RESEARCH COMMUNICATION

Limited Value of Vaginal Cytology in Detecting Recurrent Disease After Radical Hysterectomy for Early Stage Cervical Carcinoma

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Abstract

The objective of this study was to evaluate the value of vaginal cytology in routine surveillance for recurrent cervical cancer after surgery. We reviewed the medical records of 565 patients with stage IB-IIA cervical cancer who were treated with radical hysterectomy and pelvic lymphadenectomy (RHPL) and attended follow- up at Chiang Mai University Hospital between January 2000 and May 2006. With the median follow-up of 35 months (range 1-76 months), 23 (4%) patients developed recurrence. The interval from surgery to detection of recurrence ranged from 5-61 months with a median of 23 months. Of the total 4,376 vaginal smears, 5 (0.1%) showed abnormal cytology but only 1 had malignant cells and tumor recurrence. The sensitivity and specificity of vaginal cytology for detection of recurrence were 4.3% and 99.3%, respectively. In conclusion, vaginal cytology has limited value in detection of recurrence after RHPL for early-stage cervical cancer.

Key Words: Vaginal cytology - post operative surveillance - radical hysterectomy - early stage cervical carcinoma

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Introduction

Most patients with early stage cervical cancer are successfully treated with radical hysterectomy. However approximately 11-17% developed recurrence after operation (Ansink et al.,1996; Krebs et al., 1982; Soisson et al.,1990; Wilailak et al., 1993). The important goal of post operative surveillance is to early detect the patients with recurrence in order to improve the survival (Shingleton et al., 1987). The surveillance program usually consists of clinical history taking, physical examination, vaginal cytology and radiological studies. The value of vaginal cytology is controversial in routine follow-up practice. Some reports showed the limited diagnostic value of vaginal cytology in detection of pelvic recurrence (Bodurka-Bevers et al., 2000; Krebs et al., 1982) while some reports recommended routine vaginal cytology because it was simple, painless, and inexpensive (Larson et al., 1988; Soisson et al.,1990) .

In our institute, after surgical treatment for early stage cervical cancer, the patients were scheduled to attend follow up clinic every 3 months in year 1, every 4 months in year 2, every 6 months in years 3-5, and every year after that. Vaginal cytology has been routinely performed in every visit for a long period without evaluation of its value. To identify the benefit of such practice, this study was accordingly conducted to assess the value of vaginal cytology in terms of sensitivity and specificity for detection of recurrent disease after radical surgery.

Materials and Methods

The medical records of cervical cancer patients who underwent radical hysterectomy with pelvic lymphadenectomy (RHPL) and attended follow up at Chiang Mai University Hospital between January 2000 and May 2006 were reviewed. The patients received adjuvant concurrent chemoradiation (CCRT) when either nodal metastasis or parametrial involvement was found. Patients who had lymphovascular space invasion (LVSI) and deep stromal invasion also received adjuvant CCRT. Patients with positive vaginal margin received intravaginal brachytherapy using a high-dose-rate by remote control after-loading technique. Brachytherapy was usually given in 2-7 fractions with a total dose of 4-6 Gy/0.5-0.75 cm below the vaginal mucosa. Patients who had only LVSI received post operative cisplatin chemotherapy. After the completion of treatment, the patients were followed up with the routine schedule mentioned above.

At every visit, surveillance consisted of clinical history taking, physical and pelvic examination, and Papanicolaou

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smear of the vaginal cuff. Biopsies and radiographic imaging were done to investigate an abnormal finding or doubtful symptom when deemed necessary.

The recurrences were divided into 3 categories. One was regional recurrence defined as the recurrence in the area of vaginal cuff, bladder, rectum, pelvic and inguinal nodes and/or pelvic sidewall. The second one was distant recurrence that included all tumor recurrences outside the pelvis and the last one was the combination of both regional and distant recurrences.

