Conization in pregnant women with uterine cervical intraepithelial neoplasia III

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Objective: To clarify whether pregnant women with uterine cervical intraepithelial neoplasia (CIN) III can be followed-up until delivery or conization during pregnancy is necessary.

Patients and Methods: We analyzed 9 pregnant patients with CIN III who were treated at the Saitama Cancer Center between 1992 and 1998. At the time of their first visit, every pregnant patient was examined by cytology, colposcopy, and directed punch biopsy. These combined methods were performed during pregnancy and after delivery in patients who wanted to be managed without conization. Conization and vaporization were performed using a YAG laser.

Results: Seven patients were managed without conization during their pregnancy. After delivery, 5 patients received conization and 2 patients received a total abdominal hysterectomy (TAH). Among these 7 patients, the clinical and cytohistological findings of all the cervices were persistent and no microinvasive carcinomas were found during the operative procedures after delivery. All of the patients had normal vaginal deliveries. Conization was performed during pregnancy in two patients. One of these patients had severe dysplasia (SD) and the other was diagnosed as having an adenocarcinomatous lesion on the basis of the biopsy specimen obtained at the time of the first visit.

Conclusion: Pregnant patients with CIN III can be safely followed-up using a combination of diagnostic techniques (cytology, colposcopy and biopsy) until and after delivery. However, when the cytohistological diagnosis during pregnancy is suspicious of cervical adenocarcinoma, further clinical evidence must be obtained before a decision regarding the need for conization can be made.

Key words: Cervical intraepithelial neoplasia — Pregnancy — Cytology — Colposcopy — Conization

I. Introduction

Recently, a close carcinogenetic relationship
between uterine cervical carcinoma and human papilloma virus (HPV) has been reported\(^1\). The incidence of uterine cervical carcinoma in pregnant women is increasing as sexually transmitted diseases (STDs) become more prevalent among youths\(^2\).

Generally, conization and/or vaporization are standard treatments for patients with CIN III\(^3\). However, these methods are not always complete, and some patients experience residual lesions or relapses. Furthermore, these procedures can induce complications, such as bleeding, abortion, premature delivery, infection and/or cervical stenosis, when performed during pregnancy. Thus, these procedures can be troublesome and occasionally deteriorative to patients\(^4\).

In this study, which considers the quality of life of pregnant patients, we analyzed whether pregnant women with CIN III could be safely managed without conization during their pregnancy.

II. Patients and Methods

We analyzed 9 pregnant patients with CIN III who were treated at the Saitama Cancer Center between 1992 and 1998. At the time of their first visit, each patient was examined by cytology, colposcopy, and directed punch biopsy.

The stage of CIN III was cytologically classified as IIIb, IV or V, representing severe dysplasia (SD), carcinoma in situ (CIS) and microinvasive carcinoma, respectively. In class IIIb, whose estimated histology is SD, mainly parabasal-type cells with a high nuclear/cellular ratio are found. The chromatin pattern is dense but vesicular. The nuclear rims are slightly irregular with clefts. In class IV, whose estimated histology is CIS, small parabasal squamous epithelial cells are present. The nuclear/cellular ratio is much larger, and the nuclei are enlarged and hyperchromatic. The chromatin network is coarsely granular. The nuclear rims are fully expanded with nuclear content. The background of both patterns is clear without necrosis, unless inflammation is present. Class V corresponds to invasive carcinoma. If syncytial cell groupings, cells containing nucleoli, and/or cells with dense irregular nuclear structures other than the morphologic patterns of class IV are present, these cells are likely to have originated from a microinvasive carcinoma.

The colposcopical definitions proposed by the International Federation of Cervical Pathology and Colposcopy (IFCPC) were adopted\(^5\). After the application of acetic acid, acetowhite changes appear. In acetowhite epithelium (W), subepithelial vessel patterns are difficult to see. In punctation (P) and mosaic (M) epithelium, however, punctation vessels such as hairpin types or mosaic patterns, respectively, are distinct. In major changes, the acetowhiteness is thick and partly elevated, while the vessel patterns are more pronounced and irregular in P and M. The surface contour is uneven.

The histological diagnoses were performed according to the WHO classification\(^6\). CIN III includes SD and CIS. In this study, we used both systems of nomenclature, SD and CIS, and CIN III.

