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ORIGINAL ARTICLE

Squamous intraepithelial lesions and squamous cell carcinomas detected by endometrial sampling: Pap test correlation and outcome data

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Introduction Squamous intraepithelial lesions (SIL) and squamous cell carcinomas (SCC) can rarely be detected in endometrial sampling. We reviewed all cases of SIL and SCC detected solely on endometrial biopsies and curettings to determine their significance and whether these findings were detected on prior or concurrent Papanicolaou (Pap) test.

Materials and methods Endometrial samples with detached fragments of SIL and SCC over a 13-year period were reviewed, along with prior and/or concurrent Pap tests, human papillomavirus status, and subsequent pathology results. Cases with concurrent cervical or endocervical sampling that showed SIL or SCC were excluded.

Results Fifty patients had endometrial biopsies and/or curettings with SIL or SCC. Thirty-six patients (72%) had concurrent or previous Pap tests within 1 year prior to the endometrial sampling. The Pap test was negative for intraepithelial lesion or malignancy in 44% of patients (16/36) and atypical squamous cells of undetermined significance in 22% of patients (8/36). The source of the SIL and SCC in endometrial sampling was cervical SIL in 18 patients, cervical SCC in 14 patients, endometrioid carcinomas in 3 patients, metastatic carcinoma in 1 patient, and not definitively identified in 14 patients.

Conclusions The majority of SIL and SCC in endometrial samples are from the cervix. Prior and concurrent Pap tests were often negative for intraepithelial lesion or malignancy in patients with SIL and SCC detected by endometrial samples. This suggests that SIL and SCC detected on endometrial sampling may detect a subset of cervical SIL/SCC that are more proximal in the endocervical canal and are not sampled with conventional Pap tests.

This study was selected as a platform presentation at the American Society of Cytopathology Annual Scientific Meeting in Dallas, Texas, in November 2014.

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Introduction

Rarely, squamous intraepithelial lesions (SIL) and squamous cell carcinomas (SCC) can be detected in endometrial biopsies and curettings as incidental findings. The significance of this finding has not been previously studied and is not always clear. The differential diagnosis includes contaminating cervical SIL or cervical SCC, uterine endometrioid carcinomas with squamous differentiation, primary SCC of the endometrium, or SCC metastatic from another site.

This study retrospectively reviewed our experience with cases of SIL and SCC detected solely on endometrial sampling to determine their origin and significance. Additionally, the findings were correlated with recent Papanicolaou (Pap) test and HPV results. This paper guides the pathologist in analyzing this infrequent, but important finding.

Materials and methods

Endometrial biopsies and curettings with SIL or SCC over a 13-year period were included in the study. Cases with concurrent cervical and endocervical sampling that showed SIL or SCC were excluded. The electronic medical record was reviewed to determine the clinical indication for sampling and to verify an endometrial source.

The pathology reports of all cases were reviewed with subsequent surgical pathology and Pap test reports with a mean follow-up of 6 years (range 1-13 years). Concurrent and/or previous Pap tests within 1 year were also reviewed. High-risk human papillomavirus (HPV) status performed either concurrently or within 1 year prior to the endometrial sampling was also reviewed for all cases. HPV tests were performed on cervical specimens using the Hybrid Capture 2 High-Risk HPV DNA Test (Qiagen, Valencia, Calif) method.

Results

Seventy-six of 47,150 patients who had endometrial biopsies and/or curettings performed between 2000 and 2013 at a single institution showed SIL or SCC. Twenty-three cases were excluded due to concurrent cervical SIL or SCC on surgical pathology specimens. Three cases were excluded after review of the electronic medical record suggested that these may be endocervical specimens. Therefore, a total of 50 cases of SIL or SCC on endometrial samples were included in our study. Forty-six of the cases had endometrial sampling only and 4 cases had concurrent cervical surgical pathology sampling that was negative for SIL or SCC. The average age was 51 years with a range of 20 to 85 years.

Two patients had a history of cervical SIL, 1 had cervical intraepithelial neoplasia, grade 1 (CIN 1) 2 years prior to endometrial sampling and 1 had CIN1 1 month prior to endometrial sampling. One patient had a prior history of vulvar high-grade squamous intraepithelial neoplasia (classic VIN 3) 5 months prior to endometrial sampling. The previous Pap test for the patient with VIN 3 was negative for intraepithelial lesion or malignancy ([NILM] high-risk HPV: negative) and the subsequent cervical biopsy showed CIN 1. No other patients had a history of SIL of the female genital tract prior to endometrial sampling.

Table 1 Clinical indication for endometrial sampling.

Clinical indication	Number
Postmenopausal bleeding	29 (58%)
Menometrorrhagia/abnormal bleeding	7
Thickened endometrial strip	3
Pap test result: 2 EM present in a patient over 40 years old, 1 atypical EM	3
Ectopic pregnancy	2
Missed abortion	1
Uterine synechiae	1
Pelvic mass with anemia	1
Not provided	3

Abbreviation: EM, endometrial cells.

The indication for endometrial sampling was postmenopausal bleeding in the majority of patients (29/50, 58%) (Table 1). Three patients underwent endometrial sampling due to the presence of endometrial cells in a Pap test in a patient over the age of 40. One of the 3 cases had atypical endometrial cells on Pap test. This patient's endometrial sampling showed high-grade squamous intraepithelial lesion (HSIL), as well as a 3-dimensional cluster of endometrial cells with enlarged nuclei, nucleoli, and vacuolated cytoplasm with associated neutrophils.

On endometrial sampling, 18 patients (36%) had low-grade squamous intraepithelial lesion ([LSIL] CIN 1), 10 patients (20%) had HSIL (CIN 2), 9 patients (18%) had HSIL (CIN 3), 8 patients (16%) had SCC, and 5 patients (10%) had poorly differentiated carcinomas with focal squamous differentiation. Non-neoplastic endometrial tissue was present in 70% of cases (33/47 cases available for review) (Figs. 1-2).

Thirty-four of the 37 patients with SIL (92%) had subsequent pathologic sampling, either surgical pathology or Pap tests. The source of the SIL and SCC in endometrial sampling was cervical SIL in 16 patients, cervical SCC in 14 patients, primary endometrial carcinomas in 3 patients, metastatic carcinoma in 1 patient, and not definitively identified due to negative follow-up in 13 patients (Table 2). Of the 12 cases with no confirmed source for the squamous abnormality detected on endometrial sampling, 10 were LSIL and 3 were HSIL.

Thirty-six of the 50 patients (72%) had concurrent or previous Pap tests within 1 year prior to the endometrial sampling (Table 3). The Pap test results were negative for intraepithelial lesion or malignancy (NILM) in 16 patients, atypical squamous cells of undetermined significance