Cervical Carcinoma with Prominent Endometrial and Uterine Corpus Involvement: A Report of 2 Unusual Cases

Zeba Ahmed, Sarah Read-Jones, Aneeshya Kandiyil and Shatrughan Sah

Department of Histopathology, University Hospitals Coventry & Warwickshire NHS Trust, Coventry, UK

NHS
University Hospitals Coventry and Warwickshire
NHS Trust

INTRODUCTION

Primary cervical carcinoma with extensive uterine corpus involvement (endometrial or endomyometrial) is a rare phenomenon, with only a few isolated case reports and occasional case series described in literature.[1-5] This can lead to misclassification as primary endometrial carcinoma with cervical extension (FIGO stage II) and inappropriate treatment. This pattern of invasion has unknown prognostic significance due to its rare incidence and does not currently impact FIGO staging. We present 2 cases of cervical carcinoma (adenocarcinoma and squamous cell carcinoma) entirely replacing the endometrium, lower uterine segment and focally myometrium mimicking an endometrial primary.

CASE HISTORY

	Case 1	Case 2
Year of resection	2020	2022
Age	55 years	60 years
Clinical presentation	Postmenopausal bleeding (PMB) with irregular polypoid area in endocervical canal but endometrial cavity normal on hysteroscopy	Cervical smear: moderate dyskaryosis. PMB. Ulcerated cervix on speculum examination
Biopsy diagnosis	HPV associated grade 1 endocervical adenocarcinoma (EAC)	HPV associated grade 2 cervical squamous cell carcinoma (SCC)
Scan findings	CT, MRI pelvis and PET scans: cervical tumour extending to LUS, 10 mm nodule at endometrial fundus, stage IB3	TV USS and MRI: Cervical tumour extending to LUS, tumour margins evaluation difficult due to iso-signal to the adjacent myometrium, secondary hydrometra, endometrium 6 mm, stage IB2
Management	Radical hysterectomy with pelvic lymphadenectomy and adjuvant chemoradiotherapy	Radical hysterectomy with pelvic lymphadenectomy. Patient declined adjuvant radiotherapy
Final diagnosis on hysterectomy	HPV associated grade 2 endocervical adenocarcinoma, SILVA pattern C. One of 21 pelvic lymph node with metastatic adenocarcinoma, FIGO stage IIIC1	HPV associated grade 3 squamous cell carcinoma, 26 pelvic lymph nodes tumour free, FIGO stage IB3
Follow up	Remains disease free after 2 years	Ongoing post-resection follow up
Unusual feature	Extensive involvement of the lower uterine segment (LUS), endometrium, focal superficial myometrium & adenomyosis and endometrium, simulating endometrial endometrioid adenocarcinoma.	Extensive involvement of LUS and endometrium, myometrium and right cornu by invasive carcinoma.

HISTOPATHOLOGY

CASE 1

Biopsy- Endometrial and cervical curettings (2020): complex atypical glands infiltrating the stroma in keeping with adenocarcinoma. Immunohistochemistry (IHC): Positive- PTEN, ER (focal weak), PR (very focal weak), CEA (focal), p16 (block type), p53 Wild type positive.
LLETZ (2018): Shallow and deep LLETZs from stenosed cervix revealed minimal endocervical tissue with HPV changes in ectocervix but no evidence of adenocarcinoma.
Cervical biopsy (2017): similar morphology and immunohistochemistry to biopsy in 2020.
Resection- Macroscopy: tumour involved the entire cervix, extends to LUS and a 20 mm endometrial polypoid lesion. Microscopy: entire cervix replaced by adenocarcinoma, continued into the LUS, endometrium, focal superficial myometrium and adenomyosis, Silva pattern C, extensive lymphovascular invasion, 1 out of 21 pelvic lymph node with metastatic carcinoma (1/21). Immunohistochemistry: similar findings as seen in biopsies. FIGO stage IIIC1.

CASE 2

Biopsy- Cervical biopsy: HPV associated grade 3 squamous cell carcinoma (non-keratinising basaloid type). Immunohistochemistry: Positive- BerEP4, p63, p16 (diffuse block type).
Resection specimen- Macroscopy: a circumferential polypoid tumour in the cervix extending to LUS and uterine body. Microscopy: cervix with a grade 3 SCC, non-keratinising, basaloid type, CIN3, extended to the LUS and endometrium; carcinoma involved the right cornu and the uterine body myometrium, focal vascular and perineural invasion, 26 pelvic lymph nodes tumour free. Immunohistochemistry: positive- BerEP4, CK5/6, p63, CD138 (in both cervical and endometrial, invasive and non-invasive) and p16 (diffuse block positive). FIGO stage IB3.

