

Case Report

Endometrial serous tubular carcinoma extending into uterine leiomyoma in a post-menopausal woman: a case report and literature review

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Received January 19, 2017; Accepted November 26, 2017; Epub December 15, 2017; Published December 30, 2017

Abstract: Objectives: To describe an extremely rare case of endometrial serous carcinoma extending into the uterine leiomyoma. Case presentation: A 66-year-old postmenopausal Chinese woman complained of abnormal vaginal bleeding. Ultrasound showed a polypoid lesion in the uterine cavity and a different mass in the uterine wall. After surgery, histological and immunochemical exam confirmed the diagnosis of endometrial serous tubular carcinoma extending into uterine leiomyoma. Conclusions: We preferred the term "endometrial serous tubular carcinoma extending into uterine leiomyoma" for this rare case.

Keywords: Endometrial serous tubular carcinoma, uterine leiomyoma

Background

Type II endometrial carcinomas were firstly described by Hendrickson et al. [1] in 1982. They have different clinicopathological features and genetic backgrounds from type I carcinomas [2]. Type II carcinoma is clinically aggressive, accounting for a disproportionate number of recurrences and deaths [2]. Generally, it has pathological histotypes including serous adenocarcinomas and clear cell adenocarcinomas [2, 3]. Here we report an unusual case of endometrial serous tubular carcinoma extending into the leiomyoma of the uterus, which have never been reported previously. Our findings support the concept that true endometrial serous carcinoma can manifest as tubular glands as advocated by Darvishian et al. [4] previously.

Case report

A 66-year-old postmenopausal Chinese woman with normal weight complained of abnormal vaginal bleeding for two months. Menopause had commenced at the age of 56. She was 5 gravida, 2 para and denied any hormone

replacement therapy previously. Her pelvic physical examination and serum tumor biomarkers, including CA125, CA199, AFP and CEA, were all unremarkable. Transvaginal ultrasonography showed a 1.7×1.7×1.3-cm polypoid lesion protruding into the uterine cavity, which seemed to be adhered to a 2.2×2.2×2.0-cm mass localized in the left uterine wall (**Figure 1**). The prior curettage biopsy revealed endometrial adenocarcinoma. Thus, she underwent staging surgery including hysterectomy, bilateral salpingo-oophorectomy, omentectomy, pelvic and para-aortic lymphadenectomy.

Gross inspection indicated a 1×1×0.5-cm mass in the uterine cavity and a 3×2×2-cm mass in the left uterine wall. The former mass had a solid and gray cut surface originated and invaded the superficial myometrium. The latter lesion was localized in the uterine myometrium, but protruded into the uterine cavity and connected with the former. It had a smooth, soft, fleshy and gray cut surface with the central area of hemorrhage and necrosis.

Microscopically, the mass in the uterine cavity showed a glandular structure with a single layer

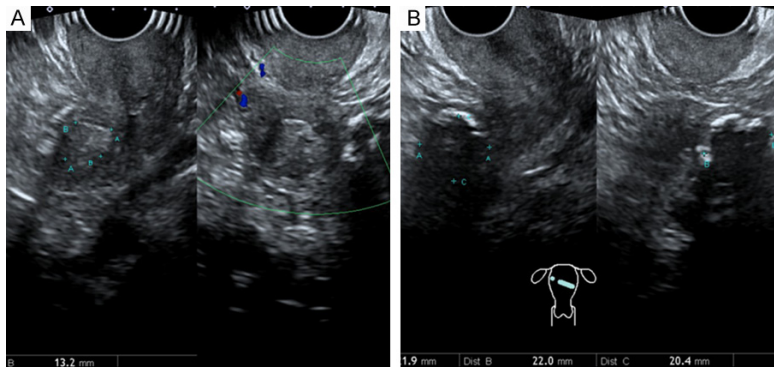


Figure 1. Polypoid lesion protruding into the uterine cavity (A) and another mass localized in the left uterine wall (B).

