Case Report

Unusual Extension of Superficial Spreading Squamous Cell Carcinoma of Cervix to Uterus, Paraovarian, Paratubal Tissue, and Vaginal Surface: A Unique Case Report

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Abstract

Superficial spreading cervical squamous cell carcinoma (SCC) is a rare phenomenon with few cases reported in the literature. The present case report briefs the findings of superficial spreading cervical SCC in postmenopausal women. A 65-year-old postmenopausal woman presented with bleeding per-vaginum for 1–2 months. On examination, the cervix was healthy with no visible growth. She was diagnosed with an endometrial malignancy on magnetic resonance imaging. On endometrial and cervical biopsy, histopathology revealed cervical intraepithelial neoplasia III in ectocervix with SCC in endocervical and endometrial curetting. The patient underwent modified radical hysterectomy with bilateral pelvic lymphadenectomy and histopathology revealed superficially spreading cervical SCC with tumor cells involving endometrium, myometrium, paratubal, paraovarian, vaginal margins without extending to pelvic, and para-aortic lymph nodes. The patient was further managed successfully with adjuvant chemoradiotherapy. Superficial spreading cervical SCC is very rare phenomenon. Its spread is not only limited to endometrium but can extend to involve myometrium, paratubal, paraovarian, and vaginal tissues.

Keywords: *Cervix, endometrium, human papillomavirus, hysterectomy, squamous cell carcinoma*

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Introduction

Globally, cervical cancer is the 14th among all cancers and the 4th most common gynecological cancer[1] with an overall percentage of new cases at 0.7%.[2] It is most commonly associated with persistent human papillomavirus (HPV) infection, accounting for 99% of all cases.[1] Histopathologically, squamous cell carcinoma (SCC) and adenocarcinoma are the two common subtypes of cervical cancer, with SCC accounting for 95% of all cases.[3]

An unusual and rare presentation of cervical SCC is superficially spreading carcinoma, in which the tumor cells spread superficially to the inner surface of the uterus replacing the endometrium. In rare circumstances, it can spread to ovaries, fallopian tubes, and vagina.[4,5] The exact data about superficially spreading cervical SCC are very scarce and hence, it is not included in the 2020 World Health Organization (WHO) Classification of Female Genital Tract Tumors or the 2018 International Federation of Gynecology and Obstetrics (FIGO) cervical cancer staging system.[6] Superficial spreading cervical SCC stains positively for p16, which is an important immunohistochemical marker of HPV, indicating the role of HPV infection in its pathogenesis.[7] Because of its rarity, the exact molecular pathogenesis is not known, but studies have shown the role of CD138 or syndecan-1, a cell-surface heparan sulfate proteoglycan involved in cell-to-cell and cell-extracellular matrix interactions.[8] CD138 is normally expressed in epithelial

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cells, including stratified squamous epithelium. In cervical cancer, decreased expression of this marker is associated with tumor invasion and progression. Loss of expression of CD138 is one of the early events in cervical carcinogenesis as evidenced by decreased expression of CD138 in microinvasive and invasive SCC compared with cervical intraepithelial neoplasia (CIN) I, II, and III.[9]

The present case report briefs the unusual finding of a superficially spreading cervical SCC in a postmenopausal woman.

Case Report

A 65-year-old, P_4L_4, postmenopausal woman with a history of menopause for the last 20 years presented to the gynecological outpatient department with complaints of on and off heavy bleeding per vaginum for 1–2 months. She had no other complaints of abdominal pain, weight loss, or bowel and bladder symptoms. On general examination, she was of fair build with no other comorbidities. On per abdominal examination, the abdomen was soft and nontender, with no mass/lump felt, no organomegaly, or lymphadenopathy. On local examination, the labia majora and minora were hypopigmented at places. On per speculum examination, the cervix and vagina were grossly healthy with no growth or lesion visible over the surface of the cervix. There was minimal blood-tinged discharge seen coming through the cervical os. On per vaginal examination, the uterus was anteverted, atrophic, and mobile with bilateral fornixes free. All her routine investigations including complete blood counts, blood sugars, liver and renal function tests, and viral markers for HIV, and hepatitis B and C were negative and within normal limits. Pap smear report revealed negative for intraepithelial lesion or malignancy. On transvaginal sonography, the uterus was atrophic with an endometrial thickness of 7–8 mm. Bilateral ovaries were atrophic. Her magnetic resonance imaging of the abdomen and pelvis revealed a normal-sized uterus with an endometrial thickness of 7 mm. An irregularly enhancing lesion in the posterior fundic region of endometrium, showing diffuse restriction with an ill-defined junctional zone (indicating invasion of the myometrium), suggestive of endometrial malignancy. The patient was planned for endometrial and cervical biopsy, and histopathological reports revealed cervical intraepithelial neoplasia-III (CIN-3) of the ectocervix with endocervical and endometrial curetting showing features of SCC. Hence, with the provisional differential diagnosis of endometroid adenocarcinoma with squamous metaplasia, or cervical SCC, the patient was planned for staging laparotomy with modified radical hysterectomy and bilateral pelvic lymphadenectomy.

