

Endometrioid Carcinoma of the Uterine Corpus With a Micropapillary Component: A Novel Prognostic Factor For Metastasis

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Abstract. *Background/Aim:* Micropapillary pattern is a morphologically distinctive form of carcinoma composed of small, hollow, or morula-like clusters of cancer cells surrounded by clear stromal spaces. The neoplastic cells characteristically display a reverse polarity, also known as an “inside-out” growth pattern, that is linked to higher frequencies of lymphovascular invasion and lymph nodal metastasis. To the best of our knowledge, it has not been previously recognized in uterine corpus. *Case Report:* We report 2 cases of endometrioid carcinoma of the uterine corpus with a micropapillary component. In these cases, histological examination identified an endometrioid carcinoma that had invaded the myometrial layer. The carcinoma cells that constructed the micropapillary components were immunohistochemically positive for EMA. They lined the stromal facing surface of the cell membrane, confirming the inside-out growth pattern, and D2-40 immunohistochemistry confirmed lymphovascular invasion of carcinoma cells. *Conclusion:* We believe that the micropapillary pattern linked to higher frequencies of lymphovascular invasion and lymph nodal metastasis may be one of the most important invasive patterns in endometrioid carcinomas of the uterine corpus for

predicting aggressive malignant potential, prognosis, and recurrence, although further, larger studies are required to evaluate its clinical significance.

To understand the biological essence of malignant neoplasms, researchers have studied their epidemiology, pathogenesis, histopathology, cytology, diagnostic molecular pathology, prognosis, and treatment. In histopathology, of the various invasive structural patterns seen in malignant neoplasms, the micropapillary pattern is one of the most well-known and clinically important.

The micropapillary pattern was first described in breast cancer, where this peculiar tumor growth pattern was referred to as having an exfoliative appearance (1). It is a morphologically distinctive form of carcinoma composed of small, hollow, or morula-like clusters of cancer cells surrounded by clear stromal spaces. The neoplastic cells characteristically display a reverse polarity, also known as an “inside-out” growth pattern, whereby the apical poles of the cells face the stroma, not the luminal surface, and epithelial membrane antigen (EMA) immunostaining shows this polarity reversal (2, 3). This pattern is linked to higher frequencies of lymphovascular invasion and lymph node metastasis (2, 3). The micropapillary pattern has been reported in multiple organs, including the breast, urinary bladder, lung, colon, and uterine cervix (3-9). To the best of our knowledge, it has not been recognized in the uterine corpus. We report two cases of endometrioid carcinoma of the uterine corpus with a micropapillary component.

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Key Words: Micropapillary, endometrioid carcinoma, uterine corpus.

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Case Report

Case 1. A 56-year-old female presented with post-menopausal bleeding at the University of Yamanashi Hospital. Biopsy and cytology of the endometrium revealed a diagnosis of adenocarcinoma. Her medical history indicated breast cancer (invasive breast carcinoma of no special type) in her 50s treated by surgery, adjuvant endocrine therapy with tamoxifen,

and radiation therapy. Pathological examination after surgery confirmed that the breast cancer had no micropapillary component. Subsequently, she underwent modified radical hysterectomy, bilateral salpingo-oophorectomy and lymph node dissection. Gross examination showed an ambiguous change of the endometrium (Figure 1A). The cut surface of the uterus had an unclear, infiltrative appearance.

Histological examination of the affected area identified an endometrioid carcinoma that had invaded the myometrial layer. This tumor displayed glandular architecture composed of columnar cells with pseudostratified large and markedly hyperchromatic nuclei (Figure 1B). The carcinoma cells in the invasive area formed micropapillary components (Figure 1D).

The endometrioid carcinoma cells were immunohistochemically positive for estrogen receptor (ER) (Figure 1C). Meanwhile, the micropapillary component cells that lined the stromal facing surface of the cell membranes were immunohistochemically positive for EMA confirming the inside-out growth pattern (Figure 1E). These cells were immunonegative for ER. We confirmed lymphovascular invasion of carcinoma cells by D2-40 immunostaining (Figure 1F). Pathological examination indicated that she did not have nodal metastasis (pelvic lymph node with para-aortic lymph node) at the time of surgery.

