Cervical Adenocarcinoma In situ Presentation of the Case and Review of Incidence, Recurrence Rate and Therapeutic Options

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Abstract

Cervical adenocarcinoma in situ (AIS) is a premalignant lesion that was first described by Helper in 1952 in his review of adenocarcinoma of the cervix. The following year Friedel reported two women who had undergone therapy for squamous cervical lesions and had concomitant cervical AIS. These authors postulated that this glandular lesion was a precursor to invasive adenocarcinoma similar to preinvasive squamous cell carcinoma in situ. An increase in the incidence of cervical AIS has been reported in recent years. In this fact may contributed an increased prevalence of HPV 18, the pathologist’s awareness of the lesion and an increase in use of oral contraceptives.

Keywords: Cervix; Adenocarcinoma in situ; Glandular dysplasia; Invasive adenocarcinoma

Introduction

Cervical adenocarcinoma in situ (AIS)

Adenocarcinoma in situ of the cervix (AIS) is a premalignant lesion that was first described by Helper in 1952 in his review of adenocarcinoma of the cervix [1]. The following year Friedel reported two women who had undergone therapy for squamous cervical lesions and had concomitant cervical AIS [2]. These authors postulated that this glandular lesion was a precursor to invasive adenocarcinoma similar to preinvasive squamous cell carcinoma in situ. An increase in the incidence of cervical AIS has been reported in recent years [3-5]. In this fact may contributed an increased prevalence of HPV 18, the pathologist’s awareness of the lesion and an increase in use of oral contraceptives.

Diagnosis and pathogenesis

The diagnosis of cervical AIS seems to be difficult and most of the time occurs as an incidental finding in a specimen of a cone biopsy or cervical cone excision coexistent with cervical squamous lesion. When lesion of glandular epithelium is reported in a smear test the following steps are suggested: colposcopy – biopsy – endocervical curettage and cold knife cone of the cervix in order to define the margins, the depth of the lesion and excluding the invasive cervical cancer. The incidence of cervical AIS has been estimated to be from 1/8000 to 1/475,000. In several studies that we reviewed [6,7,8-13] 85%-100% papanicolaou tests were abnormal. Lee et al. calculated the sensitivity of Papanicolaou tests for cervical adenocarcinoma in situ to be from 55% to 72% [14]. The results of the endocervical curettage performed in women with AIS were reported on 185 patients in six studies [15,16,9-11,12,17,]. The false negative rates ranged from 10% to 67% with an overall rate of 48% [15,9-12]. The pathogenesis of cervical AIS has not been completely delineated. On the other hand squamous cell carcinoma in situ has been well studied and the progression of dysplasia to invasive disease is very clear defined. The rare incidence of AIS makes very difficult the delineation of natural history of glandular dysplasia which could consist the precursor of cervical AIS [18-25].