Patients who wished to be managed without conization during their pregnancy were examined every two or three months by cytology, colposcopy, and, if necessary, biopsy.

Conization and/or vaporization were performed using a YAG laser. A power of 25 W for conization and 40 W for vaporization was used.

III. Results

The clinical, cytological, colposcopical and histological findings for all patients are shown in Table 1. Patients were referred to us during their first or second trimester because of abnormal cytology findings diagnosed by their private doctors.

All of the initial cytological smears suggested a histological diagnosis of SD or CIS except for Case No. 3, whose cytological classification of IIIa suggested moderate dysplasia. Repeated smears from the seven patients managed without conization during their pregnancy were class IIIb or IV, suggesting SD or CIS, respectively (Photo. 1-Case No. 1).
## Table 1 Clinical findings during pregnancy and after delivery

<table>
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<th>Cases</th>
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*1 Colpo = Colposcopy  
*2 Cyto = Cytology  
*3 Histo = Histology  
*4 Operation = Conization  

SD = Severe Dysplasia  
MoD = Moderate Dysplasia  
CIS = Carcinoma in situ  
MiD = Mild Dysplasia  
AIS = Adenocarcinoma in situ  
CC = Chronic Cervicitis  

The 3rd and 4th smears in Case No. 4 were suggestive of microinvasive carcinoma.

During every colposcopical examination, acetowhite epithelium (W), punctation (P) and/or mosaic (M) findings were detected. All findings were considered to be major except for Case No. 8. As the columnar epithelium could be seen in every patient, the colposcopical findings were considered to be satisfaction. Colposcopically overt carcinoma, which is suggestive of early invasive carcinoma, was not observed (Photo. 2-Case No. 1).

The pre-delivery histological diagnoses were SD...
Photo. 1 Cytology (Case No. 1).
  a: pregnancy 16 weeks (III b)
  b: pregnancy 29 weeks (IV)
  c: postpartum 7 months (IV)

Photo. 2 Colposcopy (Case No. 1).
  a: pregnancy 16 weeks (M)
  b: pregnancy 21 weeks (W)
  c: postpartum 7 months (W)
or CIS in all patients. The histological diagnosis of Case No. 6 was moderate dysplasia, but her smear strongly suggested SD. Among the 7 patients who were followed-up during pregnancy, none had microinvasive carcinoma. Their clinical findings persisted until the operative procedures were performed (Photo. 3-Case No.1).

All seven patients had normal vaginal deliveries. After delivery, their cytological, colposcopical and histological findings were the same as their pre-delivery findings, with no signs of either progression or disappearance. Five patients were treated with conization, and 2 patients received a TAH. All final histological diagnoses were CIS except for Case No. 2, whose diagnosis was SD. The cytological features of Case No. 4 during the 28th and 36th gestational week corresponded to a class V rating, suggesting microinvasive carcinoma. However, this patient was observed until delivery without performing a conization because the histological diagnoses of the biopsies performed during the same periods were CIS.

Conization was performed during pregnancy in two patients (Case No. 8 and 9). The pre-treatment histological diagnosis of Case No. 8 was mild dysplasia (MiD), but her smear strongly suggested SD. The conized specimen was classified as SD. The second patient showed adenocarcinomatous lesions in her initial biopsy specimen. Her conized specimen had both squamous cell carcinoma in situ (CIS) and adenocarcinoma in situ (AIS).

Comparison of the cytology, colposcopy, and punch biopsy findings showed no major discrepancies and only one degree of discordance.

IV. Discussion

A close carcinogenetic relationship between uterine cervical carcinoma and human papilloma virus has been reported\textsuperscript{11}, and these sexually transmitted diseases are widespread in youths. Furthermore, the early detection of uterine cervical carcinoma is easy because of extensively adopted mass-screening methods using Pap smears\textsuperscript{5}. Conse-
quently, the incidence of uterine cervical carcinoma in pregnant women has been increasing.

Although even pregnant patients with stage Ib uterine cervical carcinoma can be managed without therapeutic procedures until full-term delivery, prompt treatment is usually recommended in cases of advanced cervical carcinoma to save the patient’s life. However, the treatment of pregnant women with cervical intraepithelial neoplasia (CIN III) is always a concern. Whether management and follow-up until full-term delivery with only regular checks and no surgical procedures or prompt conization during pregnancy is advisable for correct diagnosis and treatment remains uncertain.