Case 2. A 55-year-old female presented with post-menstrual bleeding at the Yamanashi Kosei Hospital. The adenocarcinoma was diagnosed by biopsy and cytology of the endometrium. Her medical history indicated high-blood pressure and palmoplantar pustulosis. Subsequently, she underwent modified radical hysterectomy, bilateral salpingo-oophorectomy and lymph node dissection.

Gross examination showed an exophytic mass (70×55 mm) of the uterine corpus (Figure 2A). The cut surface of the uterus had an unclear, infiltrative appearance. Histological examination identified an endometrioid carcinoma that had invaded the myometrial layer. This tumor displayed glandular architecture with columnar cells containing pseudostratified, large, and markedly hyperchromatic nuclei (Figure 2B). Carcinoma cells also constructed micropapillary components in the carcinoma invasive area (Figure 2D).

The endometrioid carcinoma cells were immunohistochemically positive for ER (Figure 2C). Meanwhile, micropapillary component cells were immunohistochemically positive for EMA, as in Case 1 (Figure 2E), and focal and weakly positive for ER. The lymphovascular invasion of carcinoma cells was confirmed by D2-40 immunostaining (Figure 2F). Pathological examination indicated that she did not have nodal metastasis (pelvic lymph node) at the time of surgery.

The Research Ethics Committee of the Faculty of Medicine, University of Yamanashi approved this case report (approval number: 2665).

Discussion

We reported two cases of endometrioid carcinoma of the uterine corpus with the micropapillary component. The myoinvasive cases of endometrioid endometrial adenocarcinoma were classified on the basis of the 5 patterns of invasion: infiltrating glands, microcystic elongated and fragmented (MELF), broad front, adenomyosis like, and adenoma malignum (10). Gland infiltration was associated with higher stage, lymphovascular invasion, and recurrence (10). MELF pattern consisted of characteristic glands with a microcystic appearance or elongated structure and a compressed, sometimes slit-like lumen (11). The cancer cells lining these glands had conspicuous eosinophilic cytoplasm, squamoid appearance, or flattened and endothelial cell-like appearance (11). The presence of MELF pattern was associated with lymphovascular invasion and lymph node metastasis (11).

The uterus is divided into corpus and cervix. Stewart et al. reported eight cases of uterine cervical carcinomas with micropapillary component (9). The micropapillary component of the primary uterine cervical carcinomas was usually focal and sometimes initially overlooked. The metastatic carcinomas in the four patients with recurrence or disseminated disease all showed a pure micropapillary pattern. The authors indicated that micropapillary elements in uterine cervical carcinomas have aggressive malignant potential, similar to micropapillary carcinomas in general. Meanwhile, both of our cases had lymphovascular invasion confirmed by D2-40 immunostaining which indicates that the micropapillary component in the uterine corpus may be associated with lymphovascular invasion and lymph node metastasis. Although we believe that the micropapillary pattern is most likely a sixth important invasive pattern in endometrioid carcinoma of the uterine corpus following the 5 patterns listed above, further, larger studies are needed to evaluate its clinical significance.

Conflicts of Interest

The Authors declare no competing interests regarding this study.

Authors' Contributions

KM collected and analyzed the data and drafted the manuscript. KO, KT, HF and TK analyzed the data and contributed to the final draft of the manuscript. All Authors read and approved the final manuscript.

