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Case Report

Endometrial glandular dysplasia - A unique entity of gynecologic pathology: Case report and literature review

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Abstract

Based on morphologic and molecular findings, lesions that bridge between the resting endometrium and serous endometrial intraepithelial carcinoma (EIC) were designated as 'Endometrial glandular dysplasia (EmGD)' in 2004. EmGD may represent the earliest change in the development of endometrial serous carcinoma (ESC). Recently reported that about 20% of women with ESC had a history of breast cancer and the incidence was higher in patients who were at younger age. A 50-year-old woman who had an history of breast cancer and taking tamoxifen for several years was referred to clinic. Hysterectomy was performed. The microscopic examination showed an atrophic endometrium with endometrial glands and surface epithelium lined by atypical cells showing nucleomegaly, nuclear hyperchromasia, rare nucleoli, and no significant stratification. Rare papillae formation and atypical mitotic figures were present. p53 expression were evaluated by immunohistochemistry in these cells. EmGD can be diagnosed by routine microscopic evaluation and requires the careful exclusion of morphologic mimics, such as metaplastic processes and EICs. Characteristics of p53 and MIB-1 immunostains of EmGD may be of diagnostic usage in surgical pathology practice. Recognition of EmGD potentially offers the opportunity to prevent the development of the associated malignancy and may provide an opportunity to improve the management of uterine serous carcinoma.

Key words:

Endometrial glandular dysplasia, precancerous, serous carcinoma

Introduction

Endometrial cancers are the most common gynecologic malignancy in developed countries [1]. There are two major histologic types; endometrioid carcinoma and papillary serous carcinoma [2]. There are two well-known precursor lesions of endometrioid carcinoma; endometrial intraepithelial neoplasia and atypical endometrial hyperplasia [3,4]. Based on morphologic and molecular findings, lesions that bridge between the resting endometrium and serous endometrial intraepithelial carcinoma (EIC) were designated as 'Endometrial glandular dysplasia (EmGD)' in 2004 [5,6].EmGD is the first morphologically identifiable precursor lesion of endometrial serous carcinoma (ESC) [6]. ESC originates from latent precancerous lesions (p53 signature glands), progresses to precancerous lesions (EmGD), then to early serous cancer (EIC) and finally to fully developed cancers [6]. In the previous studies it is said to be that history of breast cancer may be a potential risk factor for the development of ESC in younger women [7].It is believed that both tumors have a common genetic predisposition and both are related with the unopposed estrogen stimulation [8].Tamoxifen had a possible carcinogenic effect on endometrium in patients with breast cancer. On the other hand, patient with ESC hand a significantly high prevalence of previous breast cancer history [9]. Especially patients under 55 year-old with ESC had a history of breast cancer in Liang et al's study [10]. Here in we report a challenging case with a history of breast cancer and tamoxifen treatment.

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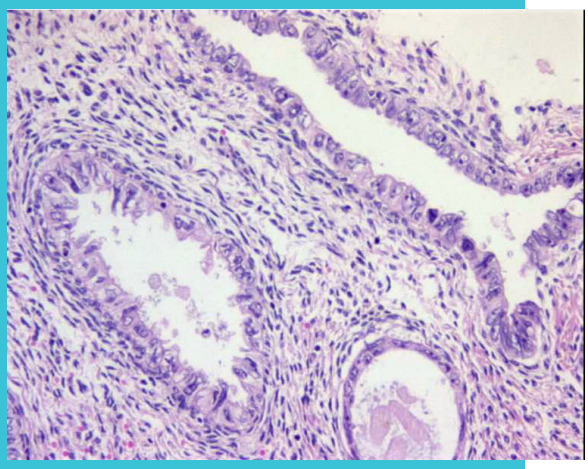
Case presentation

A 50-year-old woman, who had a history of breast

cancer and taking tamoxifen for several years referred to clinic and hysterectomy was performed. The microscopic examination showed an atrophic endometrium with endometrial glands and surface epithelium lined by atypical cells showing nucleomegaly, nuclear hyperchromasia, appreciable but non-prominent nucleoli, and no significant stratification (Figure 1). There were no atypical mitotic figures. Rare papillae formations were present. Immunohistochemically p53 expression was detected in these cells (Figure 2).

