Vaginal Intraepithelial Neoplasia III Detected After Hysterectomy for Benign Conditions

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Because primary vaginal cancer is rare, many experts discourage routine cytologic sampling of the vaginal vault following hysterectomy for benign circumstances. The following report describes a case of vaginal intraepithelial neoplasia III (VAIN III) detected by a vaginal vault Papanicolaou smear obtained from an asymptomatic 57-year-old woman 23 years after she had a total abdominal hysterectomy for a benign condition. As VAIN III is a true vaginal cancer precursor, the innocent disregard of recommended screening practices averted significant morbidity and possibility mortality for this otherwise healthy woman.

Key words. Vaginal diseases; vaginal neoplasia; vaginal smears.

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Primary carcinoma of the vagina is uncommon, estimated to comprise less than 0.5% of all malignancies,[1] and 1% to 2% of female genital tract malignancies.[2] Most (85%) afflicted women are older than 50 years of age.[3] Except for more advanced cases in which vaginal bleeding and vaginal discharge may be noted, many patients remain asymptomatic.[2,3] Primary carcinoma of the vagina is often detected unexpectantly during evaluation for other lower genital tract conditions. Because of the rarity of the disease, the older population affected, and the silent nature of early disease stages, meaningful surveillance proves challenging for patients, clinicians, and the health care system.

The Papanicolaou (Pap) smear, originally collected directly from the vagina, is the most effective test for detection of carcinoma of the vagina. In contemporary practice, true vaginal smears are not often performed. Generally, routine vaginal smears are performed only for women who have been exposed in utero to diethylstilbestrol (DES) and for women who have had a hysterectomy for cervical neoplasia.[4-7] Vaginal smears are also occasionally obtained for hormonal status evaluation. Few women are screened regularly by vaginal cytologic sampling if they have had a hysterectomy for benign conditions. Some authors advocate boldly against Pap smear testing in this circumstance because they believe it is unnecessary unless the surgery was for cervical dysplasia or cancer.[8,9] The following report illustrates a case of vaginal intraepithelial neoplasia III (VAIN III) detected by a vaginal vault Pap smear in a woman who had had a hysterectomy many years earlier for a benign condition.

Case Report

A 57-year-old woman, gravida 7 para 5 abortus 2, presented for an initial visit history and physical examination. She denied vaginal bleeding and pelvic pain. She was not currently sexually active because of her husband's impotence induced by diabetes mellitus.

Her medical history was notable for multiple surgical procedures: total abdominal hysterectomy in 1970 for chronic cervicitis with cystourethrocele and chronic pelvic congestion; bilateral salpingo-oophorectomy, appendectomy and Burch procedure in 1983 for vaginal relaxation and menopause; and two postabortion dilation and curettage procedures. She had no chronic medical problems.

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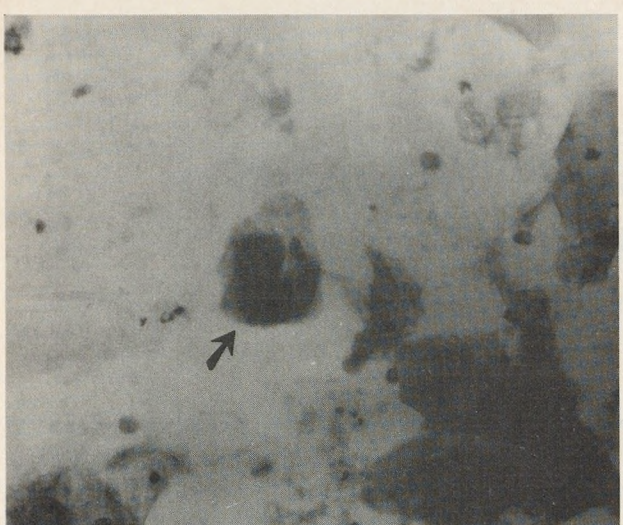

Figure 1. The Pap smear was interpreted as severe squamous dysplasia with human papillomavirus changes indicative of VAIN III. The vaginal smear contained squamous cells with enlarged, hyperchromatic nuclei. Compare the abnormal cell (arrow) with the adjacent normal intermediate squamous cell (Pap stain; ×400).