Although conization or the LEEP (loop electrosurgical excision procedure) method is a standard treatment for CIN III, many complications can occur when conization is performed during pregnancy. These complications can include bleeding, abortion, infection and/or cervical stenosis. Second, complete removal of the carcinoma without leaving any residual lesions is not always possible using conization. Third, new lesions sometimes reappear after the operation. Finally, some cervical lesions disappear during pregnancy or after delivery, meaning that conization performed during pregnancy is not always necessary.

In this study, the following facts regarding the clinical treatment of pregnant patients with CIN III were clarified. First, a correct diagnosis is possible using a combination of diagnostic methods (cytology, colposcopy, and biopsy), even in pregnant women. Second, taking cytological smears during pregnancy is easy and safe. We used cotton-swabs to obtain the smears. Sufficient cells can be obtained using this method to make a diagnosis without massive bleeding or abortion. Third, as cervical eversion is conspicuous during pregnancy and the columnar epithelium can be seen over the entire cervix, cervical lesions can be completely observed and adequate biopsies obtained from suspicious lesions that may have progressed. This enables invasive diseases to be ruled out. Finally, CIN lesions persist during pregnancy and after delivery without further progression or disappearance.

In the follow-up of pregnant women with CIN III, prompt diagnosis and the detection of progressive or invasive carcinoma over a short period of time is important. Although hormonal changes during pregnancy can be observed in smears, the cytological and histological diagnostic criteria for CIN III in pregnant women are the same as those of nonpregnant patients. Colposcopical findings are stressed during pregnancy. After delivery, the lesions become smaller in some cases but cannot be missed if adequate care is taken. Although the interval between CIN III and invasive carcinoma is not clear, several years are thought to be required for progression. Moreover, pregnancy has not been shown to accelerate their progression. Since conization during pregnancy can induce several therapeutic problems, we believe that it should be avoided when possible to increase the quality of life of pregnant women. Based on our results and those of reported literature, we would like to propose that pregnant women with squamous CIN III be managed using combined diagnostic techniques that have been shown to be reliable.

In comparison with squamous cell carcinoma, the incidence of patients with uterine cervical adenocarcinoma is low. We are unable to draw any conclusions regarding this disease because only one case of adenocarcinoma was observed in this study. Early adenocarcinomatous lesions cannot be reliably diagnosed using only cytology and/or colposcopy. In situ adenocarcinoma has a multifocal development and can spread to small, deep or superficial glands in addition to being associated with squamous neoplasia. However, when the cytological and histological diagnosis during pregnancy is suspicious, cervical adenocarcinoma, further clinical evidence must be obtained before a decision regarding the need for conization can be made. With respect to surgical procedures, conization should be performed using either a laser or cold knife method. Excising “coin” tissue using the superficial LEEP method is not advised because deep glandular
lesions can be easily missed\textsuperscript{13,14}.

抄 録

目的：子宫颈癌上皮内癌变（CIN III）合併妊娠に妊娠中、円雉切除術を施行せずに経過観察を可能かどうかを検討した。

症例と方法：症例は1992年から1998年までに当科で治療したCIN III合併妊娠9例について検討した。初診時に全症例について細胞診、コルポ診、鰐の組織診を施行した。妊娠中円雉切除術なしに経過観察を希望した患者には、この3方法を妊娠中および分娩後に施行した。円雉切除術と蒸散術はYAGレーザーを使用した。

結果：妊娠中円雉切除術をせずに経過観察をした症例は7例である。これら7例のうち5例は円雉切除術を、2例は腹式単純子宫全摘術を分娩後に受けた。この7例の子宮頸部の臨床的、細胞組織学的所見は手術時まで継続し、微小浸潤癌は発見されなかった。全例とも正常分娩をしている。他の2例には妊娠中に円雉切除術を施行しており、初回の生検標本で、1例には高度異型上皮、もう1例には上皮内癌が認められた。

結論：CIN III合併妊娠に妊娠中、分娩後も、細胞診・コルポ診・組織診を組み合わせた検査により安全に経過観察ができる。ただし、細胞組織学的子宮頸部病変を疑う症例においては、さらなる検討が必要であると考えられる。

References

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