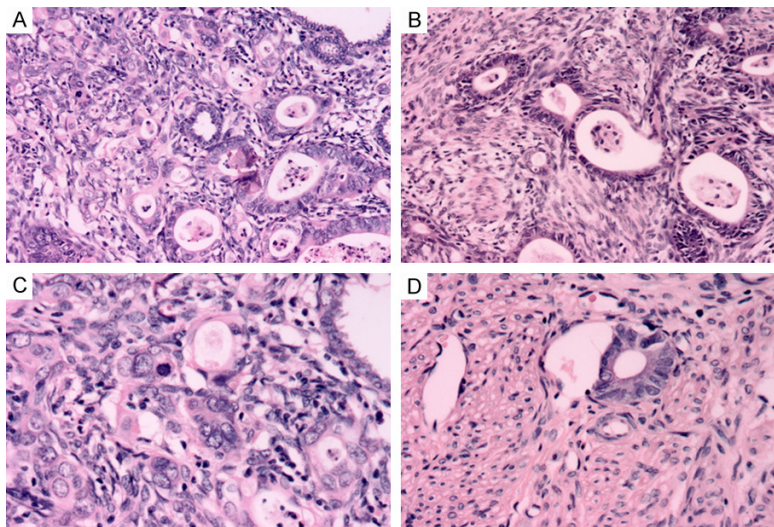


Figure 2. The infiltrative neoplastic growth was comprised of tubulocystic patterns. Carcinoma cells are arranged in a single layer. These atypical cells had large round to oval nuclei (A: 200 \times). The leiomyoma invaded by atypical glands (B: 200 \times). Mitotic figures (C: 400 \times) and lymphovascular invasion (D: 400 \times).

of cuboidal and columnar neoplastic cells. These tumor cells were characteristic of rounded nuclei, clumped chromatin, prominent nucleoli and numerous mitotic figures. Lymphovascular invasion can be seen. The mass in the uterine wall was composed of atypical neoplastic glands invading the interlaced bundles of smooth muscle fibers resembling a submucosal leiomyoma. These neoplastic glands showed the same features as that of former mass (Figure 2). The size and shape of the bilateral fallopian tubes and ovaries were macroscopically normal, and no malignant cells were identified in subsequent peritoneal washings. Evidence of dissemination was not observed in the abdominal cavity. The omentum, pelvic and

periaortic lymph nodes were normal.

The neoplastic cells in both lesions showed an identical immunostaining pattern including strong positive staining for p53, p16, the phosphatase and tensin homolog deleted on chromosome ten (PTEN), insulin-like growth factor mRNA-binding protein 3 (IMP-3) and β -catenin, and negative staining for estrogen receptor (ER) and progesterone receptor (PR) and the high Ki67 index (Figure 3). These features were typical of endometrial serous carcinoma.

Taken together, this case was consistent with an endometrial serous tubular carcinoma invading superficial myometrium and uterine submucosal leiomyoma (stage IA, pT1aN0M0).

Discussion

Endometrial serous tubular carcinoma extending into uterine leiomyoma is rare. This carcinoma is difficult in distinguishing from low-grade endometrioid carcinomas in morphology due to its well-differentiated tubulogl-

angular morphology [4]. The case we described here is consistent with serous carcinoma as determined by its morphology and characteristic immunophenotyping. We reviewed the current English literature and found only 8 similar cases [4]. The clinical and pathological features were summarized in Table 1.

Serous carcinoma is often composed of papillary architectures, and such pure form was called as uterine serous papillary carcinoma previously. Serous carcinoma can also show a gaping gland pattern characteristic of irregular glands with gaping lumina instead of papillae. In our case, the tumor exhibited a tubuloglandular growth pattern lined by a single layer of

