Appendiceal Adenocarcinoma Involving the Uterus and Mimicking Primary Endometrial Atypical Gastric-Type Mucinous Proliferation : A Rare Case Report

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Case Report

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Abstract

Gastric/gastrointestinal-type mucious lesion in the endometrium may be mostly primary or cervix gastric-type adenocarcinoma involvement. Gastriointestinal and pancreatobiliary adenocarcinoma involving the endometrium is rare. We report a rare appendiceal adenocarcinoma of a 55-year-old female, involving the uterus, mimicking primary endometrial gastric-type lesion. Endometrial lesion was associated with a polyp, which was composed of significant complex papillary architecture and crowed glands resembling lobular endocervical glandular hyperplasia (LEGH), with cytologically abundant pale eosinophilic cytoplasm and atypical nuclear. Mucinous epithelium cells of endometrial lesion was diffusely positive for MUC6, CK7 and negative for p16, PAX8, ER, NapsinA. This histologic morphology and immunophenotype show gastric-type differentiation. Meanwhile, the appendiceal tumor exhibited conventional intestinal type manifestation but focal invasive adenocarcinoma with abundant pale eosinophilic cytoplasm and focally immunoreactivity for MUC6. On the basis of morphologic and immunoreativity examination of the endometrial and appendix, We believe that the diagnosis of atypical mucinous proliferation of gastric-type of endometrium arising from appendiceal adenocarcinoma can be established. Patient died of disease at 3 months after surgery.

Introduction

Gastric/gastrointestinal-type neoplasms in the endometrium are associated with gastric-type mucinous metaplasia of native endometrium epithelium and may an independent primary entity[1]. The diagnosis precondition of primary gastric type endometrium tumor is that extraendometrium tumor involvement should be excluded, such as cervix gastric-type adenocarcinoma and digestive system origin [1–2]. In this report ,we demonstrated appendiceal adenocarcinoma involving the endometrium in the form of atypical mucinous proliferation of gastric-type of the endometrium, resembling primary endometrial gastric-type mucinous lesion.

Clinlcal Summary

A 55-year-old female presented with abdominal pain lasting one year after menopause was admitted to our institution. CT-scan revealed cystic lesion in the appendix with focal calcification and a cystic mass in the left ovary. NO abnormal was detected in the hepatobiliary systems, pancreas and spleen. Ultrasound examination showed hypoechoic mass in the right posterior wall of the uterine cavity. The Serum tumor marker including CA19-9 (100.4U/ml), CA125 44.9 (U/ml) was slightly elevated. The patient underwent appendectomy, total hysterectomy, bilateral salpingo-oophorectomy.

Pathological Finding

Gross examination, histologic observation and immunohistochemical staining(CDX2, CK20, CK7, MUC2, MUC6, p53, PAX8, p16, ER, NapsinA,CgA) are performed.

The appendix measured 5cm in length and 2.5cm in diameter. the appendix is highly dilated and filled with gelatinous mucus without obvious rupture. Histologic morphology showed the transition from low-grade mucinous neoplasm to invasive adenocarcinoma. In the appendix wall area, irregularly fused atypical glands composed of mucinous epithelium with moderate-severe nuclear atypia, eosinophilic foamy cytoplasm and increased mitotic figures was observed in desmoplastic stroma (Figure1A, B). A polyp-like mass in the uterine cavity was about 2*1*0.7cm in size(Figure1C). Histologically, the endometrial lesion associated with a polyp exhibited complex papillary architecture and crowded glandular growth pattern, which was cytologically characterized by abundant pale eosinophilic or clear cytoplasm resembling plyoric glands and nuclear atypic with nuclear enlargement, hyperchromatin and prominent nucleoli（Figure1D). In focal area, the coexistent of native endometrial and mucinous epithelium in individual gland can be found, suggesting mucinous metalplasia (Figure1E). No mucinous glands was present in the myometrium. The left ovary demonstrated a cyst mass with a single-chamber measuring about 8*7*2cm, morphologically features supporting borderline mucinous neoplasm(Figure1F). Bilateral whole tubal sample were detected and mucosal mucinous metaplasia is observed. Various degree of mucinous epithelium expression of gastric-type marker MUC6 in this case are demonstrated （in the Figure 2). The immunohistochemical results is listed in the Table 1

Table 1
immuhistochemistry results for tumor involvement sites

IHC	Ovary	Endometrium	Left fallopian tube	
CK20	+	focal+	Focal1 +	—
CDX2	+	focal+	Focal 1+	—
CK 7	+	+	+	+
MUC6	focal+	focal+	+	focal+
MUC2	+	focal+	—	—
p16	—	—	—	—
ER	—	—	—	—
NapsinA	—	—	—	—
P53	Wilde-type	Wilde-type	Wilde-type	Wilde-type
CgA	Scatter +	Scatter +	Scatter +	Scatter +
PAX8	-	-	-	-

Discussion

In the endometrial neoplasia, the presence of mucinous epithelium is rare and should be paid attention. Extrauterine tumor involvement or cervix mucinous neoplasm extension should be firstly excluded[1–2].

