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Case Report

Malignant endometrial polyps: Report of two cases and review of literature with emphasize on recent advances

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Abstract

Endometrial polyps are common pathologic findings in gynecologic pathology practice. Although malignant changes in these lesions are uncommon, numerous studies confirmed this association especially with endometrial serous and clear cell carcinoma. Two cases of malignant endometrial polyps in association with presumed precursor lesion in one of them are presented.

KEYWORDS: Polyps, Adenocarcinoma, Papillary, Endometrium.

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Endometrial polyps are common pathologic findings in gynecologic pathology and their prevalence range is between 16% to 34% depending on characteristics of the population studied and detecting methods.[1] Polyps are biphasic benign endometrial lesions that classically have been defined as 'benign nodular protrusions above the endometrial surface, consisting of irregularly distributed endometrial glands and stroma'.[2] Specific rearrangement of 12p15 and 6p21 resulting in HMGI-C and HMGI(Y) dysregulation have been reported in stromal cells of endometrial polyps.[3-7] Overall the prevalence of malignant and premalignant lesions found in the endometrial polyps ranges from 0.8% to 4.8%.[8-11] There are numerous studies, which confirm association of uterine serous papillary carcinoma with endometrial polyps especially the larger and symptomatic ones.[12,13] In the report of Ferrazzi et al,[13] the histotype of the single case of cancer on polyp and the 3 cases of polypoid cancer in asymptomatic women were endometrioid carcinoma. In contrast, 9 out of 29 cases of cancer on polyps and polypoid cancers in symptomatic patients showed clear cell histology. The frequency of malignant endometrial polyps increased with age and reached statistical significance in the age group > 65.[14]

This is a report of histologic and immunhistochemical features of two cases of endometrial polyps in postmenopausal women revealed serous and clear cell carcinoma with review of literature, emphasizing on precursor lesions and recent advances on the molecular pathways.

Case Report

Case 1

A 65-year-old lady referred to our center for managing an abdominal pain she had for a 6 months period and right side adnexal mass. Imaging studies revealed a solid and cystic mass in right adnexa m. 108×65×64 mm indistinguishable from uterine border. Total hysterectomy with bilatereal salpigo-oopherectoy in association with complete staging procedure was done. Rt. and Lf. ovarian masses, m. 10 × 6 and 6 × 5 cm, respectively, with frozen pelvis was found in laparatomy. Gross examination of the received specimens revealed multiple discrete tumoral tissue m. up to 3 cm in diameter. Opening of the uterus showed an endometrial polyp m. 5 mm in diameter with soft consistency.

