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GYN Pathology

**Metastatic endocervical adenocarcinomas simulating primary ovarian surface epithelial neoplasms.**

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**Background:**

Metastatic adenocarcinomas in the ovaries derived from both female genital tract and extragenital organs can demonstrate deceptive patterns of invasion simulating primary ovarian surface epithelial neoplasms, including both atypical proliferative tumors and carcinomas. Endocervical adenocarcinomas uncommonly metastasize to the ovaries but some examples simulating primary ovarian surface epithelial neoplasms (mucinous and endometrioid types) have been described. Endocervical adenocarcinomas typically lack expression of hormone receptors and diffusely express p16 in conjunction with the presence of integrated high-risk human papillomavirus (HPV) DNA. In contrast, well differentiated ovarian surface epithelial tumors are considered etiologically unrelated to HPV infection and those of endometrioid type usually express hormone receptors. Therefore, HPV DNA detection and immunohistochemical expression of p16 and hormone receptors are potentially useful for distinguishing metastatic endocervical adenocarcinomas in the ovary from primary ovarian epithelial neoplasms.

**Design:**

The clinicopathologic features of 5 cases endocervical adenocarcinomas with ovarian metastases were analyzed. The presence of HPV DNA was assessed by in situ hybridization (ISH; probes for HPV 16, HPV 18, and a wide spectrum probe [HPV types 6,11,16,18,31,33,45,51]) in all cases and additionally by polymerase chain reaction (PCR) in one case. Immunohistochemistry (IHC) for hormone receptors (ER and PR) and p16 was performed.

**Results:**

Two ovarian metastases presented concurrently with the primary endocervical tumors, 2 presented subsequent to the endocervical primaries, and one presented as a virilizing ovarian tumor during pregnancy prior to diagnosis of the endocervical primary. All of the ovarian tumors were unilateral; they ranged in size from 2.1 to 30 cm (median 9 cm). Four of the ovarian tumors were described as multicystic with a smooth capsule; one had focal solid areas and one was focally papillary. In all cases the ovarian tumors were initially diagnosed as or thought to possibly represent independent primary ovarian surface epithelial tumors (atypical proliferative (borderline) tumors or carcinomas of endometrioid (4) or mucinous (1) type). Microscopically they displayed variably sized cysts with some areas lined by a single layer of epithelium, some having papillary/villoglandular architecture, and others exhibiting cribriform glands. These patterns simulated atypical proliferative tumors with intraepithelial carcinomas; destructive stromal invasion was not present. Adenocarcinoma in situ was identified in all of the endocervical tumors. Depth of invasion in the endocervical tumors ranged from 2 mm to 1.2 cm. The 3 minimally invasive endocervical tumors were initially interpreted as adenocarcinoma in situ and were not recognized as unequivocally invasive even when evaluated in conjunction with the histologically identical ovarian tumors. Three of 4 evaluable ovarian tumors and 4 of the 5 endocervical tumors were positive for HPV by ISH; one endocervical tumor and the corresponding ovarian tumor were negative for HPV by ISH

but HPV was detected by PCR. There was concordance of HPV type in each case. Three evaluable endocervical tumors and 2 evaluable ovarian tumors were diffusely positive for p16. Four of the 5 endocervical tumors and 3 of 4 evaluable ovarian tumors were negative for both ER and PR; in one case both tumors were focally positive for both ER and PR.

**Conclusions:**

Endocervical adenocarcinomas can metastasize to the ovaries even when minimally invasive in the endocervix. These metastatic endocervical adenocarcinomas can simulate primary ovarian atypical proliferative tumors and carcinomas of endometrioid and mucinous types. The presence of HPV DNA, diffuse expression of p16, and lack of hormone receptor expression are useful for identifying these ovarian tumors as metastatic endocervical adenocarcinomas.