NHS
University Hospitals of Derby and Burton
NHS Foundation Trust

Uterine PEComa: A Case Report

Kate Smallwood ST7 in O&G
at Royal Derby Hospital

Introduction

University Hospitals of Derby and Burton NHS Foundation Trust

- PEComa: Perivascular Epithelioid Cell Neoplasm

" a mesenchymal tumor composed of histologically and immunohistochemically distinctive perivascular epithelioid cells"

WHO 2002

The Case

University Hospitals of Derby and Burton NHS Foundation Trust

- 56 year old
- 2ww referral for bleeding on HRT
- Para 2: NVDs
- PMH: GORD, stress incontinence Tx with Bulkamid, anxiety (PS=0)
- Surgical Hx: Appendicectomy
- Drug Hx: Oestrogen, Progesterone, Testosterone, Venlafaxine

Initial Investigations

University Hospitals of Derby and Burton NHS Foundation Trust

- Nov 2019:
  - TV USS: ET 5.6mm
  - Hysteroscopy, solitary polyp removed
  - CA125 = 15

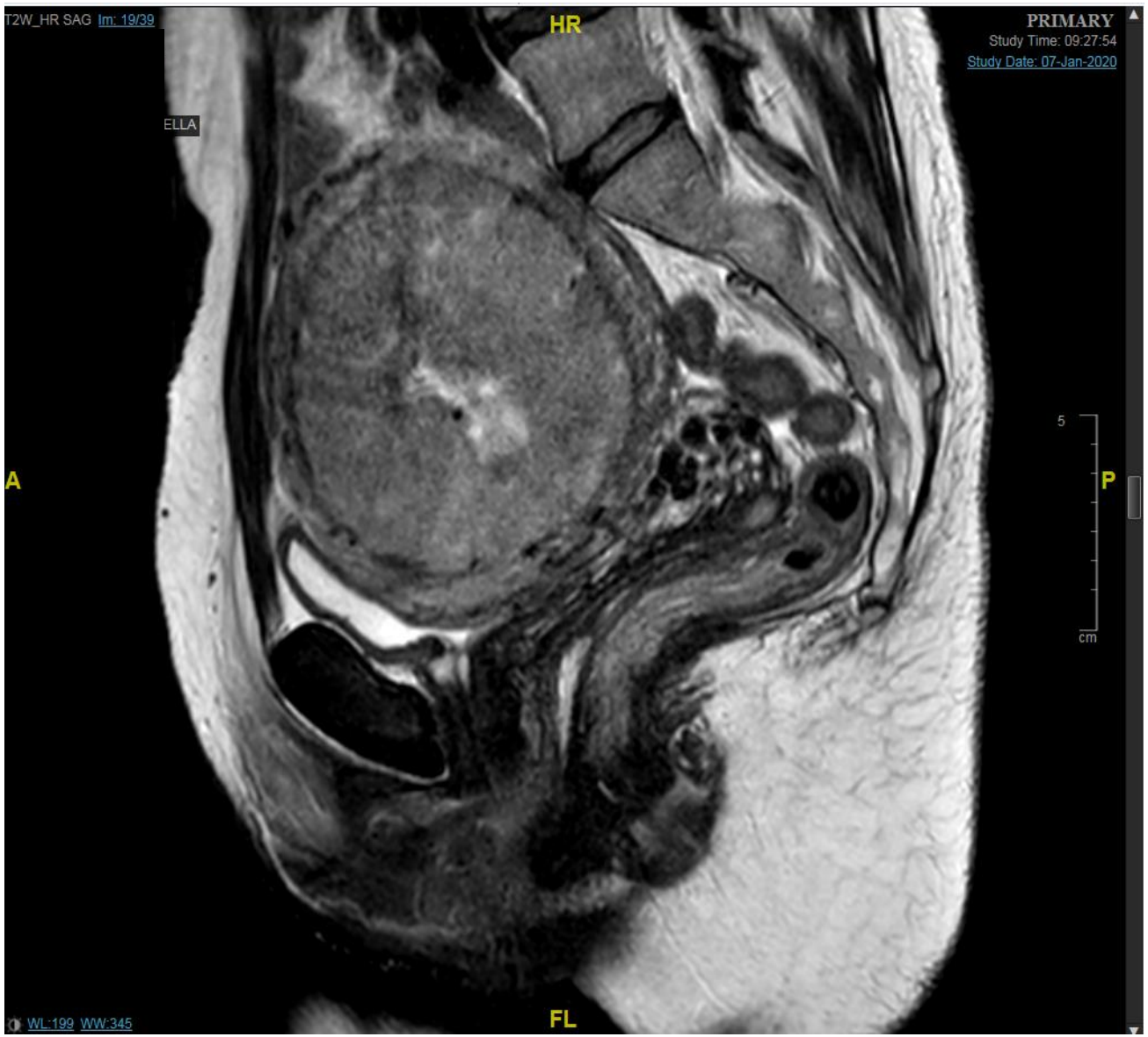
MDT

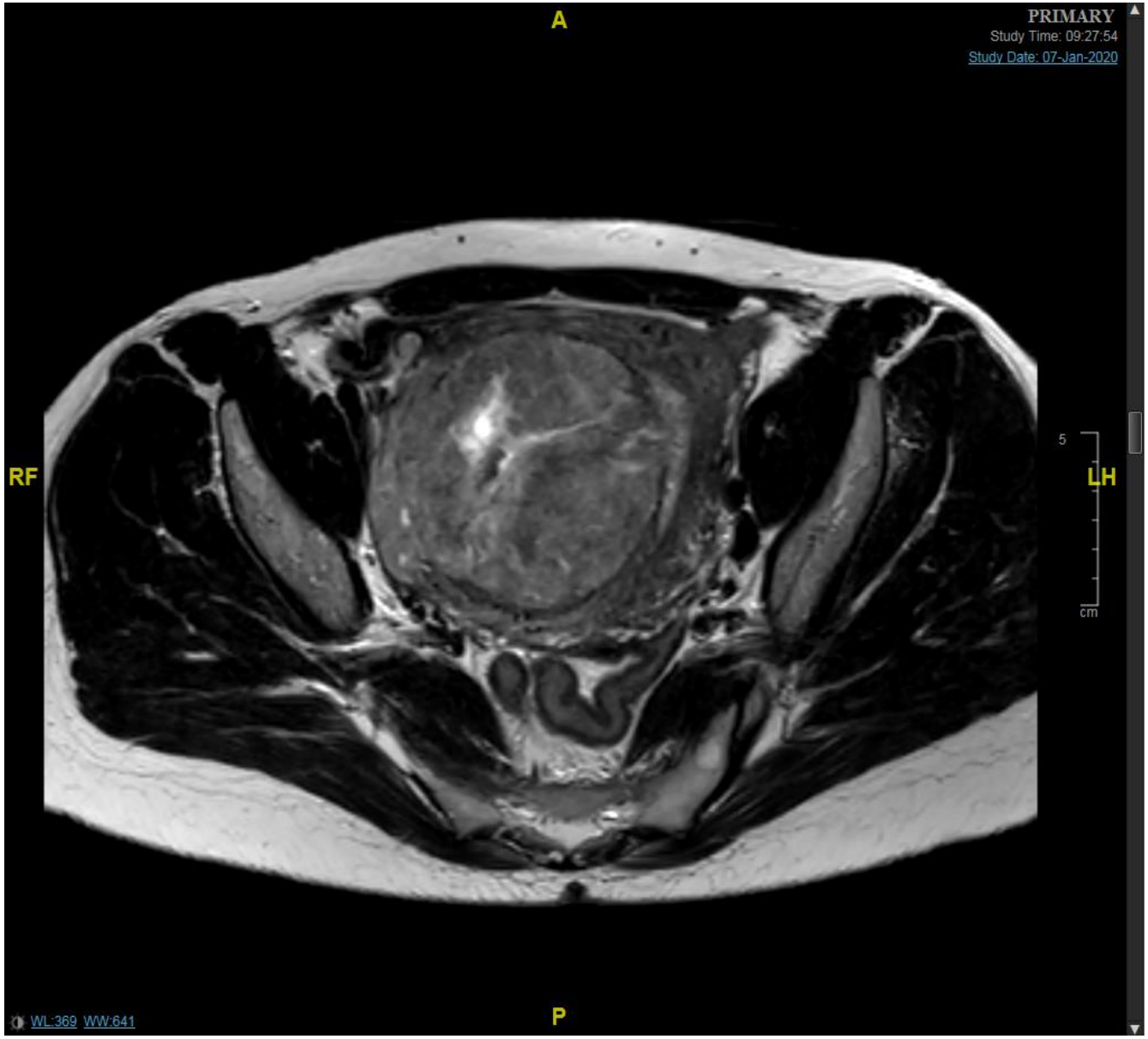
University Hospitals of Derby and Burton NHS Foundation Trust

- Dec ‘19
  - Histology – the features and immune profile are mostly in keeping with malignant perivascular epithelioid cell neoplasm.
  - Second opinion sought from an expert at the Royal Marsden Hospital: Likely PEComa with a differential diagnosis of leiomyosarcoma
  - Recommend MRI and CT CAP

MRI

- Large well defined vascular mass confined to the endometrial cavity 8.3 x 7.9cm. Could be a fibroid but intermediate signal intensity is concerning
- No obvious pelvic spread, no LN

