Mixed carcinoma of the uterine corpus, the 'real deal' versus the 'imposter'

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BACKGROUND

- **Mixed carcinoma of the uterine corpus** was removed from the 4th Edition of WHO classification as a distinct entity, however, it has been re-introduced in the 5th Edition.
- **Definition**: Carcinoma composed of two or more discrete histological types of endometrial carcinoma, where at least one component is either serous or clear cell. Rare <10% of all endometrial cancers.
- **Diagnostic criteria**: At least two spatially distinct histotypes of endometrial carcinoma must be identified by histology and immunohistochemistry *(desirable)*.
- Most carcinomas that look "mixed" morphologically represent a single neoplastic-type with areas morphologically mimicking another tumour type.
- We present 2 interesting cases that fulfill the above diagnostic criteria for mixed carcinoma of the uterine corpus.

CASE PRESENTATION

CASE 1

73 year old female presented with postmenopausal bleeding.	
MRI	2-3 cm cervical mass. Left tubo-ovarian mass.
Endometrial biopsy	FIGO Grade 2 endometrioid adenocarcinoma.
Macroscopy	Lower uterine segment polyp ~20mm

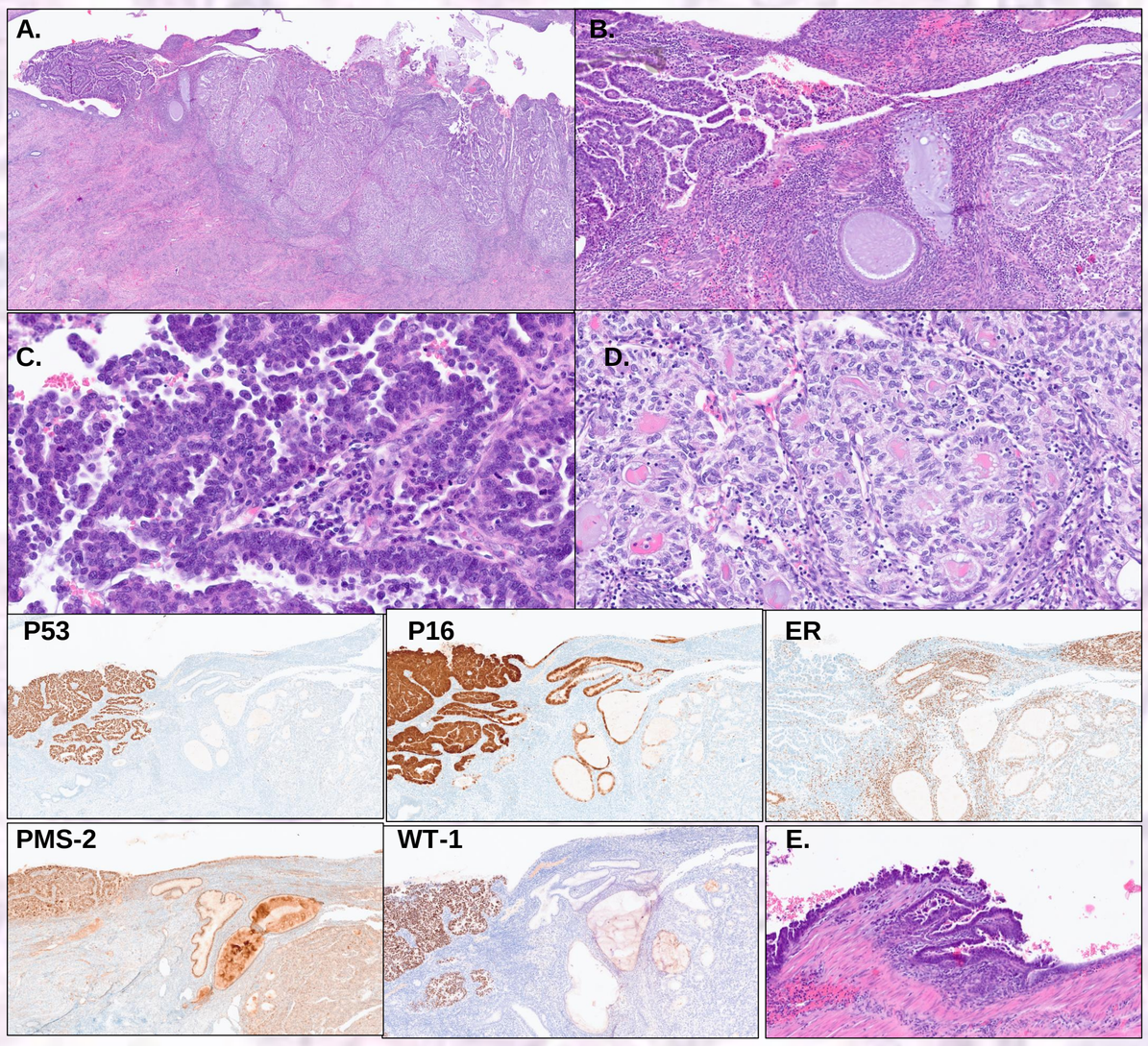

Figure 1: **A&B.** Low and intermediate power view of lower uterine segment tumour with two spatially distinct histotypes. **C.** Component 1 - glandular and micropapillary architecture, high grade cytological atypia and brisk mitoses. **D.** Component 2 - glandular and focal solid architecture, low to moderate cytological atypia and infrequent mitoses. **P53** positive abnormal 'mutation-type' in C, 'wild-type' staining in D. **P16** block positive in C, negative in D. **ER** negative in C, weak positive in D. **PMS-2** retained in C, very weak interpreted as 'lost expression' (MMR-deficient) in D. **WT-1** positive in C, negative in D. **E.** Fallopian tube revealed STIC lesion.

FINAL DIAGNOSIS of uterine tumour: MMR-deficient FIGO Grade 2 endometrioid endometrial adenocarcinoma (FIGO stage II) and metastatic high grade serous carcinoma of fallopian tube origin.

THE IMPOSTER

CASE 2

87 year old female presented with postmenopausal bleeding.	
Imaging	Not available
Endometrial biopsy	High grade serous and endometrioid carcinoma with possible clear cell component.
Macroscopy	friable polypoid endometrial tumour ~30mm