Figure 1.

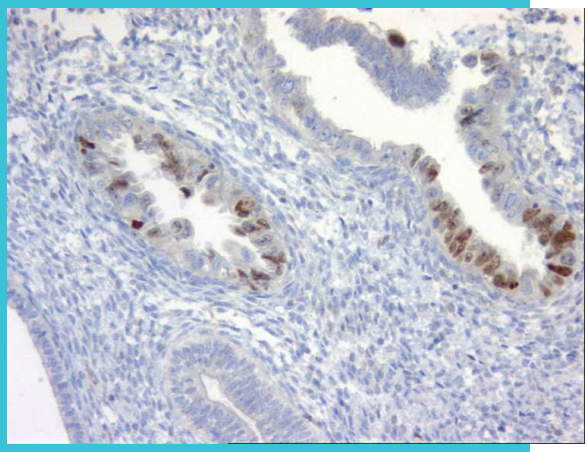


Morphologic appearance of endometrial glandular dysplasia (HEX200)

Discussion

EmGD is proposed as a putative precursor lesion of ESC and morphologically seems to be in the noninvasive counter part of EICs. There is not a clear cut relation between EmGD and serous carcinomas, but there are some clues pointing this relationship. In literature 90% of ESCs and 80% of serous EICs shows p53 tumor suppressor gene mutations [11,12]. Over than half of the EmGDs showed p53 protein over accumulation and about 33% showed loss of heterozygosity of TP53 [6]. In Jia et al's study p53 mutation was 43.2% [13]. EmGD lesions mostly showed intermediate scores of p53 and MIB-1 in comparison with serous EIC and resting endometrium [14]. In our case endometrial epithelium was also expressing P53 suggesting P53 gene mutation. As it is known P53 alternation benign endometrium is extremely rare [13]. It is previously reported that EmGDs have a 9 to 60 months window period developing an ESC or serous EIC [15]. Therefore, P53 immunohistochemical staining or P53 protein based immunoassays may be useful for early detection of endometrial serous carcinomas. EmGD is characterized by mild dysplasia, occasional loss of nuclear polarity and no atypical mitotic figures. In differential diagnosis of EmGD most challenging one is reparative epithelial changes. Reparative epithelial glands do not show the architectural patterns and atypical cells than those found in EmGD. EmGD can be diagnosed by routine microscopic evaluation and requires the careful exclusion of morphologic mimics, such as papillary syncytial, tubal, and eosinophilic metaplasia and EICs [5,6]. Recently reported that about 20% of women with ESC had a history of breast cancer and the incidence was higher in patients who were younger age [7]. In our report patient had a breast cancer and EmGD together.

Figure 2.



p53 staining of Endometrial glandular dysplasia (DABX200)

This is compatible with literature but it is known that tamoxifen has an opposite effect on the breast and the endometrium. Among tamoxifen treated breast cancer patients the hyperplasia incidence was 1.3-20% and in 0-8% of cases carcinoma

was developed after less than 2 years follow-up [16]. Tamoxifen treatment may be the reason of endometrial alternation in endometrium; Because of this further studies are needed to clarify the relationship between breast cancer and ESC. EmGD is usually focal [17]. Also in our case the lesion was in a small focus. From this point of view not only histopathological properties but also size of the EmGD causes diagnostic challenging. Because of this severeal serial cuts and total examination of endometrium should be done in tamoxifen treated cases. Finally p53 mutation in EmGD provides the most important evidence of its being precancerous lesion of ESC development. And also this points out that p53 gene is the one of the most important promoters of the initiating the endometrial carcinogenesis. Accurate diagnosis of ESC precancerous lesions provides the early detection and effective treatment of aggressive endometrial cancer.

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Conflict of Interest Statement
The authors declare no conflict of interest

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