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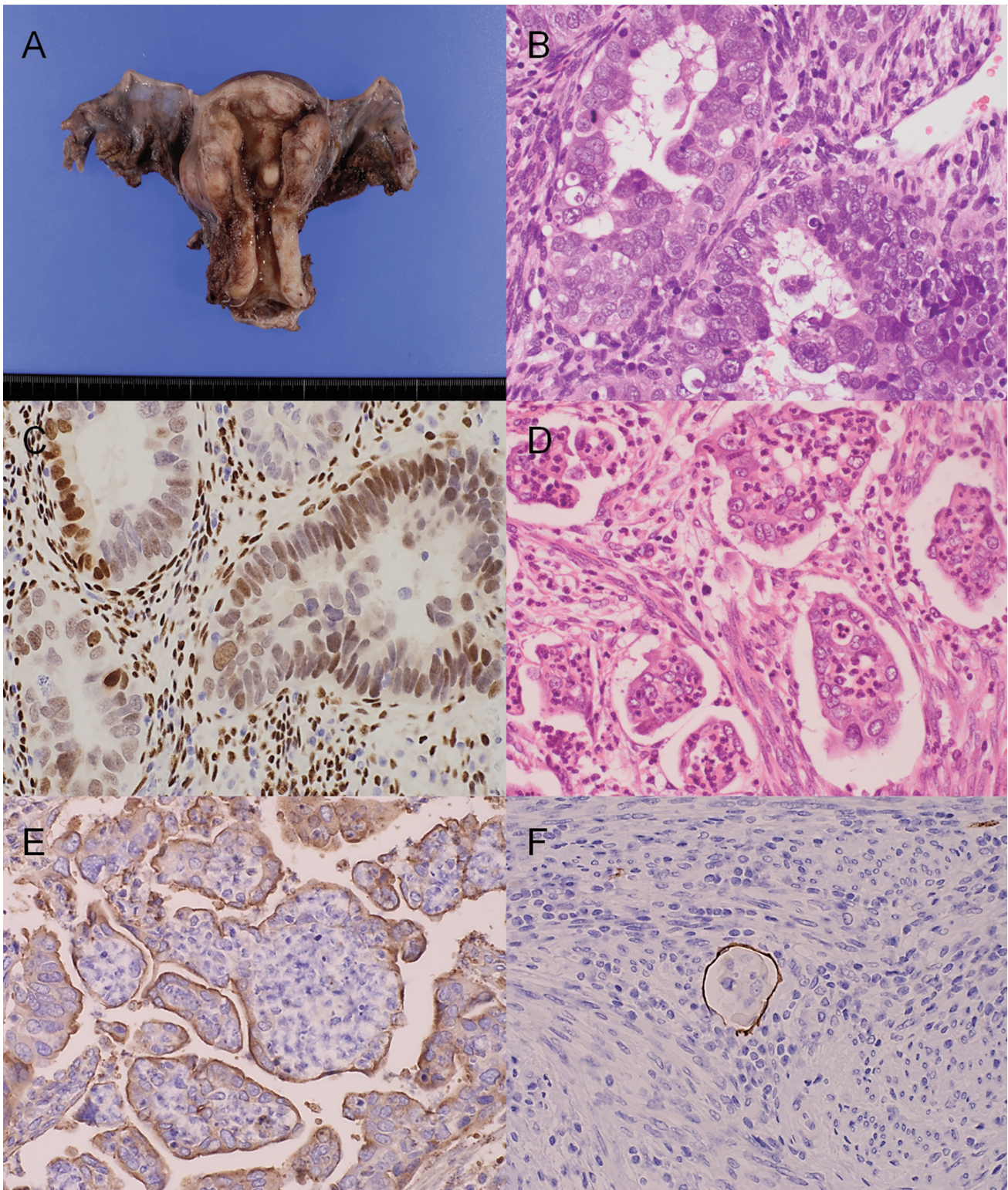


Figure 1. Case 1. Gross examination showed an ambiguous change of the endometrium (A). Histopathologic findings showed endometrioid carcinoma component (B, 400 \times), ER immunopositivity in the endometrioid carcinoma (C, 400 \times), micropapillary component (D, 400 \times), EMA immunopositivity in the micropapillary component (E, 400 \times), and lymphovascular invasion of carcinoma cells confirmed by D2-40 immunostaining (F, 400 \times). ER, estrogen receptor; EMA, epithelial membrane antigen.