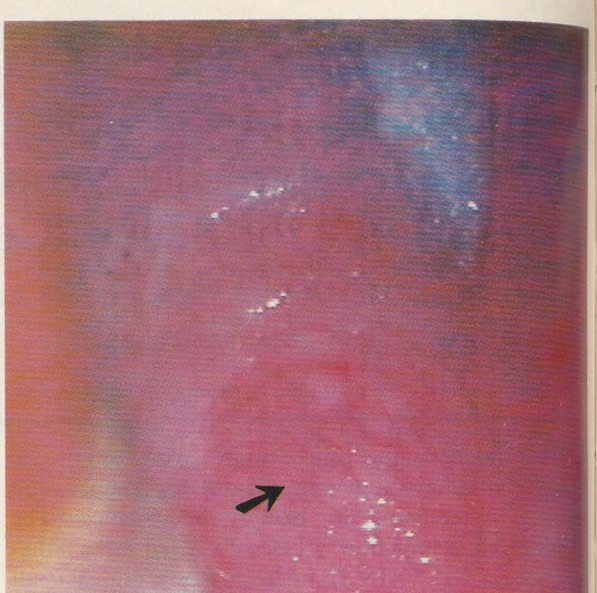

Figure 2. The vaginal lesion following 5% acetic acid application. There are dense acetowhite epithelium, smooth margins, and a moderately coarse punctation vascular pattern (arrow).

Her family history was of interest because her grandmother had had cervical cancer and another distant relative had developed vulvar cancer. A physical examination revealed a healthy middle-aged woman. A Pap smear was obtained from the normal appearing vaginal vault. Otherwise her physical examination was unremarkable.

Her Pap smear was interpreted as severe squamous dysplasia with human papillomavirus (HPV) changes indicative of VAIN III (Figure 1). She was then scheduled for colposcopic examination for apparent vaginal disease.

With further questioning, the patient denied a history of venereal warts. She claimed smoking one pack of cigarettes per day. Her age of first sexual intercourse was 19, and she reported only one lifelong sexual partner. She denied a history of abnormal Pap smears, cancer, and radiation therapy.

A careful colposcopic examination was performed of the vagina, vulva, and perineum. A small area of keratosis was noted in the right posterior vaginal vault during the saline examination. Following 5% acetic acid application, a 2-cm × 3-cm area of acetowhite epithelium was observed in the adjoining region (Figure 2). A moderately coarse punctation vascular pattern with wide intercapillary distances was noted. Petechial hemorrhages associated with trauma were also seen in the proximal vagina. One-half strength Lugol's iodine solution was then applied to the vagina with cotton swabs. Multifocal iodine-negative lesions were observed within a larger area of light brown epithelium in the right vaginal vault (Figure 3). Three histologic specimens of the iodine-negative vaginal lesions were obtained by biopsy. Hemostasis was established by applying silver nitrate and a paste of Monsel's (ferric subsulfate) solution. The colposcopic evaluation was VAIN III, possible microinvasive carcinoma.

The histologic specimens (Figure 4) were interpreted as VAIN III with condylomatous changes that correlated with the cytology report and colposcopic evaluation. The patient was referred to a gynecologic oncologist for treatment. Because of concern about the possibility of an occult invasive lesion, the patient underwent a partial vaginectomy. The resulting vagina was shortened to approximately 5 cm. Her postoperative recovery was unremarkable. The resected vaginal mucosa showed extensive residual VAIN ranging from VAIN I to VAIN III with no stromal invasion. Vaginal intraepithelial neoplasia was present at some resection margins.

Discussion

Vaginal intraepithelial neoplasia is typically detected by an abnormal cytology report.[10,11] The disease is most commonly noted in the sixth decade of life.[10–12] Patients are usually asymptomatic,[10,11] but vaginal bleeding, dyspareunia, postcoital spotting, and leukorrhea are occasion