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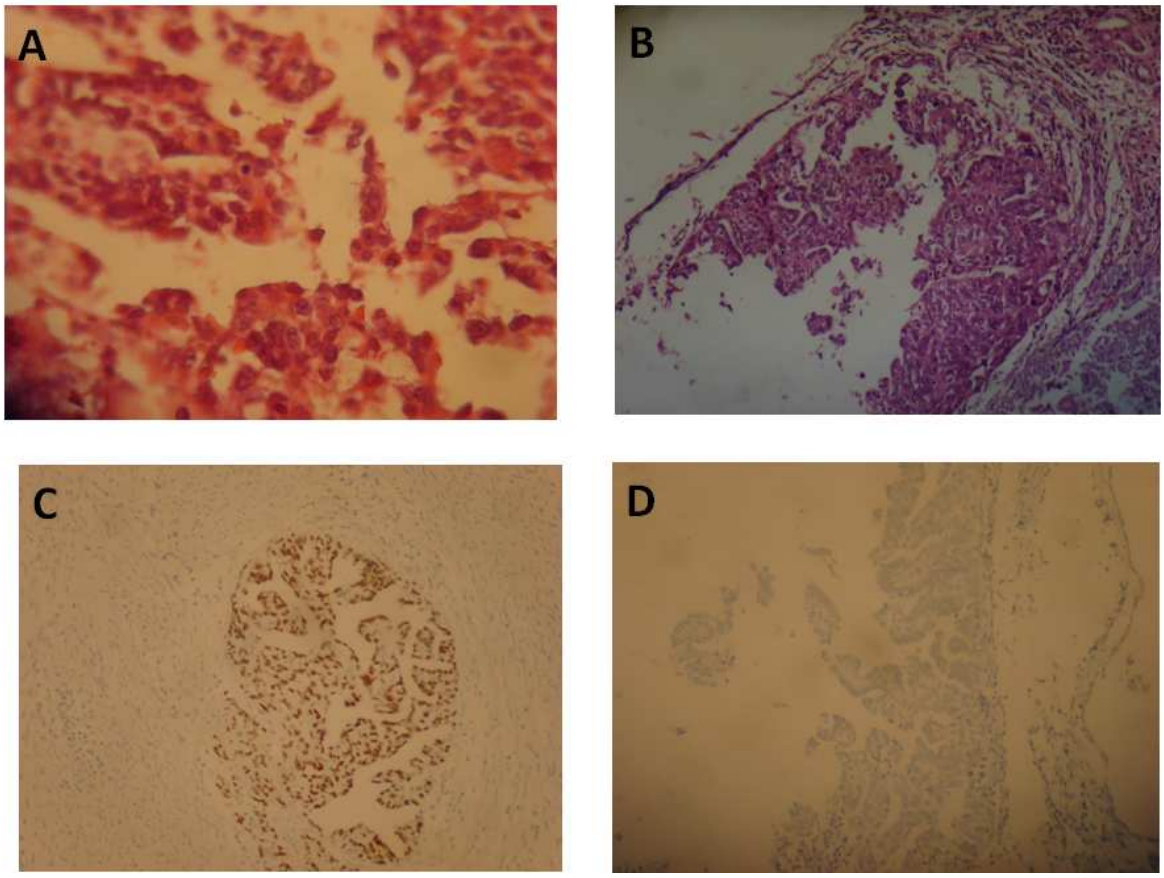

Figure 1. High grade ovarian serous carcinoma (A), the endometrial polyp with small foci of serous carcinoma (B), myometrial invasion by the serous carcinoma showing p35 positive staining (C) and small focus of serous papillary carcinoma in the endometrial polyp with negative p53 staining (D).

Cervix was unremarkable and gross appearance of the omentum was metastatic. Microscopic examination of the specimens revealed bilateral high grade ovarian serous carcinoma (Figure 1A), endometrial polyp with small foci of serous carcinoma (Figure 1B), massive full thickness myometrial invasion by the serous tumor (Figure 1C), lymphovascular space involvement, omentum metastasis, metastatic lymph nodes and positive ascetic fluid for malignant cells. Immunohistochemistry staining for P53, Ki-67, estrogen receptor and progesterone receptor was done. The invasive foci in the myometrium were positive for P53 (Figure 1C), estrogen receptor and progesterone receptor. Ki67 staining showed 30% positivity in these foci. In contrast the foci of serous carcinoma in the endometrial polyp were negative for P53 (Figure 1D). Unfortunately we missed the carcinomatous foci of the endometrial polyp in Ki-67, estrogen receptor and progesterone receptor staining due to repeated sections for IHC staining.

Case 2

A 53-year-old lady with chief complaint of vaginal bleeding for 6 months period referred for further evaluation. Ultrasound study revealed mild increased endometrial thickness (10 mm) with no remarkable change in the cervix, myometrium or adnexa. Endometrial biopsy was done and histologic examination revealed endometrial clear cell carcinoma with serous carcinoma components in association with fragments of endometrial polyp m. up to 5 mm in diameter (Figure 2A, 2B). Total abdominal hysterectomy with bilateral salpingooopherectomy in association with staging procedure was