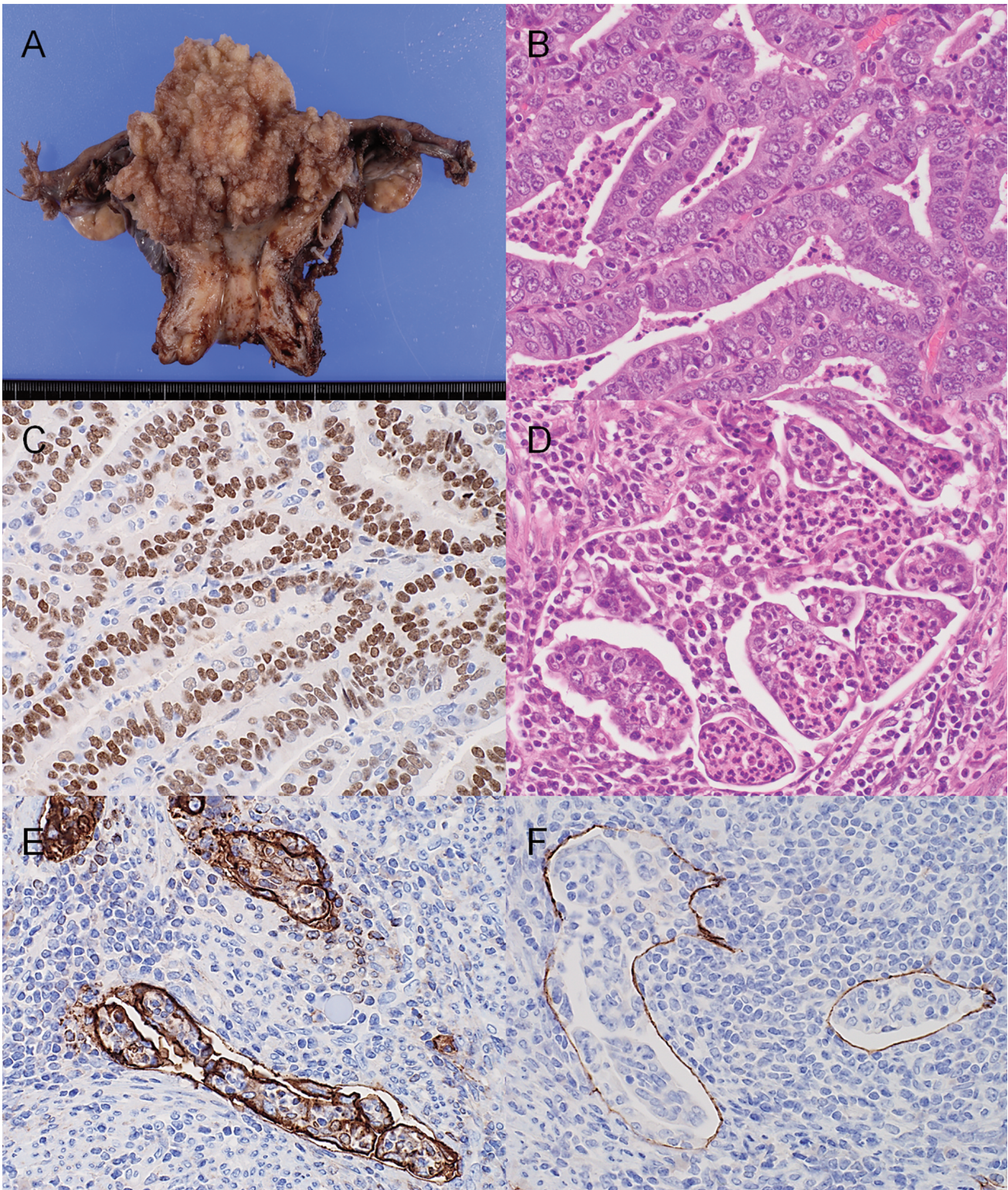


Figure 2. Case 2. Gross examination showed an exophytic mass (70×55 mm) of the uterine corpus (A). Histopathologic findings were endometrioid carcinoma component (B, 400×), ER immunopositivity in the endometrioid carcinoma (C, 400×), micropapillary component (D, 400×), EMA immunopositivity in the micropapillary component (E, 400×), and lymphovascular invasion of carcinoma cells confirmed by D2-40 immunostaining (F, 400×). ER, estrogen receptor; EMA, epithelial membrane antigen.

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