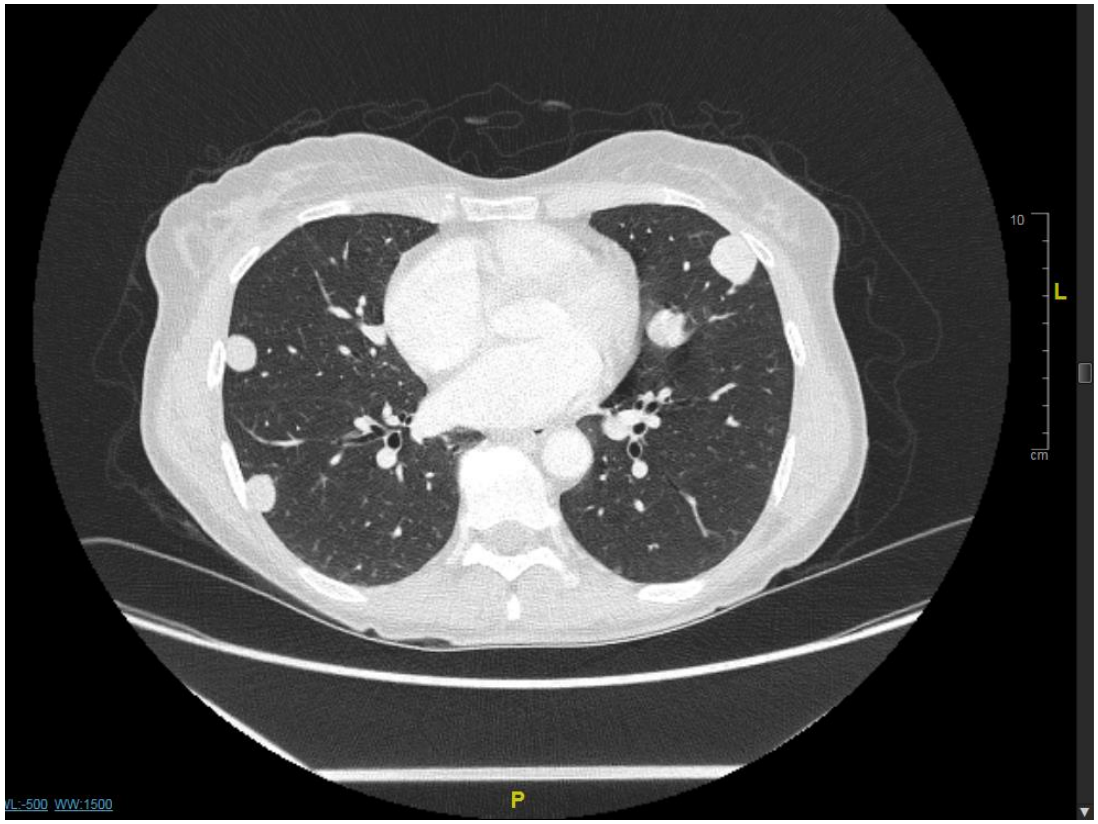

T2W_HR SAG Im: 19/39
HR
PRIMARY
Study Time: 09:27:54
Study Date: 07-Jan-2020
ELLA
A
P
5
cm
WL:199 WW:345
FL


A
PRIMARY
Study Time: 09:27:54
Study Date: 07-Jan-2020
RF
LH
5
cm
WL:369 WW:641
P

CT Scan

University Hospitals of Derby and Burton NHS Foundation Trust

- Diffuse pulmonary metastasis



Initial Surgery

- 13/1/20: TAH BSO and omental biopsy
- Histology:
  - Macro: Nodular tumour within the uterus with areas of necrosis
  - Micro: predominantly of epithelioid cells but with focal spindle cells. Marked nuclear atypia with numerous mitotic figures
  - Immuno: Strongly positive for HMB45 and Melan-A in keeping with malignant PEComa

Adjuvant Treatment

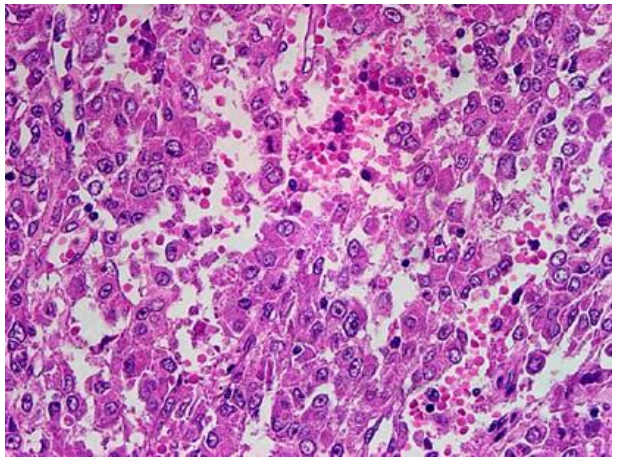
University Hospitals of Derby and Burton NHS Foundation Trust