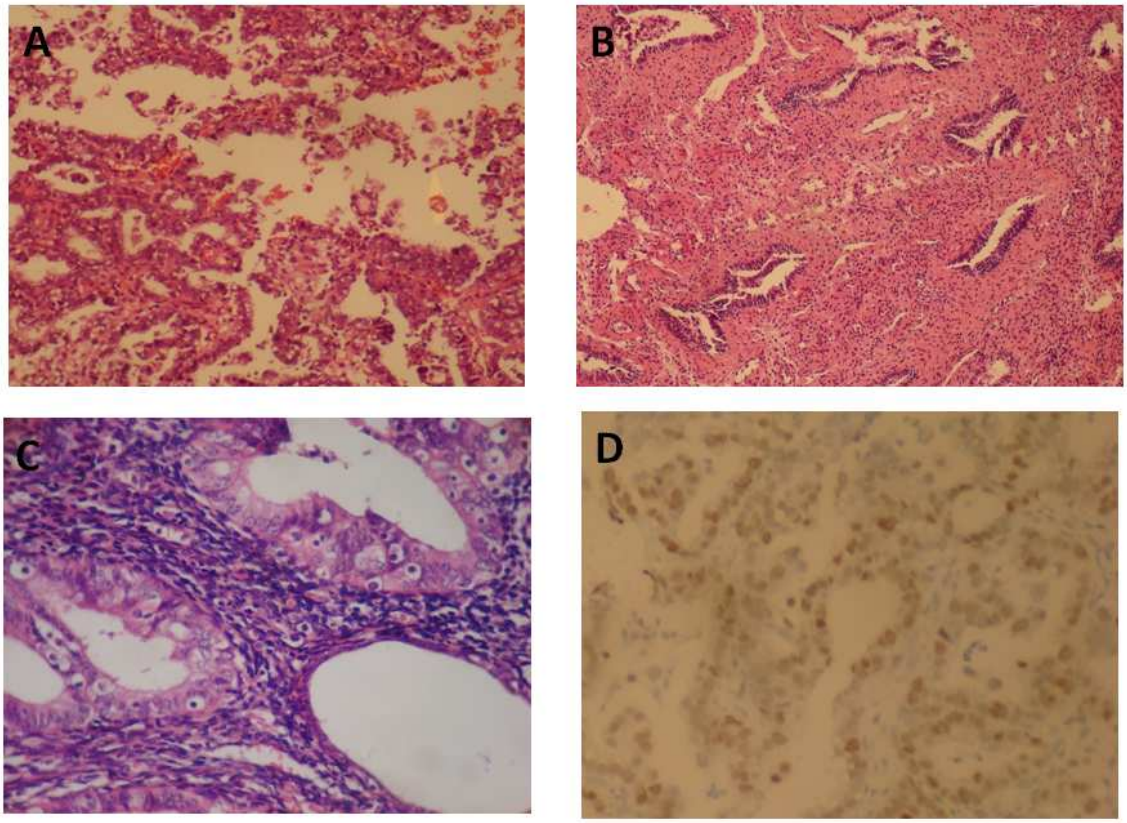

Figure 2. Foci of endometrial clear cell carcinoma in the endometrial biopsy (A), a fragment of endometrial polyp in the endometrial biopsy (B), clear cell endometrial glandular dysplasia, EmGD (C) and positive p53 reaction in the clear cell carcinoma (D).

done. Gross examination of the specimens revealed unremarkable endometrial cavity and the myometrium, cervix and ovaries showed no pathologic change. Microscopic examination of the endometrium showed endometrial glands with dysplstic nuclei and clear cytoplasm (clear cell glandular dysplasia) with no invasive component (Figure 2C). Figure 2D shows p53 positivity in clear cell carcinoma obtained by endometrial biopsy. The received omentum, lymph nodes, peritoneal biopsies, and peritoneal washing cytology were negative for malignancy.

Discussion

In a series including 455 patients with endometrial polyp diagnosed by hysteroscopy, endometrial adenocarcinoma was found in 2.7%, although they did not indicate the type of reported malignancy.[15] In another study, all of the 13 malignancies reported in the endometrial polyps were well to moderately differentiated endometriod adenocarcinoma.[16]

Although uterine serous carcnoma is an uncommon cancer, it accounts for a disproportionate number of endometrial cancer deaths. In a series studied by Hamilton et al, these tumors accounted for 10% of endometrial tumors, but comprised 39% of endometrial cancer deaths.[17] Its tendency for early spread results in upstaging of 50% to 70% of clinically stage I cancers at the time of operation.[18] Presentation of 19.7% and 31.1% of patients with uterine serous carcinoma in stage II-III, respectively in one study confirms the common perception that this histotype of endometrial carcinoma carry a worse prognosis due to advanced disease at the time of diagnosis.[19]

