Diagnostic difficulty in macroscopically invisible cervical adenocarcinoma: Case report

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Abstract. Cervical adenocarcinomas are the second most common malignant tumours of the cervix after squamous cell carcinoma. Their frequency is reported to be gradually increasing. These tumours are polypoid or papillary in 50%, diffuse or nodular in 15%, and occult (cannot be observed macroscopically) in 10-15% of the cases. We present the pathological features of three cervical adenocarcinoma cases that could not be observed macroscopically but were found by endocervical curettage.

Cervicovaginal smears of the cases were prepared by conventional methods and PAP stained. Endocervical curettage and resection materials were reexamined. One patient’s smear material could not be found. No positive findings were detected in the smears of other two cases. The carcinomas could be determined with endocervical curettage in all three cases. All cervixes were sampled and the tissues were processed as the tumour could not be seen macroscopically in hysterectomy materials. Clear cell carcinoma was diagnosed in one case and endocervical mucinous adenocarcinoma in the other two cases.

Cervical adenocarcinomas can be occult in some cases and can not be observed during macroscopic examination as in our cases. A large number of paraffin-embedded blocks should be prepared, and if necessary, all cervixes should be processed to find the tumor in such cases.

The possibility of diagnosing the tumors which cannot be seen macroscopically and cannot be determined clinically increases if the number of samples taken from the cervix is increased in hysterectomy materials and if conization can be performed after positive ECC which properly performed before endometrial sampling.

Key words: Cervix, adenocarcinoma, macroscopic examination, occult

1. Introduction

Adenocarcinomas constitute approximately 10-20% of invasive cervix tumours and their incidence has increased since the 1980s (1-6). This increase is remarkable under the age of 40 (2). The mean age of the patients is 55 and they often complain of abnormal vaginal bleeding and secretion. One third of these patients can be asymptomatic (6, 7). Epidemiologic risk factors for cervical adenocarcinoma include low socioeconomic status, multiple sexual partners (particularly before the age of 20), weight gain and oral contraceptive use (long-term) (6-8). More recent data have also implicated human papillomavirus (HPV) (6,9,10). Adenocarcinomas are macroscopically exophytic and form a polypoid or papillary mass in 50%, are nodular and can exhibit diffuse growth or ulcerate in 15%, and cannot be observed macroscopically in 10-15% of the cases. The tumours may infiltrate deeply into the wall, even in the absence of visible signs or symptoms (6). We present the pathological features of three macroscopically invisible cervical adenocarcinoma cases in this study, and discuss the reason why these tumours were macroscopically invisible, together with literature data, and address the important points for pathologists.

2. Materials and methods

Three of the seven invasive cervical adenocarcinoma cases diagnosed in our hospital between 2007 and 2008 were found to have a macroscopically invisible diffuse form. Smears belonging to two of the three cases were prepared...
with conventional methods and PAP stained. Radical hysterectomy, bilateral salpingo-oopherectomy, pelvic and paraaortic lymphadenectomy, omentectomy, peritoneal washing for cytologic examination were performed. Endocervical curettage and hysterectomy materials were fixed with 10% formalin and paraffin-embedded blocks were cut into 5-µm thick sections. The prepared sections were stained with Haematoxylin-Eosin. Cytocentrifuge samples were obtained from the abdominal irrigation fluid, fixed with 96% ethanol and stained like PAP.

3. Results

Clinical data of the cases, macroscopic features of the tumours, and the histopathological and cytological diagnoses are provided in the table 1. Also histopathological views of the tumours were shown in figure 1, 2 and 3.

4. Discussion

A significant increase in the incidence of cervical adenocarcinomas in recent years has been reported and 10-15% of these lesions are invisible (1-6). Tumours could not be observed during macroscopy in our three invasive cervical adenocarcinomas cases but recognized by endocervical curettage. The rate of cervical glandular cell anomalies determined by cytology and histopathology is less than for squamous cell anomalies and the false negative rates of PAP smear, endocervical curettage and cervical biopsies have been reported to be high by many studies in the literature. The reported false negative rates for PAP smear and for endocervical curettage are about 50% and 25 % respectively (5, 11-15). Smears were found to be negative in two of our three cases. One of our patients’ smear material could not be reached. Histopathological changes of endocervical curettage were diagnostic in two cases but suspicious in one case. These diagnostic difficulties in our cases are the reflection of the high false negative rates of diagnostic tools of cervical adenocarcinomas indicated in the literature.

