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Precis:
Microglandular hyperplasia is associated with exogenous progestin

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Abstract:

Objectives:

Although microglandular hyperplasia is a benign endocervical lesion, it may raise concern of malignancy in an inexperienced pathologist, since clinicians may not be familiar with it on a report. It has been reported to occur in association with progestational stimulation, but this has not been well studied. The purpose of the current study was to evaluate this potential association.

Methods:

This was an observational case control study of patients seen from 1/1/91 to 11/1/14 at University Hospital, Newark New Jersey. Cases of microglandular hyperplasia and controls were identified from the files of the Department of Pathology. Controls were cases of endocervical curettages for whom no microglandular hyperplasia was detected. Medical records were reviewed for evidence of exogenous progestin exposure within the prior 6 months.

Results:

89 cases of microglandular hyperplasia, and 97 controls were identified. Of the cases of microglandular hyperplasia, 26/89 [29.2%] had exposure to progestational medication, significantly greater than that of controls [10/97 (10.3%)] p=0.0014.

Conclusions:

Our data show that a significantly higher percentage of women with microglandular hyperplasia had progestin exposure than did women who do not exhibit this benign lesion. Clinicians and pathologists should be aware of this association, as well as the benign nature of the lesion.

Introduction

Microglandular hyperplasia (Figure 1) is a benign endocervical lesion that should not be mistaken for adenocarcinoma. It is of no major clinical significance, but clinicians may not be familiar with it. Indication of microglandular hyperplasia on a pathology report may raise concern of malignancy in an inexperienced pathologist, and hence must be recognized. It has been reported to occur in association with oral contraceptive pill usage, or hormone replacement therapy (1,2), thought to be due to an effect of progestin stimulation. However, previous reports often include conditions in which other nonprogestin agents are elevated, such as pregnancy, making it unclear as to whether an actual association with progestins occurs. The purpose of the current study was to determine whether exogenous progestin exposure is associated with the occurrence of cervical microglandular hyperplasia.

Methods

This was an observational case control study of patients seen from 1/1/91 to 11/1/14 at University Hospital, Newark New Jersey. The study was approved by the Rutgers Institutional Review Board, Newark Campus. Cases of cervical microglandular hyperplasia and controls were identified and selected from the files of the Department of Pathology. Cases were those diagnosed with microglandular hyperplasia during the study period. Controls were cases of endocervical curettages submitted to the Pathology Department wherein no microglandular hyperplasia was detected. Medical records were reviewed for evidence of exogenous progestational exposure within the prior 6 months. Exogenous progestin exposure was defined as progestin-releasing intrauterine devices, medroxyprogesterone acetate IM injection, or combination oral contraceptive pills or patches. The oral contraceptive pills and contraceptive patches, while combination estrogen/progestin in composition, have a progestin-dominant local effect, as evidenced by the histologic features seen in the endometrium. Differences between groups were assessed using Fisher's exact and Mann-Whitney U tests. A p value of <0.05 was considered significant.

Results

101 cases of cervical microglandular hyperplasia and 140 cases without microglandular hyperplasia were identified. Cases were deemed ineligible for this study if there was a history of pregnancy within 6 months, or if the patient was postmenopausal. In the microglandular hyperplasia group, 7 had a history of pregnancy within 6 months and 5 were postmenopausal. In the control group, 7 had a history of pregnancy within 6 months and 36 were postmenopausal. Thus, a total of 89 cases of microglandular hyperplasia and 97 controls were assessed.

Of the cases of microglandular hyperplasia, 26 (29.2%) had exposure to progestins, whereas 10 (10.3%) controls had exposure to progestins (p=0.0014). When we separated out progestin only exposure, (omitting the patients on oral contraceptive pills or patches) although the numbers of patients in each group were small, the difference was still significant (p=0.028). This held true as well with the small numbers of patients on oral contraceptive pills/patches (p=0.0178). The distribution of patients in each group by progestin is shown in Table 1. In addition, Table 1 shows the mean ages of the patients in each group, which were not different (p=0.499). The mean ages of the patients exposed to progestins in the groups were also not different (p=0.737)

Discussion

Cervical microglandular hyperplasia is a fairly common finding. It is one of a group of pseudoneoplastic endocervical glandular lesions that may mimic cervical glandular neoplasia (3). Although it is of no clinical significance, it can be challenging to diagnose. With a lack of experience, or in the case of small biopsy specimens, it may be confused with endometrial malignancy, particularly in rare cases with mitotic activity (4), or mucinous differentiation (5), in which immunohistochemistry may be helpful (6). The presence of microglandular hyperplasia may also be the cause of atypical glandular cells observed on cervicovaginal cytology assessment (7).

Little has been written about the association of exogenous progestins with microglandular hyperplasia and what has been described is conflicting. In one report, 13.2% of patients utilizing a levonorgestrel releasing IUD were found to have microglandular hyperplasia (8), whereas a second study showed that only 1.3% of those exposed to a progestin had microglandular hyperplasia (9). In an additional study, tissues from a small group of cases were examined by immunohistochemistry for estrogen and progesterone receptor (10), and the profile of the glandular epithelium was shown to be more likely to be estrogen receptor positive and progesterone receptor negative. Greeley et al., did not find an association of microglandular hyperplasia and oral contraception use or the occurrence of a recent pregnancy (2). Chumas et al, suggested that microglandular hyperplasia represents a form of reserve cell hyperplasia, and that, while it was thought that progestin exposure was involved, it was unknown if the lesion persisted after that exposure ended (11). Their report pointed out that many of their cases had not had oral contraceptive exposure, although some of those had been pregnant.

Our study has some limitations and certain strengths. The data are limited by their retrospective nature. In addition, the numbers of cases and controls are few. However, unlike other reports which included patients whose progestin exposure was due to having recently been pregnant, since tissues of pregnant patients are exposed to so many different hormones and growth factors at elevated levels in addition to progesterone, we excluded assessment of tissues from pregnant patients from our study to avoid these additional confounding variables. With a limited number of more specific cases, the current data suggest an association between exogenous progestin exposure and the presence of microglandular hyperplasia. Clinicians and pathologists should be aware of this association, as well as the benign nature of the lesion.

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