The first case reported here shows the coexistence of high grade bilateral ovarian serous carcinoma and small foci of invasive serous carcinoma in the endometrial polyp. Although metastatic spread to this endometrial polyp should be considered in differential diagnosis, the high

tendency of primary endometrial serous carcinoma to develop in endometrial polyps must be emphasized. In a study, 13 cases of primary endometrial serous carcinoma had developed in endometrial polyps and all of them except for one were limited to the endometrial polyps.[20] On the other hand, although apparently these lesions were limited in the polyps in the present study, extrauterine spread was found in four cases, three of which were microscopic. Even in the so-called intraepithelial form of serous carcinoma (endometrial intraepithelial carcinoma), the predilection and tendency for extra uterine spread has been noted.[21-24] In addition, minimal uterine serous carcinoma (including serous carcinoma with invasion limited to the endometrium and endometrial intraepithelial carcinoma) were found to involve endometrial polyps in 88% of the cases (35/40) and were confined to the polyp in 53% (21/40).[24] In an interesting case report that included 5 cases, the authors reported endometrial serous carcinoma confined to an endometrial polyp with ovarian vascular involvement.[25]

For this reason Clement and Young recommended that EIC should be considered as small foci of serous carcinoma and stressed that pathologists should indicate its malignant potential in the pathology report when it is unaccompanied by typical serous carcinoma and note its size and location.[26] It means that in all forms of uterine serous carcinoma including EIC, surgical staging should be performed regardless its location or limitation on endometrial polyp. Recently, it has been proposed that the term EIC should be discarded as a precursor lesion for endometrial serous carcinoma due to its well recognized potential for extra uterine spread. Furthermore, Endometrial Glandular Dysplasia (EmGD) has been proposed recently as a true precursor lesion for endometrial serous carcinoma.[27] In the our recent study EmGD was found in five out of 25 cases of endometrial serous carcinoma developed in endometrial polyp (unpublished data). Coexisting involvement of the endometrium or ovary is found in 10% and 5% of women with ovarian and endometrial cancer, respectively.[28] Although the presence of multifocal or multicentric serous neoplaia is possible, identical p53 mutation in multiple sites indicates metastatic origin.[29] In this case, positivity of tumor nests in the myometrium and negativity of the small foci of serous papillary carcinoma in the polyp for P53 favours independent primary tumors in both endometrium and ovaries (Figure 1C, 1D).

In the second case like the first one, the endometrial clear cell carcinoma had been developed in an endometrial polyp in association with clear cell EmGD. The criteria most commonly used for identification of serous EmGD are glands or groups of small glands in superficial endometrium or a flat layer of superficial epithelium. Since the level of atypia in these foci is not at the level of serous carcinoma, these lesions do not fit the designation of EIC. The typical changes in EmGD foci are nucleomegaly (2-4 times of resting endometrium nuclei), variably conspicuous nuclei, nuclear loss of polarity and changeable nuclear hyperchromasia.[30]

Clear cell EmGD is characterized by small glands or segments of slowly progressing nuclear atypia. Based on grade of nuclear atypia, the grades of these lesions vary from 1 to 3. Histologically, the lesions lined by cells with atypical nuclei and clear or eosinophilic cytoplasm were considered grade 3 while the lesions with grade 1 or 2 nuclear atypia were designated clear cell EmGD.[31]

Based on the molecular and immunohistochemical studies in this background,[32] it is reasonable to consider that EmGD may be the true precancerous lesion of endometrial serous carcinoma on the assumption that serous carcinogenesis in the endometrium is also identical to other carcinogenetic processes in terms of stepwiss progressing rather than "de novo" arising from resting endometrium.

Conclusions

In summary, this paper reported two cases of type II endometrial carcinoma in dualistic model of endometrial carcinogenesis in association with presumed precursor lesion in one

case developed on endometrial polyp. It should be emphasized that endometrial polyps especially the symptomatic and larger one and the polyps developed in postmenopausal patients have tendency to show malignant change. Therefore, careful histologic examination of these lesions to find premalignant and malignant lesions should be emphasized.

Conflict of Interest

Authors have no conflict of interests.

Authors' Contributions

ADT selected the cases and prepared the first draft. AV reviewed the drafts and helped as a consultant. HAE was the consultant pathologist and also helped editing the manuscript. All authors have read and approved the content of the manuscript.

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