In our study, the endometrial mucinous lesion was present in the form of poly-like growth pattern, grossly resembling primary endometrial poly. Histologic morphology exhibited complex papillary architecture and crowded glands characterized cytologically by abundant pale eosinophilic and clear cytoplasm with nuclear atypia. Although the cytologic and significant architecture features was treated as low-grade endometrioid adenocarcinoma except absence of invasive biological behavior, diffusely positivity for MUC6 and negativity for ER,PAX8 demonstrated gastric-type differentiation, suggesting possibly primary endometrial gastric lesion. In addition, the coexistent of native endometrial epithelium and mucinous cells in individual gland can be found, resembling mucinous metaplasia. These findings also give the impression of primary endometrial neoplasm. primary endometrial gastric(gastrointestinal-type) lesion is regarded as a distinct entity in a series study by Wong et al[1] they believed that benign and atypical gastric/gastrointestinal-type mucinous lesions may progress to related gastric-type adenocarcinoma, resembling the spectrum of cervix gastric-type mucinous lesions counterpart[3]. No mucinous glands was present in the myometrium in our case. On the account of the diagnostic criteria proposed by Wong et al about endometrial gastric(gastrointestinal)-type mucinous lesion, we made the diagnosis of atypical mucinous proliferation of gastric-type of the endometrium. Interestingly, in Wong et al study, these atypical endometrial mucinous lesions are closely associated with poly like our case[1]. The presentation of endometrial mucious lesion in this case strongly supported its primary because of absence of cervical and vagina involvement.

Given the presence of invasive adenocarcinoma in the appendix, appendiceal tumor extension to the uterus should be taken consider. Gastriointestinal adenocarcinoma origin mostly refer to appendiceal mucinous neoplasm in the previous literatures. We reviewed literatures about the endometrium involvement associated with appendiceal mucinous neoplasm. It is not difficult to find that the morphology of secondary endometrial mucinous was similar to that of primary appendiceal neoplasm. And the immunohistochemistry phenotype of the primary and secondary lesion was consistent, displaying the expression of intestinal type marker (CDX2,CK20) rather than primary endometrium neoplasia inmunophenotype[4–8]. Appendiceal mucinous neoplasm involving the endometrium exhibiting gastric-type differentiation is not reported in previous literatures. In present case, microscopic examination revealed focal invasion adenocarcinoma of the appendix with the characteristics of pyloric glands with pale eosinophilic cytoplasm, moderate to severe nuclear atypia. Focal immnoreactivity for MUC6 can be seen. We speculated that The Phenomenon is abnormal differentiation of tumor leading to morphological heterogeneity. This Interpretation may further suggest endometrial mucious lesion arising from appendix adenocarcinoma.

Tumors extension to the female genital tract, the ovary is commonly metastasis site. Regarding the growth pattern of appendix mucinous tumors involving the ovary, a spectrum of benign metaplastic to maligant mucinous lesions can be observed[9]. This ability of colonization native epithelium may lead to neoplasm extension[4, 5, 7, 8]. In our study, the spectrum of benign gastric-type metaplasia to atypical proliferation(boderline) in the uterus poly is observed, suggesting benign endometrial mucinous metaplasia of extrauterus tumor involvement have the equal potential of progression to borderline or even malignant, mimicking primary endometrial cancer. Atypical mucinous proliferation of gastric-type of

the endometrium is proposed as the precursor lesion of primary endometrial gastric-type adenocarcinoma like cervical LEGH counterpart[3, 10]. In addition, because of the presence of ovarian mucious borderline tumor and fallopian tube mucious metaplasia in this case, synchronous and multifocal gastric mucinous metaplasia and neoplasm of the female genital tract(SMMN-FGT) can not be excluded, some studies have been described[11]. But accompanying with independently appendix neoplasm is extremely rare.

In conclusion, according to currently research, gastric-type mucinous lesions can independently or multiply occur in various sites of the female reproductive tract. The morphology of the lesions may demonstrate benign mucinnous metaplasia, atypical hyperplasia, invasive adenocarcinoma[1, 3, 12]. In regard to invasive adenocarcinoma of the appendix presenting with morphologically heterogenous with gastric-type differentiation and the morphology and immunophenotype of the endometrium associated with appendix neoplasm in this case, appendiceal adenocarcinoma involving the endometrium resembling primary endometrial gastric-type neoplasia lesion seem to be established. Therefore, one of the diagnosis criterias for gastric-type adenocarcinoma is the absence of other primary site [1, 3, 13]. Gastric-type mucinous carcinoma(GAS) in the endocervical and endometrium have revealed poor prognosis[14]. Park et al detected 21 GAS cases by next-generation sequencing, they described frequently gene mutations in GAS. Some gene features such as KMT2D, ERBB3, RNF43 mutations associated with poor prognosis in Gastriointestinal adenocarcinoma are also present in GAS[15]. Whether the appearanece of morphological heterogeneity with gastric-type differentiation in appendix adenocarcinoma show worse prognosis, the data is limited to evaluated. More cases for further studying can help to understand the biological and the molecular mechanisms of gastric-type differentiation mucinous tumor occurring in extra-stomach.