Presentation of our case report and therapeutic approach

Our patient woman of age 36 years old came to our private medical office for a second opinion after having a second pathological smear test and a cervical biopsy which results were discordant with the results of smear test. The patient reported that she was following regular annual gynecological screening exams and she had normal smear tests from 2007 until 2010 when the results showed cervicitis. She reported that she was suggested from her gynecologist to repeat the smear test after 6 months. On 23/09/2010 the new smear test showed AGUS and was suggested colposcopy and cervical biopsy was held without any pathological finding. Antibiotic treatment was given and cryopexy was made. Finally was suggested to repeat the smear test after 6 months. On 10/03/2011 thin prep was made and the results were CIN 1-2. Cervical biopsy followed again and the results showed glandular dysplasia. We don’t have a clear information if second cryopexy was made but next thin prep reveled CIN 2-3 (HGSL) with possible involvement of glandular epithelium. With all these results that women provided to us our first thought was that the biopsies were’t taken from the proper place as long as the thin prep results insisted for the lesions. The women from her obstetrical history had one normal labor 8 years ago free personal history and no family history. Her gynaecological examination revealed cervix of a parous woman with transformation zone clearly visible, uterus and ovaries appeared normal by transvaginal ultrasound. Colposcopy was made - the transformation zone appeared very clear with an exophytic lesion on 7th o’clock position of the cervix on the glandular epithelium with high vascularization from the 7th to 12th o’clock position. From the squamous epithelium didn’t appear any serious lesion. A small loop cervical excision was made and we removed the lesion and the sublesional stroma with possible diagnosis of exophytic condylomatosus lesion of cervix and we sent it for histological examination. The histological exam showed adenocarcinoma in situ well differentiated and CIN 1/HGUS of squamous epithelium. We followed endocervical and endometrium curettage with negative for a disease results. Then large cold knife cone was made 4×3, 6×2, 5 cm. The histological examination showed adenocarcinoma in situ of endocervix from 6 o clock position until 12:00 o’clock position. No
invasive disease reported. The glandular dysplastic lesions reached the border of excision at 10:00 o’clock position. We discussed with the patient the need to repeat new cervical cone excision and also the rates of recurrence of the disease and so finally was decided total hysterectomy without salpingo-oophorectomy. The histological specimen of uterus and cervix showed glandular dysplasia from 6 to 12:00 o’clock position, multilayered epithelium, medium nuclear atypia and mitotic divisions. The surgical margins of excision of cervix was free of glandular dysplasia. Histological results showed: glandular dysplasia of endocervical epithelium. Follow up of the patient until today is clear of disease. In (Figure 1) below we summarize the management of AIS.

**Conclusions**

International literature reviewing showed two different approaches of the patient with cervical AIS. Recent reviews reported increasing in number of patient who undergone cold knife cervical cone with free of disease surgical margins having a good follow up. Very good prognosis in relation with the rate of recurrence of disease. The rate of recurrence of disease is wide from 0% to 44%. (Table 2) shows the results of several studies according to disease recurrence after conservative management. Therefore the decision of conservative therapy depends on the age and the desire of women to preserve fertility. In women with free of disease surgical margins of cervical excision and negative endocervical curretage the cervical cone must be cover all the women with free of disease surgical margins of cervical excision and on the age and the desire of the women to preserve fertility. In management. Therefore the decision of conservative therapy depends on the age of involved women and the desire for fertility preservation. We discuss and describe a case report of adenocarcinoma of cervix in situ coexistent with glandular dysplasia with no invasive disease.

**Summary**

The incidence of cervical adenocarcinoma in situ is increasing in frequency although very few cases has been described in the literature. The residual disease rates are as high as 80% when the cervical cone margins are positive which signifies the necessity gynecologist and pathologists to become familiar with these cases. Therapeutic options depending on the age of involved women and the desire for fertility preservation. We discuss and describe a case report of adenocarcinoma of cervix in situ (no invasive cancer).

*Negative endocervical margins patients were managed with cone biopsy.*

**Table 1: Residual disease and cone biopsy margin status.**

<table>
<thead>
<tr>
<th>Author</th>
<th>No of patients treated conservatively</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bertrand et al. [15]</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Poynor et al. [16]</td>
<td>15</td>
<td>7</td>
</tr>
<tr>
<td>Hopkins et al. [17]</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Wildrich et al. [7]</td>
<td>38</td>
<td>6</td>
</tr>
<tr>
<td>Deney et al. [9]</td>
<td>19</td>
<td>1</td>
</tr>
<tr>
<td>Wolf et al. [10]</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Anderson and Arffmann [12]</td>
<td>23</td>
<td>0</td>
</tr>
<tr>
<td>Im et al. [18]</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Ostor et al. [19]</td>
<td>53</td>
<td>0</td>
</tr>
<tr>
<td>Nicklin et al. [20]</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Luey et al. [21]</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Houghton et al. [22]</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>Azodi et al. [23]</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Shin et al. [8]</td>
<td>95</td>
<td>9</td>
</tr>
<tr>
<td>Total</td>
<td>297</td>
<td>27 (9%)</td>
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</tbody>
</table>

**Table 2: Disease recurrence after conservative management.**

**References**