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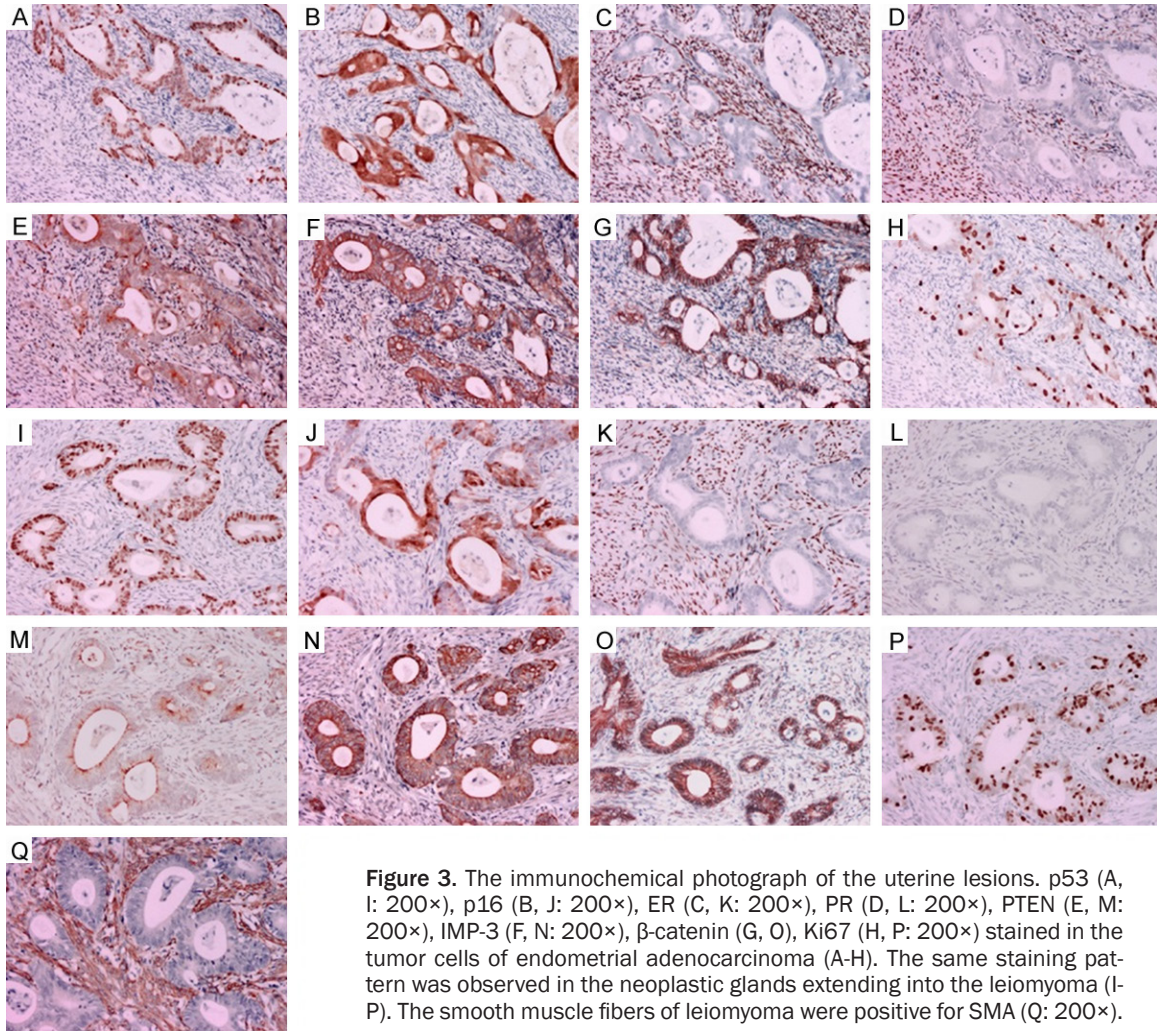


Figure 3. The immunochemical photograph of the uterine lesions. p53 (A, I: 200×), p16 (B, J: 200×), ER (C, K: 200×), PR (D, L: 200×), PTEN (E, M: 200×), IMP-3 (F, N: 200×), β -catenin (G, O), Ki67 (H, P: 200×) stained in the tumor cells of endometrial adenocarcinoma (A-H). The same staining pattern was observed in the neoplastic glands extending into the leiomyoma (I-P). The smooth muscle fibers of leiomyoma were positive for SMA (Q: 200×).

cuboidal or columnar neoplastic epithelial cells in low power resembling to that of a well differentiated endometrioid carcinoma. The most striking feature of this case is the presence of prominent atypia including large nuclei with prominent nucleoli, scant cytoplasm and numerous mitotic figures.

Several studies have demonstrated the utility of immunohistochemical markers, including p53, P16, PTEN, IMP-3, β -catenin, ER and PR, in distinguishing between the common endometrioid carcinomas and serous carcinomas [5, 6]. An immunoprofile of ER-, PR-, p53+, p16+, and/or, PTEN+, IMP3+, β -catenin+ (membrane) favors a diagnosis of uterine serous carcinoma [3-10].

p53, a tumor suppressor gene, is typically over-expressed in serous carcinomas and regarded as a surrogate marker of serous carcinomas [6,

7]. Strong and diffuse p16 immunoreactivity is a feature of HPV-related carcinomas, but can also be frequently seen in serous carcinomas [8]. IMP3 is an oncofetal protein that is involved in embryogenesis and carcinogenesis of some malignancies [9]. Zheng *et al.* [10] found that IMP3 is a novel biomarker for uterine serous carcinoma and significantly less expressed in the non-serous uterine carcinomas. PTEN is a tumor suppressor gene that maps to chromosome 10q23. Loss of PTEN expression is more commonly associated with the endometrioid subtype than with serous carcinomas [11]. β -catenin is an epithelial cell adhesion molecule. Nuclear expression of β -catenin was observed in a subset of endometrioid carcinomas but not in serous carcinomas [12].