The intraoperative findings included an atrophic uterus with bilateral atrophic ovaries and fallopian tubes [Figure 1]. The left fundal region of the uterus including the medial end of the fallopian tube and ovary appeared unhealthy with some friable deposits over them. There were no ascites and no peritoneal and omental deposits. There was no pelvic or para-aortic lymphadenopathy. Hence, peritoneal washings were taken with 100 mL of normal saline, followed by modified radical hysterectomy and bilateral pelvic lymphadenectomy. On opening, the left-sided broad ligament one solid lesion separate from the left lateral border of the uterus of size 0.5 cm × 1 cm was identified and removed. Bilateral pelvic lymphatic chains grossly appeared healthy but were removed for histopathological examination. The uterus with cervix with bilateral tubes and ovaries including the mass were removed along with the bilateral uterine arteries from their origin from internal iliac arteries, followed by infracolic omentectomy and peritoneal biopsies. Grossly, the bilateral paracolic gutters, under the surface of the diaphragm, liver, intestines, and peritoneum had no visible deposits.

On gross examination, the cervix measured 3 cm × 2 cm × 1 cm with an irregular mucosal surface and thickened wall, and the uterus measured 5 cm × 4 cm × 4.2 cm with an endometrial cavity having a distorted proliferative growth measuring 4 cm × 3 cm, infiltrating more than 50% of myometrium. The bilateral ovaries and tubes were grossly unremarkable. The vaginal cuff of 1.5 cm × 1.5 cm × 0.8 cm also appeared normal. The bilateral pelvic lymphatic chains and uterine arteries appeared healthy on gross examination.

On microscopic examination, sections of the cervix revealed severely dysplastic stratified squamous epithelial

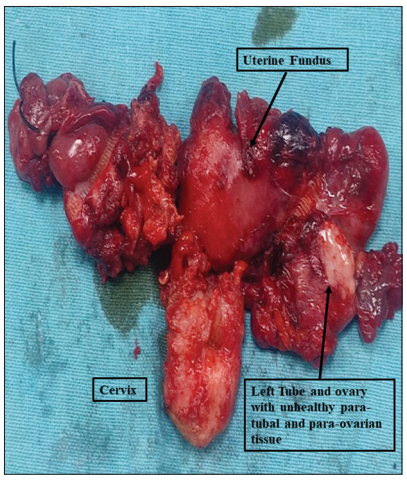

Figure 1: Gross specimen of the uterus with cervix with bilateral fallopian tubes and ovaries

lining with infiltrating tumor nests composed of atypical squamous epithelium displaying moderate pleomorphism and brisk mitotic activity. Lymphovascular space invasion was present with the depth of stromal invasion >5 mm. Sections from the isthmus and endomyometrium showed surface atypical squamous cells lining the entire uterine cavity. The tumor cells infiltrating into the myometrium showed similar morphology to that of the cervical tumor and involved >50% of the myometrium. Sections from both ovaries and fallopian tubes were histologically within normal limits. Sections from the left paratubal and paraovarian tissue revealed the presence of tumor deposits. Sections from the vaginal cuff also revealed dysplastic epithelium-lined fibrocollagenous tissue with infiltrating islands of tumor cells similar to the cervix. Sections from the omentum, peritoneum, pelvic lymphatic chains, and uterine arteries were all negative for tumor cells. The isolated solid lesion taken out from the left broad ligament showed the presence of tumor cells similar to that of the cervix [Figure 2a-f]. Hence, on gross and microscopic examination, the final diagnosis of superficially spreading SCC of the cervix with involvement of endometrium, myometrium, vagina, and paratubal and paraovarian tissues was made with the histological staging of $_pT_{3a}N_xM_x$. Immunohistochemistry with p16 was additionally conducted to validate the findings, which further supported the diagnosis of cervical SCC, most likely attributed to HPV infection [Figure 3].

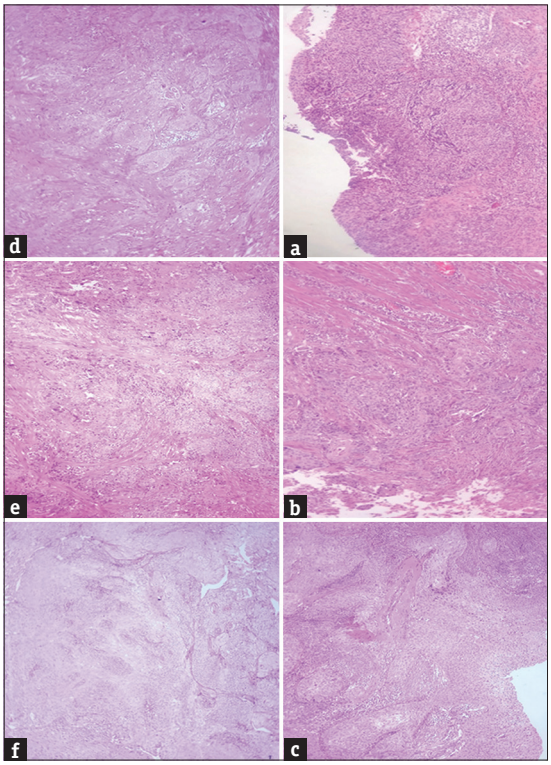

Figure 2: (a) Cervix showing full-thickness dysplasia (cervical intraepithelial neoplasia III) with the invasive focus of squamous cell carcinoma (SCC) (×100); (b and c) Endometrium showing ulcer-proliferative growth with microscopic features of SCC (×100); (d) Vaginal cuff showing full-thickness dysplasia (differentiated VIN III) with invasive SCC (×100); (e) Paratubal and paraovarian deposits of SCC (×100); (f) Pelvic soft-tissue showing deposits of SCC (×100)