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Figures

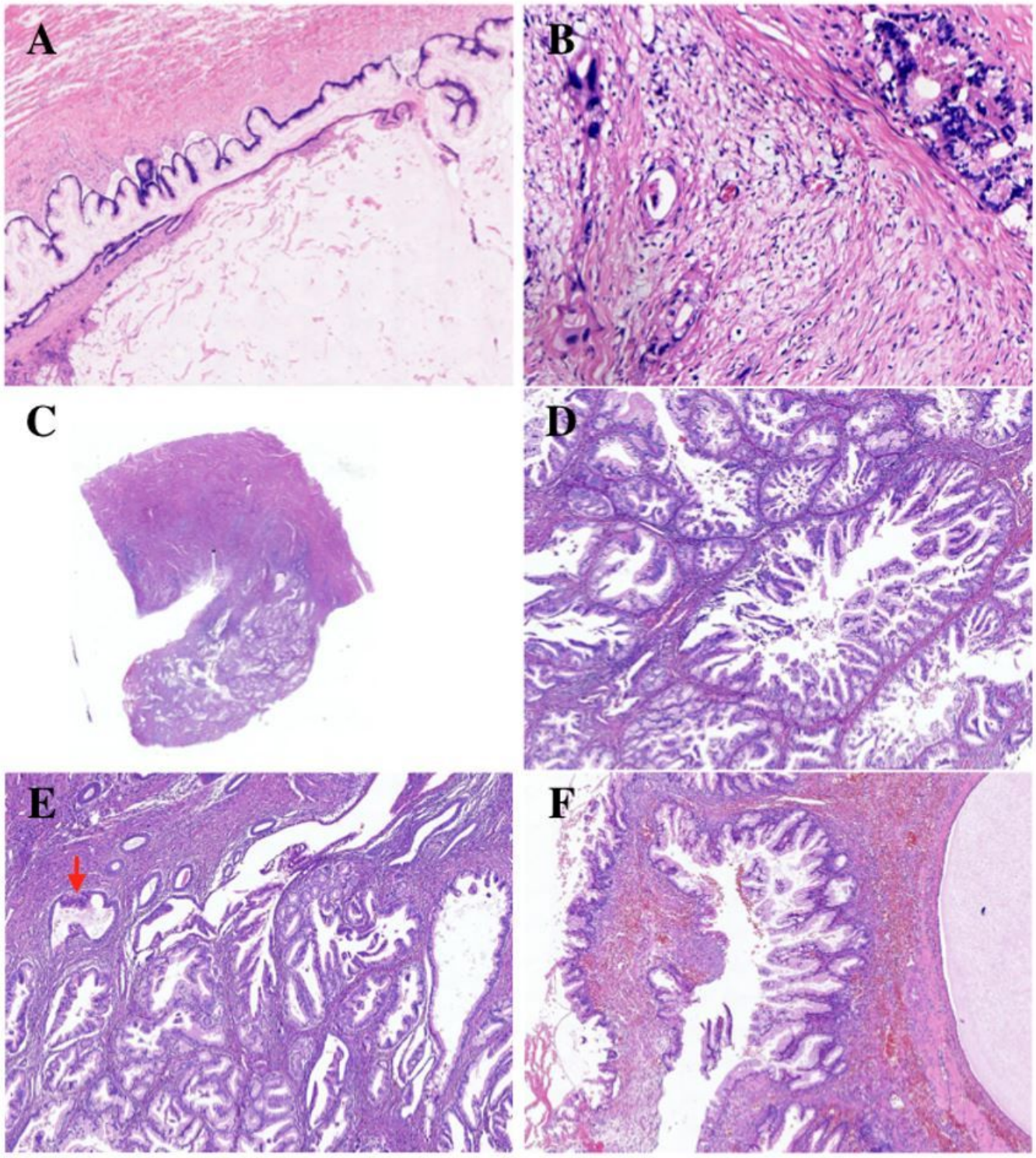

Figure 1

Histological Morphology of the appendix and the uterus poly. The area of low grade appendiceal mucinous neoplasm(LAMN)(A). Invasion carcinoma shows irregularity glands located in the wall of the appendix, with pale eosinophilic and foamy cytoplasm, moderate-to-severe nuclear atypia, desmoplastic stromal reaction is significant(B). The lesion in the endometrium is associated with a poly(C), composed of complicated irregularly glands and papillary architecture resembling lobular endocervical glandular

hyperplasia or pyloric glands metaplasia with abundant pale cytoplasm, mild-to-moderate nuclear enlargement (D,E). Focal individual gland metaplasia can be seen(red arrow). Ovary tumor shows borderline mucinous neoplasm(F).