- Lung Bx – confirmed PEComa
- Discussion with Sarcoma MDT
- Standard chemotherapy not effective
- Recommendation for Sirolimus 3mg OD – off license treatment for sarcoma
- CT Aug 2020 – pulmonary mets reduced in size

Current Status

- Continues on Sirolimus
- CT Feb 2021 – pulmonary mets increased in size
- Opinion sought from Royal Marsden Oncologist
- ?for experimental treatment

Brief History of PEComa



- Mesenchymal neoplasms
- More common in females
- Subset of sarcoma
- Commonly benign
- Appear in visceral (GI tract, uterus), abdominopelvic and retroperitoneal sites
- The perivascular epithelioid cell has no known normal tissue counterpart

- Nearly all show reactivity to HMB45 and or Melan-A as well as actin and desmin
- Gynaecological PEComa's most commonly in the uterus
- May be asymptomatic
- Radiological appearance is extremely variable
- All types of PEComa can be a feature of Tuberous Sclerosis
- Malignant PEComas tend to be aggressive and commonly metastasise

Management

- Evidence based on case reports as the condition is rare
- Surgical resection is primary treatment Hysterectomy +/- BSO
- Adjuvant treatment:
  - RT: no evidence
  - CT: varying regimes have been tried with varying results
  - mTOR inhibitors

mTOR Inhibitors

- mTOR is an atypical serine/threonine kinase
- regulates cellular metabolism, growth, and proliferation
- Two complexes mTORC1 and mTORC2
- The mammalian target of Rapamycin
- Rapamycin – antifungal metabolite produced by Streptomyces hygroscropicus
- Possesses immunosuppressive and anti-proliferative properties (targeting mTORC1)

- Increased activiation of mTORC1 is seen in numerous cancers
- Hyperactive mTORC1 is seen in tuberous sclerosis
- Sirolimus has been successful in reducing tumour size in Lymphangioleiomyomatosis (LAM) in the lung and angiomyolipomas

Royal Marsden Study

University Hospitals of Derby and Burton NHS Foundation Trust

- Benson et al 2014
- Series of 10 patients with metastatic PEComa (2 gynaecological)
- Treated with Sirolimus or Temsirolimus (70% adjuvant post surgery)
- Half of patients showed a partial response with one patients disease remaining stable
- 78% 1 year survival
- Recommends Sirolimus as first line treatment

Future Considerations

University Hospitals of Derby and Burton NHS Foundation Trust

- Considerations for disease progression:
  - Dual mTORC1/2 inhibitors (in phase 1 trials)
  - P13 kinase inhibition
  - Combination of mTOR and insulin like growth factor-1 receptor inhibitors
- Recruitment to trials is encouraged.

Summary

University Hospitals of Derby and Burton NHS Foundation Trust

- Malignant PEComa is a rare tumour
- Aggressive, metastatic potential. Poor prognosis
- Current evidence based on small case series
- Primary surgery is recommended
- Followed by mTOR inhibitors
- Treatment of recurrence isolated to clinical trials

References

- Folpe AL, Fletcher CDM, Unni KK, Mertens F (Eds.) Neoplasms with perivascular epith differentiation (PEComas), *World health classification of tumors: pathology and genetics of tumors of soft tissue and bone*, IARC Press, Lyon (2002), p. 221
- Huang S, Houghton PJ. Targeting mTOR signalling for cancer therapy. *Current Opinion in Pharmacology*, 2003, Volume 3, Issue 4,Pages 371-377,
- Musella A, De Felice F, Kyriacou AK, Barletta F, Di Matteo FM, Marchetti C, Izzo L, Monti M, Benedetti Panici P, Redler A, D'Andrea V. Perivascular epithelioid cell neoplasm (PEComa) of the uterus: A systematic review. *International Journal of Surgery. 2015,* Volume 19,Pages 1-5,
- Li J, Kim SG, Blenis J. Rapamycin: one drug, many effects. *Cell Metab*. 2014;19(3):373-379.
- Benson C ,Vitfell-Rasmussen J, Maruzzo M, Fisher C, Tunariu N, Mitchell S, Al-Muderis O, Thway K, Larkin A, Judson I. A retrospective study of patients with malignant pecoma receiving treatment with sirolimus or temsirolimus: the royal marsden hospital experience*. Anticancer research.* 2014, 34 (7) 3663-3668.