The patient withstood the surgery well and was started on adjuvant chemoradiotherapy with injection cisplatin 40 mg/m^2 weekly for 5–6 weeks along with 25 cycles of external beam radiation therapy at a dose of 50 Gray – 5 days a week. The patient is tolerating chemoradiotherapy well and is on regular follow-ups.

Discussion

Superficially spreading SCC of the cervix is a very rare entity with very few cases reported in the literature with the majority of them mainly limited to the endometrium of the uterus. The present case briefs the findings of a superficially spreading SCC of the cervix in a postmenopausal woman with tumor cells spreading to the endometrium, myometrium, paratubal, paraovarian, and vaginal margins without involving the pelvic and para-aortic lymph nodes. Similar studies reported the involvement of the endometrial, focal myometrial, bilateral tubal mucosal, fimbrial, and bilateral ovaries by superficially spreading SCC of the cervix without involvement of pelvic and para-aortic lymph nodes.[4,10] Another case report observed the superficial spread of SCC of the cervix to the fallopian tubes.[11] Similar to our report, a study reported the superficial spread of SCC of the cervix to the entire endometrium up to the fundus, salpinx, and vagina.[12]

Superficially spreading cervical SCC is characterized by the continuity of the lesion with extension mainly

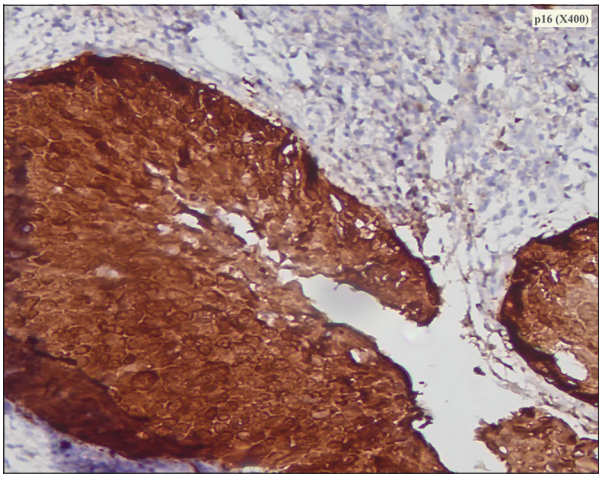

Figure 3: p16 immunohistochemistry showing block-like positivity in the invasive carcinoma island in cervix suggestive of primary squamous cell carcinoma in the cervix (×400)

to the endometrium and rarely extends to ovarian or tubal structures.[6,13] The concomitant occurrence of primary endometrial SCCs must be ruled out.[6] It is very important to differentiate primary endometrial SCC from the endometrial spread of SCC of the cervix, as the prognosis and management vary. This can be done using the following pathological criteria recommended by Fluhmann:[14] (a) lack of coexisting endometrial adenocarcinoma or primary cervical SCC; (b) the absence of connection between the endometrial tumor and cervical squamous epithelium; or (c) the absence of connection between existing cervical *carcinoma in situ* and the endometrial malignancy.[5] In the present case, a continuity was observed between the cervical lesion and lesions of the endometrium, paratubal, paraovarian, and vagina, indicating the superficial spread of SCC to these sites.

This rare variant is common in women over 50 years of age, and the most common presenting complaint is bleeding from the genital tract.[9]

The exact pathogenesis and prognosis of superficially spreading cervical SCC are not clear and hence, more clinical cases are required to formulate clinical practice guidelines for its management.[6] Furthermore, because of its rarity, there are no conclusive and optimal treatments for this disease. Based on the FIGO 2018 recommendations, a simple hysterectomy can be considered for SCC *in situ* or stage IA1 SCC without nodal involvement and an isolated focus of carcinoma *in situ* in the endometrium.[6] Studies have shown that the survival rate for superficial spreading SCC is poorer compared to invasive cervical SCC.[5]

Conclusion

Superficially spreading cervical SCC is a seldom encountered condition whose underlying causes remain unidentified. Research indicates a correlation with HPV infection and positive p16 staining. However, due to its infrequency, definitive treatment protocols for this carcinoma have yet to be established. Moreover, it has not been incorporated into the 2020 WHO Classification of Female Genital Tract Tumors or the FIGO cervical cancer staging system. Thus, in cases where SCC cells are detected in endometrial and cervical biopsies, it is crucial to maintain a suspicion of superficially spreading cervical SCC.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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