Statistical analysis of the data was carried out by using the SPSS for Windows program version 11. The vaginal cytology was analyzed to evaluate the sensitivity, specificity, positive and negative predictive values for the detection of recurrent carcinoma. The Fisher-exact test was used to assess the statistical significance of treatment and anatomical site recurrence. The study was conducted under the ethical approval of the Research Ethics Committee of Chiang Mai University Hospital.

Results

There were 585 patients in the study period. Thirty patients were excluded due to loss to follow up after the operation. Among the remaining 565 patients, the mean age was 43 years with a range of 27-74 years. The mean follow-up time was 35 (1-76) months and the mean number of Pap smears was 8 (1-15) times per cases. The majority of patients were in stage IB1 (478 patients), followed by stage IB2 (38 patients) and stage IIA (49 patients). The treatment consisted of RHPL alone in 362 (64%) patients, RHPL followed by adjuvant CCRT in 171(30.3%) patients and RHPL with adjuvant chemotherapy in 32 (5.7%) patients. Squamous cell carcinoma were noted in 379 (67.1%) followed by adenocarcinoma, adenosquamous and poorly differentiated small cell neuroendocrine in 138 (24.4%) patients, 33 (5.8%) patients, 11 (1.9%) patients, respectively.

One hundred and eighty three patients (32.4%) were considered to be high risk for recurrent carcinoma because of the nodal metastasis (99), surgical margin involvement (34) and positive parametrium (50). All of these patients received adjuvant CCRT except the 26 patients who had positive vaginal margin for high grade lesion who received only brachytherapy.

Twenty-three patients (4%) developed recurrence. The interval from the surgery to recurrence ranged from 5-61 months with a median of 23 months. Seventeen (73.9%) patients developed suspicious symptoms while six (26%) patients had recurrence detected by physical examination. Table I shows the recurrence sites related to treatment. Regional recurrences were found in 11 (47.8%) patients whereas 8 (34%) patients developed distant recurrence. Both regional and distant recurrences were noted in 4 (17.4%) patients. The anatomic sites of recurrence were not statistically different between patients who underwent radical surgery alone and those who received adjuvant treatment.

During the follow-up period, 4,376 vaginal cytology were carried out with the mean number of 8 (1-15) per case. Abnormal smears were found in 5 patients. Low grade intraepithelial lesion (LSIL) and atypical squamous cell of undetermined significance (ASCUS) on cytology were detected in 2 and 1 patients, respectively. The colposcopic examination and vaginal biopsy in these 3 patients revealed negative for lesions. One patient had high grade intraepithelial lesion (HSIL). Colposcopic examination and vaginal biopsy revealed high grade vaginal lesion. She was treated with laser abrasion followed by application of bleomycin cream. The subsequent vaginal smears after treatment were normal.

Table 1. The Recurrent Sites Related to Treatment

	Surgery	Surgery & Adjuvant	Total
Regional	3	8	11
Distant	2	6	8
Combine	2	2	4
Total	7	16	23

Fisher exact test, P = 0.64

Table 2. The Accuracy of Vaginal Smears for Detection of Recurrence

	Recurrence	No Recurrence	Total
Abnormal smear	1	4	5
Normal smear	22	538	560
Total	23	542	565

Sensitivity = 1/23 = 4.3% Specificity = 538/ 542 = 99.3%
Positive predictive value = 1/5 = 20%
Negative predictive value = 538/560 = 96.1%
False positive = 4/5 = 80% False negative = 22/560 = 3.9%

The remaining 1 patient had malignant cells on vaginal cytology. This patient was previously treated with RHPL for adenocarcinoma of the cervix followed by adjuvant cisplatin chemotherapy for several LVSI. She developed vaginal recurrence 16 months after the operation and was treated with pelvic radiation and brachytherapy. She had adenocarcinoma on vaginal cytology 15 months later. Abdominal computerization scan revealed the vaginal stump mass with bilateral hydronephrosis. Since the tumor did not respond to chemotherapy, she was then treated with palliation radiation to control pain.