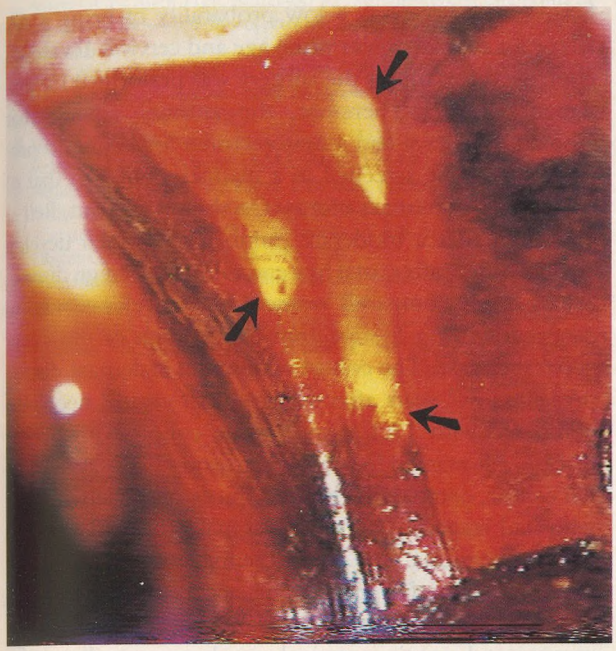

Figure 3. The vaginal lesion following application of Lugol's iodine solution. Iodine-negative or yellow epithelium (arrow) represent the dysplastic epithelium. Normal epithelium appears a mahogony brown color.

ally reported.[11,13] The lesions are generally not apparent by naked-eye examination of the vagina.[11]

Although vaginal cancer[6,7] and VAIN[12] are seldom noted in women following hysterectomy for malignant or benign conditions,[7,10] reports of women who developed vaginal cancer following hysterectomy show that 28% to 41% had had a hysterectomy initially for benign conditions.[6,7,14] It must be recognized, however, that nearly the same percentage of women in the general population of equal age will also have had a hysterectomy. Typically, VAIN is multifocal,[14] and is usually located in the proximal one third of the vagina.[10,11,14] Virally induced VAIN is also commonly associated with a multicentric disease process of the lower genital tract.[14]

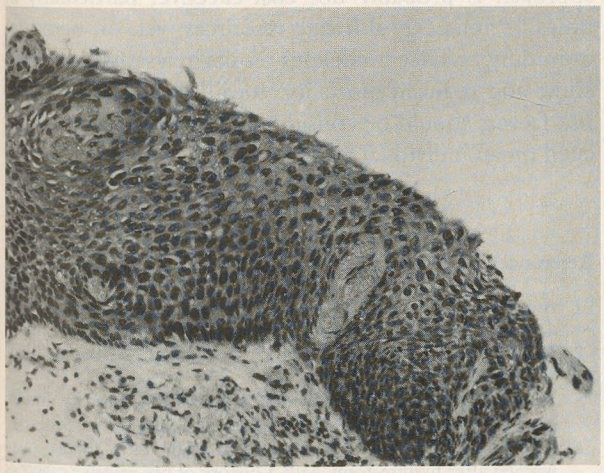

Figure 4. The histologic specimen demonstrates undifferentiated dysplastic squamous cells occupying the full thickness of the epithelium. The dysplastic cells do not breach the basement membrane (hemotoxylin and eosin stain; ×200).

Colposcopy of the vagina and directed biopsy are required to confirm a diagnosis of VAIN. The indications for vaginal colposcopy are listed in the Table.[15] The colposcopic appearance of VAIN varies according to the stage of disease.[15] In this case, a high-grade vaginal lesion was expected, based on the dense acetowhite epithelium, coarsely dilated punctation with a wide intercapillary distance, a smooth margin, and multifocal, distinct iodine-negative (a positive Schiller's test result) epithelium.[10] Mosaic vascular patterns are rarely observed in VAIN.[10] An adjoining area of keratosis was also observed by colposcopic examination. The absence of atypical vessels, papillary or exophytic projections, ulceration or erosion, and a nodular configuration limited the colposcopic evaluation to a severe, premalignant process.[15] The cytologic, colposcopic, and histologic correlation confirmed VAIN III.

The differential diagnosis included residual neoplasia previously undetected at the time of hysterectomy, recurrent disease considering the same circumstances, metastatic disease, atrophy of the vagina, trauma, infection, or vaginal adenosis.[16] The pathology report of the previously excised uterus indicated chronic cervicitis. The possibility of earlier vaginal disease cannot be excluded because there was no mention of examination by colposcopy prior to hysterectomy in the medical record. Atrophy of the vagina appears slightly iodine negative but no abnormal vascular changes or acetowhite epithelium are visualized. Trauma induced by vaginal foreign bodies may produce ulceration or keratosis, the latter of which was seen in this patient. Infection and the associated inflammatory response generally produce a patchy iodine-negative vaginal epithelium, as in the case of vaginitis or virally mediated infection. Vaginal adenosis associated with prior therapy is usually a focally red area with an amber exudate.[12]

The patient was treated by an excisional technique to confirm the preliminary diagnosis and to exclude the possibility of an occult malignancy. The histologic presence of VAIN I at the resection margin requires careful postoperative surveillance by both vaginal cytology and colposcopic examination. VAIN may also be treated by ablative methods such as laser vaporization or 5-fluorouracil cream.[10] Ablative treatment reduces operative morbidity and postoperative sexual dysfunction.[10] Excision, however, is the preferred treatment for women who have high-grade lesions and other risk factors for invasion.

