

Endocervical Adenocarcinoma *in situ* with Replacement of the Entire Corpus Endometrium

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Abstract

Adenocarcinoma *in situ* (AIS) of the uterine cervix is a premalignant glandular condition and is the precursor to cervical adenocarcinoma. Extension of endocervical AIS proximal to the endocervical canal up to the endometrium of the corpus uteri, fallopian tubes and even the ovaries is rare. In the present case we describe a very unique pattern in which AIS has spread, starting from within the endocervical canal all the way up covering the entire inner lining of the uterus and into the salpinges but not in the ovaries.

Introduction

Adenocarcinoma *in situ* (AIS) of the uterine cervix is a premalignant glandular condition and is the only known precursor to cervical adenocarcinoma. AIS and adenocarcinoma are less common than Squamous cell cervical cancer and its precursors. The average age of woman at diagnosis of cervical AIS is 36.9 years [1]. AIS is associated with high-risk human papillomavirus infection (HPV type 18 and 16) [2,3]. Also some data suggest that long-term use of oral contraceptive is associated with an increased risk of AIS [4,5]. Extension of endocervical AIS proximal to the endocervical canal up to the endometrium of the corpus uteri, fallopian tubes and even the ovaries is rare. In the literature there is only one case report that describe the presence of endocervical AIS with contiguous spread in to the lower uterine segment [6]. Our case represents such a case reported.

Case Report

A 36-year-old, para 2, Turkish woman presented with an adenocarcinoma *in situ* (AIS) detected in a cervical cytology and endocervical curettage. She had no vaginal bleeding, no abnormal discharge or postcoital bleeding. Besides the use of oral contraceptive for more than 5 years, there are no other significant past medical or surgical history. A physical examination showed a normal uterine cervix and normal uterus. A cold-knife conization was performed. (Immuno) histologic examination revealed an intestinal-type endocervical adenocarcinoma *in situ* near the squamo columnar junction with Cervical Intraepithelial Neoplasia (CIN-2) in the surrounding area. No suggestions of invasive adenocarcinoma (Figure 1). The surgical margins were negative for AIS. Immunohistochemical analysis showed strong expression of p16 (p16 is a cyclin-dependent kinase-4 inhibitor) and CEA (Carcino Embryonic Antigen) in the AIS. The expression for ER (estrogen receptor) was absent. The patient wished to preserve fertility and was closely follow-up. PAP smears six and twelve months after conization were normal. One year and 4 months after conization she visited the clinic with complaints of abnormal discharge. Endocervical curettage revealed again an intestinal-type endocervical adenocarcinoma *in situ*. She was scheduled for a hysteroscopy and endometrium curettage plus cold knife-conization. The hysteroscopy revealed a normal endometrium and the pathologic investigation of cervix conus showed minor rest lesion of AIS, no invasive adenocarcinoma. The surgical margin was negative for AIS. The endometrium showed no signs of hyperplasia, atypia or malignancy. The patient wished no longer to preserve fertility and strongly requested a hysterectomy. She underwent an uncomplicated total laparoscopic hysterectomy without salpingo-oophorectomy. Histology showed extensive endocervical AIS, involving the endocervix and the entire endometrium (Figure 2) into the tubes. The endocervical AIS tested positive for HPV 16 and HPV 45 by polymerase chain reaction analysis. Although the lesion was not invasive beyond the endometrial mucosa, the diffuse extension into the tubes with no clear surgical margin required further investigation of the tubes. In an MDT (Multi Disciplinary Team) meeting it was strongly advice to do a bilateral tubectomy. Two months later the patient underwent a laparoscopic bilateral tubectomy, biopsy of ovaries and peritoneum plus pelvic lymphadenectomy in Turkey. The pathological examination showed no evidence of AIS and no

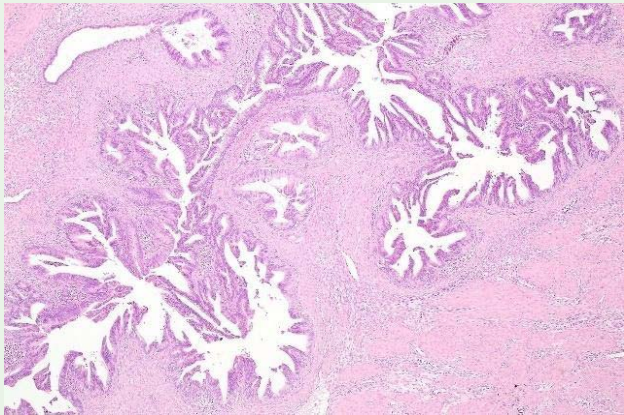


Figure 1: Adenocarcinoma in situ (AIS) of the endocervix; no invasive growth present (amplification 100 x).