Table 2 presents the sensitivity of vaginal cytology which was only 4.3% while the specificity was high at 99.3%. The positive predictive value was 20% and negative predictive value was 96%. Among 8 patients who developed recurrence at the vaginal stump , only 1 showed adenocarcinoma in the vaginal smear whereas the others revealed normal vaginal cytology. The total vaginal smears in patients with vaginal recurrence were 41. Consequently, the detection rate of vaginal recurrence by vaginal cytology was only 2.4%.

Discussion

This study showed that vaginal cytology had very low diagnostic value for surveillance of early stage cervical

cancer patients after surgical treatment. The sensitivity of the vaginal smear was only 4.3%. Unlike the report of Soisson et al (1990), the sensitivity and specificity of vaginal cytology for the detection of recurrence in their series were 13% and 100%, respectively. They noted that 2639 vaginal smears would have been performed in order to detect 2 recurrences that were successful treated with radiation therapy. Larson et al (1988) revealed that 5 of 27 (18%) recurrence patients were detected by vaginal cytology. However, Morice et al (2004) found that in only 1 of 7 asymptomatic patients was the recurrence identified by vaginal cytology. All patients in their series were treated with surgery and adjuvant radiotherapy. Nevertheless, none of the recurrence patients in the series of Bodurka-Bevers et al (2000) was diagnosed by vaginal smear. In the present study, only 1 patient had malignant cells in the follow up vaginal smear after receiving treatment for pelvic recurrence with pelvic radiotherapy. She had vaginal stump mass and was additionally treated with palliative radiotherapy after failure of 1 course of chemotherapy. The remaining abnormal vaginal smears in our series did not have tumor recurrence after further investigation.

The low sensitivity of vaginal smear after radical surgery and radiation might result from the atrophy and vaginal stenosis, and the interpretation of cytology is complicated by radiation change (Naumann et al., 1996). In addition, Owen and Duncan (1996) supposed that the vaginal cytology could be normal in patients with clinical evidence of recurrent disease on the vaginal vault because the recurrent tumor invaded the entire thickness of the vagina before the cells could be sampled by routine cytology. The sensitivity of vaginal cytology increased in the advanced stage of cervical cancer. Shield et al (1991) noted that the sensitivity of vaginal cytology in a group of 70 locally advanced stage patients who had recurrence was 33% and was high at 62% in patients with pelvic recurrence. They also mentioned that the diagnosis of post radiation dysplasia was an ominous sign. There were 6 of 15 patients with post radiation dysplasia who developed recurrence; the mean interval of recurrence was 14 months. There findings were similar to the other reports (Wentz et al., 1970). In our study, there were 3 patients with post radiation dysplasia and none of them had recurrent cancer.

Whereas vaginal cytology had low detection rate for recurrence, the symptoms and physical examination showed high detection rate at 71-84 % (Soisson et al.,1990; Bodurka-Bevers et al., 2000; Morice et al., 2004). This was similar to our series that 17 of 23 (74%) patients who developed tumor recurrence had clinically suspicious symptoms.

The recurrence rate in the present study was only 4%. This differed from the previous reports that reviewed the high recurrence rate at 11-17% after RHPL for early stage cervical cancer (Ansink et al., 1996; Krebs et al., 1982; Soisson et al., 1990; Wilailak et al., 1993). This may result from the short study period and the high number of the patients who were lost to follow up. Thirty patients in our study never returned to follow up after initial surgery. The study period in our study was 6 years while those in the previous reports ranged from 12-21 years (Ansink et al., 1996; Krebs et al., 1982; Soisson et al., 1990; Wilailak et al., 1993). The limitations of our study included the retrospective by nature and the short follow-up period. However, the large number of patients (565) in a single institute was the strength of this study. Long-term follow-up study is ongoing to confirm the results of this study.

In conclusion, the value of vaginal cytology in detecting recurrent cervical cancer after radical surgery is limited. Careful history taking and physical examination still play important roles in detection of tumor recurrence.

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