Low-grade endometrioid carcinoma is usually strongly positive for ER and PR, whereas serous

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Table 1. Summary of the clinicopathological features of endometrial serous tubular carcinoma

Authors [Reference]	Age	Stage	Pathology	Immunostain	Surgery	Radiation	Chemotherapy	Follow-up
Darvishian F, et al. [4]	Na	IB	Tubuloglandular growth pattern, high nuclear grade	p53+, PTEN+, β -catenin+ (membrane), ER-, PR-	TAH-BSO, LND	IVRT	None	NED at 37 mo
	Na	IC	Tubuloglandular growth pattern, high nuclear grade	p53-, PTEN-, β -catenin+ (membrane), ER+, PR+	TAH-BSO, LND	WPRT	None	NED at 4 mo
	Na	IA	Tubuloglandular growth pattern, high nuclear grade	p53+, PTEN+, β -catenin+ (nuclear), ER+, PR-	TAH-BSO, LND	None	None	NED at 12 mo
	Na	IIIA	Tubuloglandular growth pattern, high nuclear grade	p53+, PTEN+, β -catenin+ (membrane), ER-, PR-	TAH-BSO, LND	None	Paclitaxel/carboplatin $\times 6$	AWD at 32 mo
	Na	IIIA	Tubuloglandular growth pattern, high nuclear grade	p53+, PTEN+, β -catenin+ (membrane), ER-, PR+	TAH-BSO, LND	WPRT	Paclitaxel/cisplatin/doxorubicin $\times 6$	NED at 6 mo
	Na	IA	Tubuloglandular growth pattern, high nuclear grade	p53-, PTEN+, β -catenin+ (membrane), ER-, PR-	TAH-BSO, LND	WPRT	Doxorubicin/gemcitabine	AWD at 31 mo
	Na	IA	Tubuloglandular growth pattern, high nuclear grade	p53+, PTEN+, β -catenin+ (membrane), ER+, PR+	TAH-BSO, LND	IVRT $\times 3$	Paclitaxel/carboplatin $\times 3$	AWD at 35 mo
	Na	IA	Tubuloglandular growth pattern, high nuclear grade	p53+, PTEN+, β -catenin+ (membrane), ER-, PR-	TAH-BSO, LND	None	None	NED at 9 mo
Zhou F et al.	56	IA	Tubuloglandular growth pattern, high nuclear grade	p53+, p16+, PTEN+, IMP3+, β -catenin+ (membrane), ER-, PR-, Ki67 high	TAH-BSO, LND	None	None	NED at 12 mo

Abbreviations: NA: not available; NED, no evidence of disease; AWD, alive with disease; TAH-BSO, total abdominal hysterectomy-bilateral salpingo-oophorectomy; LND, lymph node dissection; mo, month; IVRT, intravaginal radiation therapy; WPRT, whole pelvic radiation therapy.

carcinoma is negative for both. A very high Ki67 labelling index is also more typical of serous carcinoma [13]. Using only strong and diffuse staining as evidence of a positive result, we found the tumor cells in our case were strongly positive for p53, p16, PTEN, IMP-3 and negative for ER and PR, a typical feature of endometrial serous carcinoma.

We found that both tumors in the endometrium and the leiomyoma had identical morphological and immunochemical features, implicating that the latter most probably originated from the endometrial carcinoma. The serous carcinoma extending into submucosal leiomyoma of the uterus has rarely been reported. We here characterized the term “endometrial serous tubular carcinoma extending into uterine leiomyoma” for this rare case.

The endometrial serous carcinoma must be differentiated from endometrial intraepithelial carcinoma (EIC) because of their common glandular structures and marked cytological atypia. EIC has been alternatively regarded as in situ serous adenocarcinoma and is considered to usually occur in the setting of inactive or resting endometrium and frequently involves endometrial polyp [14]. Carcinoma cells of EIC can replace the glands in the polyp and form micropapillary protrusions, but lacking apparent evidence of stromal invasion.

Conclusions

To the best of our knowledge, there are rare reports on the endometrial serous tubular carcinoma, especially extending into submucosal leiomyoma of the uterus. We concurred with the term “endometrial serous tubular carcinoma” for this case. Surgery is the principal treatment. Adjuvant chemotherapy and/or radiotherapy have been given in some cases, but the role is controversial.

Acknowledgements

This research was supported by Department of Education of Zhejiang Province, China, under grant number Y201328159.

Disclosure of conflict of interest

None.

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