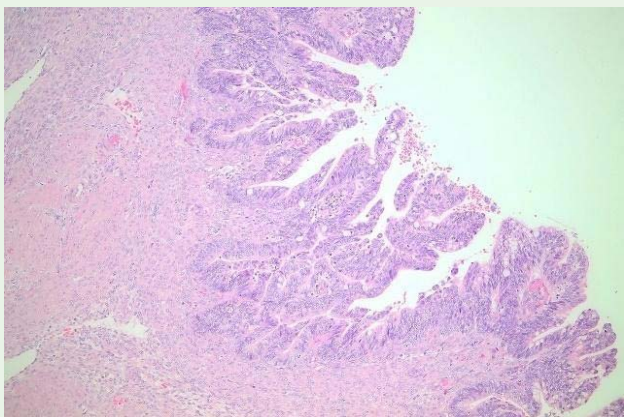


Figure 2: AIS overgrowth of the endometrium without invasion.

invasive adenocarcinoma. These slides were reviewed by the gynecologic pathologists in our department and confirmed no (pre) malignancies.

Discussion

Adenocarcinoma *in situ* of the cervix is nearly always asymptomatic and is generally not visible upon gross examination. It is typically detected due to an abnormal finding on cervical cytology.

Adenocarcinoma *in situ* (AIS) of the uterine cervix typically arises in the transformation zone with contiguous extension proximal within the endocervical canal. Ten to 15 percent of patients with AIS have multifocal disease (“skip” lesions) with foci of AIS that are separated by at least 2 mm of normal mucosa [7]. Jennifer et al. [6] reported a case of a 38-year old woman with endocervical AIS spreading contiguously into the endometrium with a “skip” lesion high in the uterine fundus (80 mm from the transformation zone). The highest reported focus of AIS in the endocervix (measured from the ectocervix) was 30 mm [8]. In our case we describe a very unique pattern in which AIS has spread, starting from within the endocervical canal all the way up covering the entire uterine wall with in the salpinges but not in the ovaries. This has never been described before.

Although the most common HR-HPV types found in endocervical AIS and adenocarcinoma are HPV 18 and HPV 16, we detected HPV16 and HPV 45 in the tissue section. Castellsague et al. [9] describe in their report that women infected with HPV 35, 45, 51 and 58 were statistically significantly and strongly associated with cervical adenocarcinoma. Distinction of an “metastatic” adenocarcinoma *in situ* from a primary endometrial cancer can be problematic in tissue sections due to overlapping morphology of endocervical adenocarcinoma (*in situ*) and endometrial carcinomas. Yemelyanova et al. [10] explain in their report some useful techniques (presence of HPV DNA, Immunohistochemistry for strong expression of p16 and decreased or absent expression of hormone receptors) for clarifying the origin of endocervical adenocarcinoma.

Two cases of extensive AIS with ovarian metastases were reported by Chang et al. [11]. One was a 34-year old woman with cervical biopsy positive for AIS with fourteen months later in a follow-up setting, a well-differentiated intracystic adenocarcinoma of the left ovary. She was 12 years disease-free after oophorectomy, despite limited systemic therapy. The second one was a 30-year old woman with a laser cone excision that showed AIS with negative margins. Three years later cervical biopsy revealed recurrent AIS. Six years later hysterectomy showed extensive endocervical AIS, involving endocervix and endometrium. Because of the diffuse extent a follow-up bilateral salpingo-oophorectomy was performed which showed adenocarcinoma of the right ovary. She was alive and well after chemotherapy and radiotherapy, with no evidence of recurrent disease, 9 months after diagnosis of ovarian metastases. In our case although there was some extension into the salpinges, ovarian biopsy, peritoneum biopsy and pelvic lymph nodes (10 nodes on the right side and 16 nodes on the left side) did not show invasive disease requiring adjuvant therapy. Follow-up with vaginal cytology and high-risk HPV testing of the vaginal fornix is planned at 6 and 24 months.

Informed Consent

Informed consent was obtained from the patient for publication of this case report and accompanying images.

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