Table. Indications for Vaginal Colposcopy

1. An abnormal Pap smear report following treatment of cervical neoplasia
2. An abnormal Pap smear from the vaginal vault following hysterectomy
3. An abnormal Pap smear in a woman with a satisfactory cervical colposcopic examination and normal cervix
4. Cervical neoplasia in an immunocompromised woman
5. Vulvar neoplasia
6. An abnormal gross visual inspection or abnormal palpation of the vagina
7. Intrauterine exposure to diethylstilbestrol (DES)
8. Lower genital tract evidence of human papillomavirus (HPV) infection

Adapted with permission of Educational Systems Inc, from Campion MJ, Ferris DG, diPaola FM, Reid R, Miller MD, eds. Modern colposcopy: a practical approach. Augusta, Ga: Educational Systems Inc, 1992.

These factors would include older women, smokers, women with a history of recurrent dysplasia, immunocompromised women, and women who are considered a compliance risk.

The etiology of VAIN and vaginal neoplasia appears multifactorial. Predisposing factors for vaginal neoplasia include HPV infection, intrauterine DES exposure, immunosuppression, chronic trauma, tobacco abuse, and lower genital tract radiation therapy.[17] Women with a history of premalignant and malignant cervical disease have an increased risk for vaginal neoplasia. Exposure to a carcinogen in the lower genital tract conveys the risk of carcinogenesis to all sites. This "field effect" occurs because of common embryologic origin of the involved epithelium.[15] Squamous cell carcinoma is the most common malignancy encountered (>90%), followed by adenocarcinoma and melanoma.[2,3] By convention, a diagnosis of primary vaginal cancer cannot be made if the patient had a previous malignancy of the vulva or cervix.

There is some consensus on the role of vaginal cytology surveillance following hysterectomy for cervical neoplasia. Few women develop neoplasia at the vaginal cuff, and the majority who do are usually identified by Pap smear in the first two postoperative years.[4,5,18] Consequently, some authors suggest biannual Pap smears for the first two postoperative years and then reversion to regular screening, provided normal cytology results are obtained.[5] There is less consensus on the role of vaginal cytology screening in women subsequent to hysterectomy for benign conditions. Many authors recommend that these women require no surveillance.[8,9] In a small case-controlled study, Herman et al[8] demonstrated that hysterectomy conveys a low probability of being a risk factor for vaginal cancer when age and cervical disease are controlled for, unless the surgery was performed for malignant disease. Therefore, the authors suggest that women who have had a hysterectomy for benign conditions should be screened in a manner similar to that of women with an intact uterus. On the other hand, Bell et al[7] found that a moderate number of women develop vaginal cancer after total hysterectomy for benign disease. Stuart et al[6] compared women who developed vaginal cancer following hysterectomy for benign or malignant cervical disease. The cohort with initial malignant disease presented 5.7 years after surgery with vaginal neoplasia, compared with 13.1 years for the cohort with benign disease. All women in the former group had stage I vaginal cancer, compared with two thirds of the latter group who had stage II or greater vaginal cancer, denoting a poorer prognosis. One could assume less aggressive cytologic postoperative monitoring accounted for this discrepancy. Although controversial, many authors strongly recommend routine vaginal cytology surveillance for women who have had a hysterectomy for benign disease.[10,13,14]

In the present case, many would argue that the resident physician appeared to discount the broadly accepted but controversial practice of not obtaining vaginal vault cytology from women who have had a hysterectomy for nonmalignant disease. Certainly, the practice elicits a low yield of disease based on the infrequent nature of vaginal neoplasia. The risk of VAIN progressing to invasive cancer, especially in the absence of previous intrauterine exposure to DES, is rather small. This seemingly aggressive approach is probably not cost-effective, particularly in times of limited health care resources, yet, on occasion, exceeding practice guidelines results in a satisfactory outcome and reduced mortality. Ideally, patients' potential risk factors should be considered, and each patient managed on an individual basis.

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