

Pilomatrix-like high-grade endometrioid carcinoma (PiMHEC)
A three-case series highlighting morphologic heterogeneity and CTNNB1 mutation



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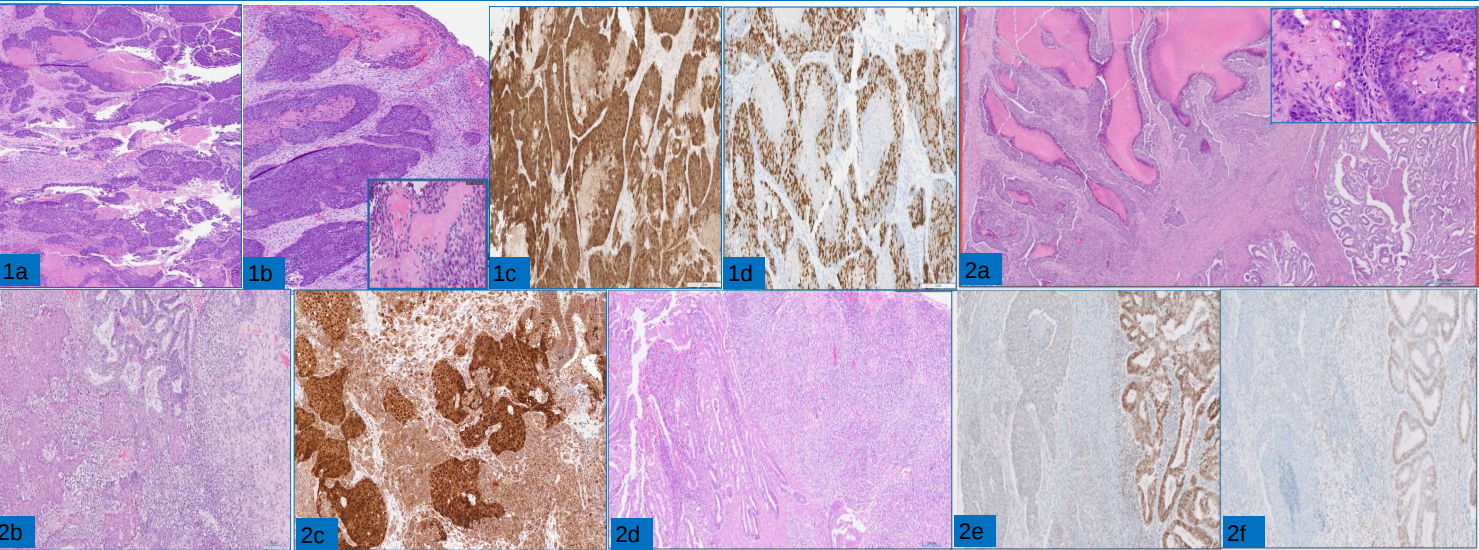
Introduction

Pilomatrix-like high-grade endometrioid carcinoma (PiMHEC) is a recently described, under-recognised aggressive variant of endometrioid carcinoma (EC). To date, only six publications describing approximately 25 cases have been reported in the literature.¹⁻³ We present three cases- including classical, mixed, and shadow cell-poor variants- highlighting diagnostic pitfalls and expanding the morphologic spectrum of this entity. We report a case with unique combination of PiMHEC, leiomyosarcoma, low-grade EC including corded-hyalinized endometrioid carcinoma (CHEC).

Clinical Findings

Case	Age (yrs)	Clinical presentations	Biopsy diagnosis	Hysterectomy diagnosis	FIGO stage	Treatment	Follow-up
1	51	Pelvic pain, weight loss	PiMHEC	Not applicable	IVB	Chemotherapy x 3 cycles	4 months, metastasis to parotid & bones
2	76	Post menopausal bleeding	Grade 1 EEC	Carcinosarcoma (carcinoma-90%, PiMHEC+G2 EEC+CHEC; leiomyosarcoma-10%)	IVB	Chemotherapy+ Radiotherapy	Died of brain metastasis, after 13 month
3	56	Post menopausal bleeding	Grade 1 EEC	PiMHEC	IIIB	Not applicable (Lymph node & omental metastasis)	Died of renal failure and sepsis, after 10 days of surgery

Microphotographs



Case 1: Figures 1a &1b- Endometrial & vaginal biopsies with nests of basaloid high grade tumour cells & geographic necrosis, inset, 1b-shadow cells with abundant pale eosinophilic cytoplasm and ghost-like nuclear contours; 1c- diffuse nuclear β -catenin and 1d- CDX2 positivity in basaloid cells.
Case 2: Figures 2a- PiMHEC with comedo-like necrosis and low-grade EEC infiltrating myometrium (Inset- shadow cells within PiMHEC); 2b- PiMHEC, low-grade EEC and CHEC components; 2c- β -catenin IHC, PiMHEC intense nuclear, CHEC moderate nuclear and EEC membranous positivity; 2d- low grade EEC and leiomyosarcoma; 2e-PAX8 & 2f-ER IHC: positive in low grade EEC, negative in PiMHEC.

Pathological Features				Immunohistochemistry & Molecular Findings			
Features	Case 1	Case 2	Case 3	Markers	Case 1	Case 2	Case 3
Low grade(LG) component	No	Yes	Yes	PAX 8	-ve (Negative)	Basaloid -ve/ LG (low grade) +ve	Basaloid -ve/ LG +ve
Basaloid component	Yes	Yes	Yes	ER	-ve	Basaloid -ve/ LG +ve	Basaloid -ve/ LG +ve
Shadow cells	Yes	Yes	No	PR	-ve	Basaloid -ve/ LG +ve	Basaloid -ve/ LG +ve
Necrosis	Yes	Yes	Yes	B-catenin	+ve (Nuclear)	+ve (Nuclear)	Not done
Myometrial invasion	Not applicable	>50%	>50%	CDX2	>50% of tumour	Focal	Focal
Vascular invasion	Not applicable	Extensive	Extensive	p53	Wild-type	Wild-type	Wild-type
				MMR	Proficient	Deficient (POLE -ve)	Proficient
				CTNNB1	Mutated	Mutated	Mutated

Discussion

The series illustrates remarkable morphological diversity, with one case showing a combination of grade 1 EEC, CHEC, PiMHEC and a sarcomatous component, emphasizing the challenges of accurate diagnosis due to intratumoral heterogeneity and important morphologic mimickers. CTNNB1 mutation was identified in all three cases; similar alterations have been reported in both CHEC and PiMHEC, supporting a shared Wnt/ β -catenin - driven molecular pathway and possible lineage relationship.³ Despite the presence of low-grade elements, the PiMHEC component represents the biologically aggressive element, likely driving tumour progression, metastasis and overall clinical outcome.²⁻³ Recognition of PiMHEC is important to avoid diagnostic pitfalls and to facilitate appropriate clinical management.

References

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