (EORTC 55874) Gynecological Cancer Group Study -improved locoregional control in adjuvant radiotherapy (24% vs 47%) compared with the observational group, especially in early-stage disease (FIGO stages I–II). However, no difference in either overall or disease-free survival was demonstrated .
- Prospective randomized control trial phase III (GOG Protocol 150)(recurrence rates and survival are not altered by the addition of adjuvant therapy in patients with UCS, although there were a significant increase in late adverse events in adjuvant RT (WAI) and increased vaginal recurrences in the chemotherapy group. Five-year probability of relapse was 58% vs 52% for the WAI vs CIM, and the estimated recurrence rate in CIM was 29% lower than the WAI patients)

FOLLOW UP

- Recurrence rate of 37% with stage I UCS patient needs a regular follow up

- Recurrent disease is usually shown to be carcinomatous rather than sarcomatous. ER and PR status are usually negative so of limited value but should be checked as the occasional patient shows positivity.

Thank you