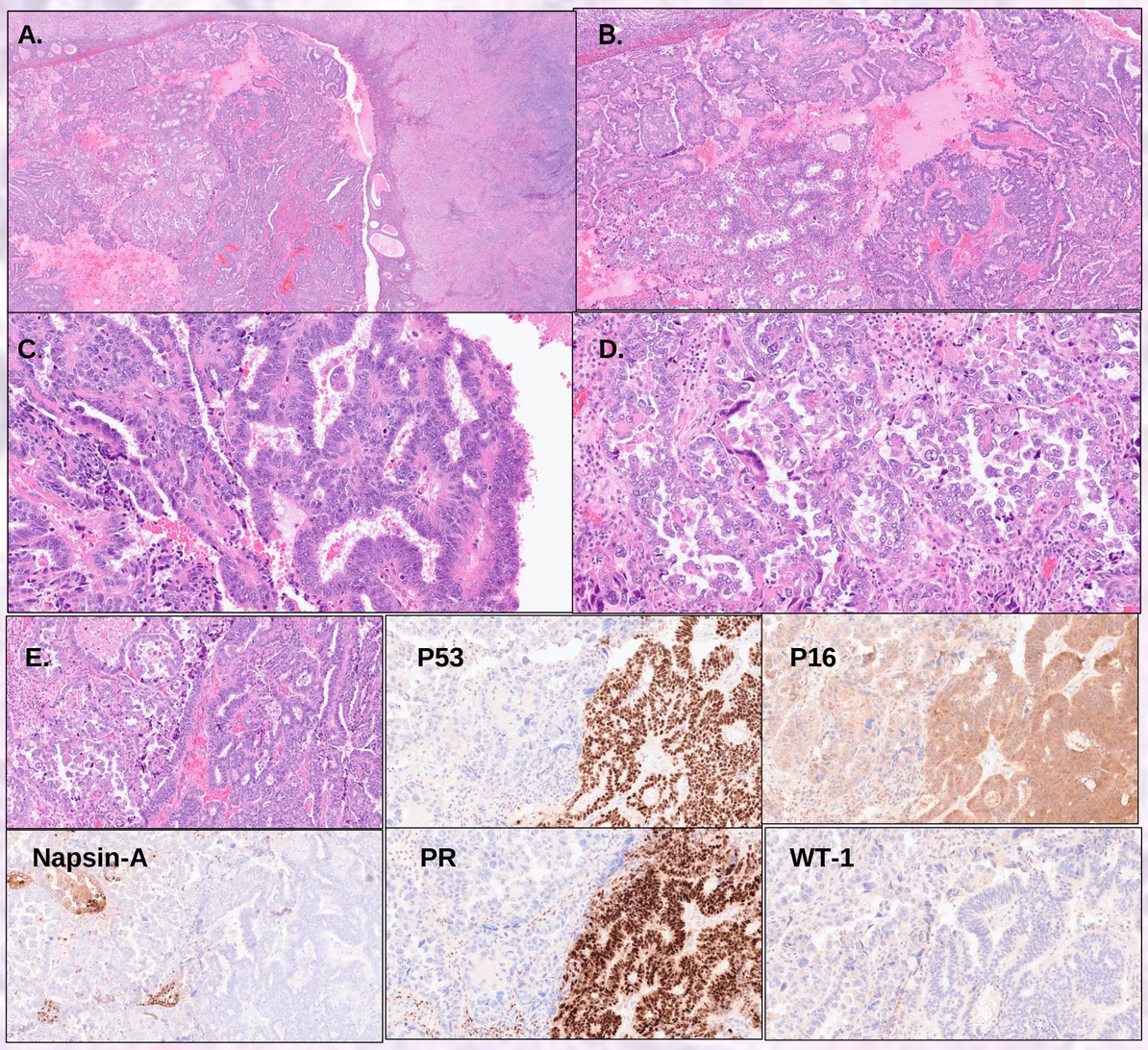

Figure 2: **A&B.** Low and intermediate power view of polypoid endometrial tumour with two spatially distinct histotypes. **C.** Component 1 - glandular architecture, columnar epithelium, moderate to high grade cytological atypia and brisk mitoses. **D.** Component 2 – tubulocystic architecture, clear and hob-nail cells and high grade cytological atypia. **E**. Both components intimately associated. **P53** positive abnormal 'mutation-type' in C, 'wild-type' staining in D. **P16** block positive in C, negative in D. Napsin negative in C, focally positive in D. **PR** positive in C, negative in D. **WT-1** negative in both components.

FINAL DIAGNOSIS: Mixed endometrial uterine serous and clear cell carcinoma. FIGO Stage II.

THE REAL DEAL

DISCUSSION & LITERATURE REVIEW

- True cases of mixed carcinoma of the uterine corpus are exceedingly rare, and commonly result in interobserver disagreement in endometrial cancer subtyping.
- **Diagnosis of exclusion:**

1. Not to be used for pathologically distinct tumour types, such as dedifferentiated endometrial carcinoma or carcinosarcoma.
2. Not to be used for morphologic variants of endometrioid carcinoma that simulate serous carcinoma (eg, villoglandular or papillary variants of endometrioid carcinoma) or clear cell carcinoma (eg, clear cell change in endometrioid carcinoma).
3. Not be used for cases with ambiguous morphology that defy classification.

- **Pathogenesis:** Some may represent collision tumors composed of genetically independent tumors while others may represent progression or divergence from a common origin.
- It is recommended not to use a specific quantitative threshold (for e.g. >5%) to exclude cases that clearly exhibit prototypical features of serous carcinoma or clear cell carcinoma. Any amount of serous carcinoma or clear cell carcinoma qualifies as a mixed carcinoma.

LEARNING POINTS

- Diagnostic criteria are not to be followed in isolation. Always consider the clinical picture in its entirety.
- Immunohistochemistry is recommended to help confirm the subtype of each component, using the suggested markers (positive and negative) for each individual subtype.

REFERENCES

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