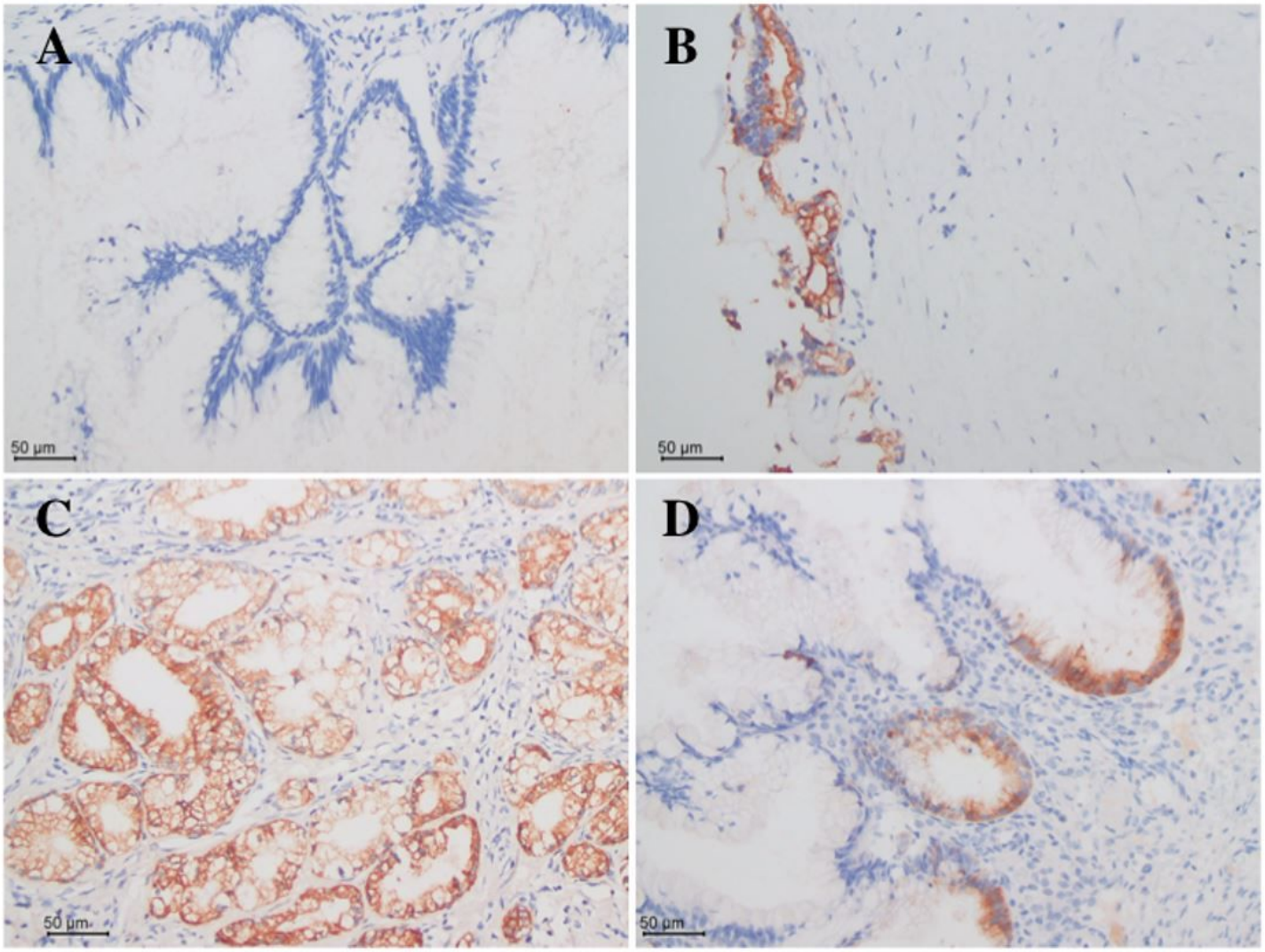

Figure 2

various degree of mucinous epithelium expression of gastric-type marker MUC6 in this case. LAMN shows negative(A), but invasion carcinoma is focal positive(B). diffuse immunopositivity for MUC6 highlight in the endometrial mucinous epithelium cells(C). Ovarian mucinous cell show focal positive.

+, more than 25% tumor cells positive; focal+, less than 25% tumor cells positive; P53 ,wilde type(more than 0% but less than 80% tumor cells positive).