MICROPHOTOGRAPHS

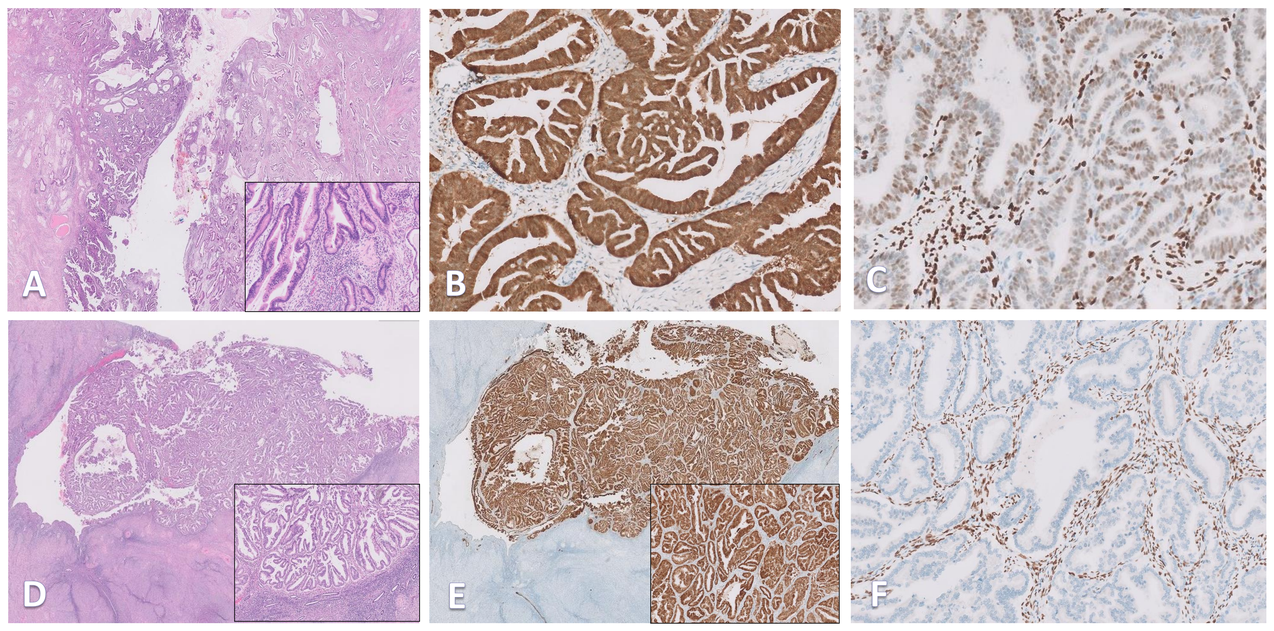

Figure 1 (Case 1): Resection specimen- (A-C) **Cervical AC**: (A) complex atypical glands replacing entire cervix (inset high power), (B) Abnormal block type p16 positive, (C) focal weak ER positive. (D-F) **Endometrial AC**: (D) Adenocarcinoma extensively involving endometrium, focal superficial myometrium & adenomyosis (inset high power), (E) Abnormal block type p16 positive (inset high power), (F) ER flat negative.