The literature lacks satisfactory information explaining why some of the cervical adenocarcinomas can be macroscopically invisible. The findings that could be related to reasons are the nodular form and diffuse growth, mimicking the normal histology of the cervix by creating abnormal glandular forms and not

<table>
<thead>
<tr>
<th>Case</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>72</td>
<td>66</td>
<td>52</td>
</tr>
<tr>
<td>Clinical Symptom</td>
<td>PM bleeding</td>
<td>PM bleeding</td>
<td>PM bleeding</td>
</tr>
<tr>
<td>PAP Smear Diagnosis</td>
<td>NILM</td>
<td>NILM</td>
<td>-</td>
</tr>
<tr>
<td>ECC Diagnosis</td>
<td>Clear cell carcinoma</td>
<td>Adenocarcinoma</td>
<td>Endocervical type mucinous adenocarcinoma</td>
</tr>
<tr>
<td>Preoperative radiologic evaluation (magnetic resonance imaging)</td>
<td>No evidence of gross tumour</td>
<td>No evidence of gross tumour</td>
<td>No evidence of gross tumour</td>
</tr>
<tr>
<td>Cervix Macroscopy</td>
<td>Normal</td>
<td>Irregular Endocervix</td>
<td>Normal</td>
</tr>
<tr>
<td>Tumor Dimensions</td>
<td>1x 0.4 cm</td>
<td>1.8x1 cm</td>
<td>2.1 cm</td>
</tr>
<tr>
<td>Histopathological Diagnosis</td>
<td>Clear cell adenocarcinoma</td>
<td>Endocervical type mucinous adenocarcinoma</td>
<td>Endocervical type mucinous adenocarcinoma</td>
</tr>
<tr>
<td>Cervical Surface Epithelium</td>
<td>Normal</td>
<td>Tumor present + HSIL</td>
<td>Normal</td>
</tr>
<tr>
<td>Transformation Zone</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Endometrium</td>
<td>Atrophy</td>
<td>Atrophy</td>
<td>Poor proliferative</td>
</tr>
<tr>
<td>Lymph Node Metastasis</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Malignant Cells in Abdominal Fluid</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Ovaries</td>
<td>Normal</td>
<td>3 cm fibroma on the right</td>
<td>Normal</td>
</tr>
<tr>
<td>Omental Metastasis</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

PM: Postmenopausal. NILM: Negative for Intraepithelial Lesion or Malignancy. ECC: Endocervical curettage. TZ: Transformation Zone.
causing a desmoplastic reaction. Although focal desmoplastic reaction has been reported in some macroscopically invisible cervical adenocarcinomas, the majority of these tumours have not shown desmoplastic reaction (6). The growth was diffuse and created glandular structures in all three of our cases. Desmoplastic reaction was not present in the tumour of the first cases while chronic inflammation in the periglandular regions and fibrosis were observed at minimal levels in the second cases.

One third of cervical adenocarcinoma cases may be asymptomatic (6, 16). Our three cases presented at the hospital with symptoms of postmenopausal bleeding.

Taking two sections one from the anterior and one from posterior walls of the cervix and preparing two paraffin-embedded blocks have been found to be adequate for histopathological diagnosis in macroscopic examination of uteri of cases without a history of cervical carcinoma and dysplasia. Few numbers of sections can cause high false negative rates in the pathological diagnosis of cervical adenocarcinomas that cannot be identified with a smear or biopsy or are macroscopically invisible cervical tumours. Because the tumours had been observed in the endocervical curettage materials in our tree cases we put the whole cervixes in process and examined. In this way we could manage to define the tumours and their dimensions. So we think that it is proper to put the whole cervixes in process in cases with positive endocervical curettage in terms of suspicion of cervical adenocarcinoma but without macroscopically visible tumours.

Since recent studies about the management strategies of small-volume stage I cervical cancer tend to point less radical surgery possibilities, cervical conization may be diagnostic and curative for the cases who have positive ECC which is properly performed just before
References