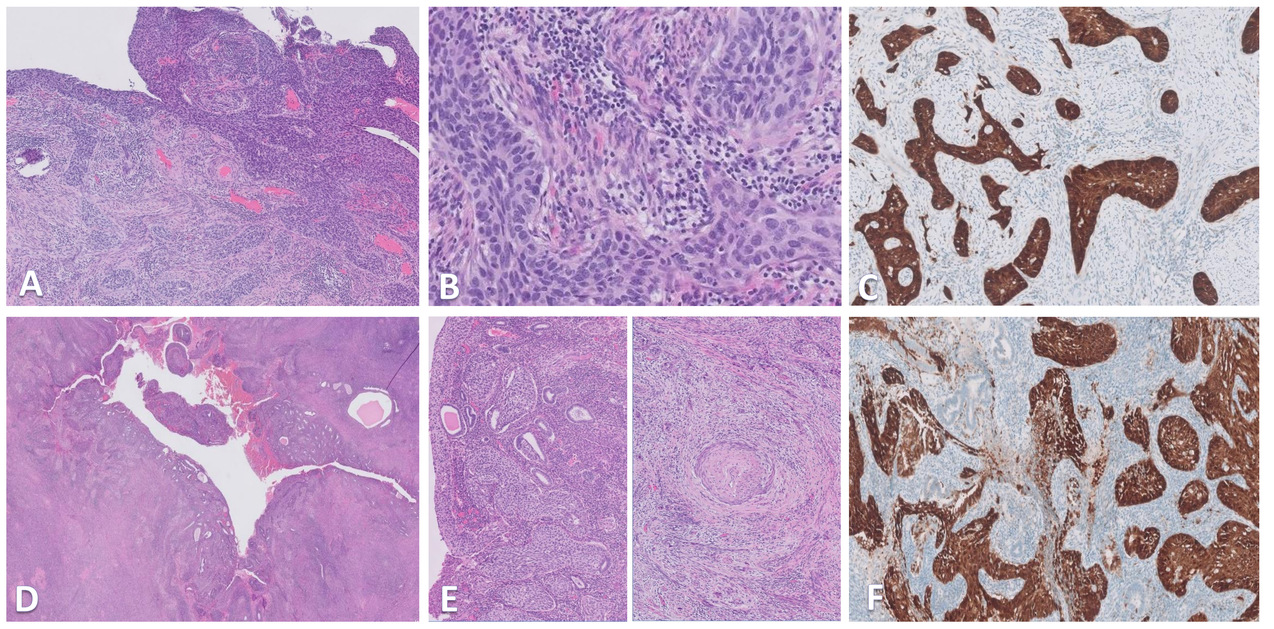

Figure 2 (Case 2): Resection specimen- (A-C) **Cervical SCC:** (A) SCC replacing entire cervix, (B) SCC in cervix (high power), (C) Abnormal block type p16 positive. (D-F) **Endometrial SCC:** (D) SCC extensively involve endometrium & myometrium, (E) High power with endometrial (left) and myometrial (right) involvement, (F) Abnormal block type p16 positive (background endometrial glands negative).

DISCUSSION

Endocervical adenocarcinoma (EAC) with extensive uterine corpus involvement can be difficult to distinguish from endometrial carcinoma (EEC) on morphology.[1] Studies have demonstrated the value of p16, HPV DNA and hormone receptors (ER, PR) with most (90%) of EAC showing block positivity for p16, HPV DNA detection, weak to absent ER, PR and in contrast strong ER, PR positivity and patchy p16 expression in EEC.[1,2,6]
Recently Bagde et al[3] reviewed 48 cases cervical SCC involving the endometrium reported in the literature and found 50% of the cases with superficial spread to endometrium without myometrial involvement and 70.45% of the cases had stage IB or less. Our case had deep myometrial invasion with FIGO stage IB3. Extensive endometrial and deep myometrial involvement by cervical SCC can be misdiagnosed as endometrial SCC or EEC with extensive squamous differentiation on endometrial biopsy. Diffuse block type positivity for p16 and detection of HPV DNA would help to finalise the diagnosis of cervical SCC as endometrial SCC and EEC usually show non-block type p16 and absent HPV DNA.
Various mechanisms such as cervical stenosis, CD138 (cell surface adhesion molecule),[4] transformation of endometrial cells to squamous cells and loss of heterozygosity markers in endometrial cells indicating monoclonal origin of both tumours,[5] have been proposed for endometrial spread of cervical SCC.[3] In our case CD138 was positive in both invasive SCC and CIN 3.

CONCLUSION

Careful morphologic evaluation, allied with clinico-pathologic correlation and the judicious use of ancillary tests, will help avoid diagnostic pitfalls and allow accurate diagnosis. Larger studies of such cases would help inform in formulating guidelines and prognosis.

REFERENCES

1. Yemelyanova, A et al. Endocervical adenocarcinomas with prominent endometrial or endomyometrial involvement simulating primary endometrial carcinomas. Am J Surg Pathol. 2009; 33: 914-24. doi: 10.1097/PAS.0b013e3181971fdd.
2. Reyes, C et al. Secondary involvement of the adnexa and uterine corpus by carcinomas of the uterine cervix: a detailed morphologic description. Int J Gynecol Pathol. 2015; 34: 551-63.
3. Bagde, MN et al. A review and case report of enigmatic superficial endometrial spread of cancer of the uterine cervix: Need for vigilance in the primary care setting. J Family Med Prim Care. 2021; 10: 3505-10. doi: 10.4103/jfmpc.jfmpc_39_21.
4. Ishida M and Okabe H. Superficial spreading squamous cell carcinoma of the uterine cervix involving the endometrium: Report of two cases with emphasis on the likely molecular mechanism. Oncology Letters. 2013; 5: 31-4.
5. Kushima M et al. Simultaneous squamous cell carcinomas of the uterine cervix and upper genital tract: Loss of heterozygosity analysis demonstrates clonal neoplasms of cervical origin. Int J Gynecol Pathol. 2001; 20: 353-8.
6. Stewart, C et al. Guidelines to aid in the distinction of endometrial and endocervical carcinomas, and the distinction of independent primary carcinomas of the endometrium and adnexa from metastatic spread between these and other sites. Int J Gynecol Pathol. 2018; 38: S75–S92. doi: 10.1097/PGP.0000000000000553

Declaration of conflict of interest: All authors confirm that this is work is not affiliated with any commercial sponsor or external organisation that could affect independence or objectivity.