

Unusual form of squamous cell carcinoma of the cervix extending *in situ* into the endometrium: Three case reports and review of literature

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ABSTRACT

Squamous cell carcinoma of the cervix is the most common gynecological malignancy in India. Direct extension from a cervical growth can involve the uterine corpus, but a superficial spread, without invasion of the underlying myometrium, is uncommon. We report three cases of squamous cell carcinoma of the cervix, with superficial extension to the whole endometrial cavity, by expansile intraepithelial growth. Clinically, two of our cases presented with pyometra and one with vaginal bleeding and discharge. The tumor had spread superficially into the entire endometrial cavity, up to the fundus, replacing the columnar epithelium totally. This was a rare phenomenon, with fewer than 30 cases reported in literature.

Key words: Cervical intraepithelial neoplasia, cervix, endometrium, superficial spreading

INTRODUCTION

Squamous cell carcinoma of the cervix is the most common gynecological malignancy in India. Recognized patterns of the local tumor spread include direct invasion of the parametrium and endometrial cavity, but a superficial spread without invasion of the underlying myometrium is uncommon.^[1] We report three interesting cases of squamous cell carcinoma of the cervix, in which there was replacement of the entire endometrial surface by an intraepithelial squamous cell carcinoma along with a review of literature. This is a very rare phenomenon, with fewer than 30 cases reported so far in the literature.

CASE REPORTS

Case 1

A 65-year-old female (Para 5, Live 4, Abortion 1), ten-year

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post-menopausal was investigated for an abnormal Papanicolaou (PAP) smear. Clinically, there was mild cervical stenosis with pyometra. There was no other significant medical history. A punch biopsy confirmed the diagnosis of an infiltrating squamous cell carcinoma of the cervix, non-keratinizing, of a large cell type. With the clinical diagnosis of cervical carcinoma, Stage I-B, Wertheim's hysterectomy was performed. The uterus weighed 70 g and revealed cervical stenosis, but no obstruction. On gross examination, the uterus and cervix measured 8 x 5 x 4 cm. The cervix was completely replaced by gray-white circumferential growth. The endometrial cavity was dilated and the endometrial surface had a gray-white corrugated appearance. Microscopically, the cervical lesion consisted of squamous cell carcinoma, moderately differentiated and extending up and over the endometrial surface of the lower uterine segment as carcinoma *in situ*, without involvement of the underlying myometrium. The tumor extended up to the right parametrium, but the vaginal cuff, both fallopian tubes, and ovaries were unremarkable.

Case 2

A 60-year-old female (Para 2, Live issues 2), five years postmenopausal, presented with a four-month history of vaginal bleeding and discharge. The pelvic examination revealed an enlarged uterus, with a firm mass occupying the cervix. A cervical biopsy revealed invasive squamous cell carcinoma, of a large cell non-keratinizing type. A radical

vaginal hysterectomy with pelvic and para-aortic lymph node dissection was performed. A 140 g uterus revealed a gross cervical lesion. The endometrial cavity was roughened with gray-white patches. Microscopically, the cervical lesion again revealed features of squamous cell carcinoma, of the large cell non-keratinizing type, extending up and lining the endometrial surface. There was no evidence of the remaining normal endometrial glands and stroma. The entire endometrial surface was totally replaced with squamous cell carcinoma *in situ*, with few small foci of microinvasion, associated with extensive inflammatory cell infiltrate. The pelvic and para-aortic lymph nodes were negative for metastasis.

Case 3

A 49-year-old female (Para 4, Live issues 4) presented with post-menopausal bleeding since the last two months, associated with foul smelling discharge. She also gave a history of burning micturition since the last one month. The patient had been menopausal for the past five years, was married at the age of 15, and had four full-term spontaneous vaginal deliveries. Her first child was delivered at the age of 18 years. There was no past medical or surgical history that was significant. Pelvic examination revealed a firm cervix, flushed with vagina. A cervical punch biopsy was performed, which revealed squamous cell carcinoma of the cervix, non-keratinizing, of large cell type. The patient underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy, and the specimen was submitted for histopathological evaluation. Gross examination of the specimen revealed a slightly bulky uterus measuring 18 x 14 x 8 cm. The external surface of the uterus appeared smooth. On sectioning of the specimen, a superficial yellowish growth was seen extending from the endocervical canal to the fundus of the endometrial cavity. Microscopically, malignant squamous cells were seen extending superficially and continuing from the cervix lip to the fundus of the uterus [Figure 1]. No vascular or lymphatic invasion was noted. The vaginal cuff also showed extension of squamous cell carcinoma in a superficial manner [Figure 2]. The fallopian tubes and ovaries were free of tumor spread.

DISCUSSION

Squamous cell carcinoma of cervix is the most common tumor of the female genital tract, comprising 70-78% of the cervical malignancies.^[2] Carcinoma of the cervix generally spreads upward to the parametrium, and through the lymphatic invasion to the uterine wall. The presence of invasive squamous cell carcinoma of the cervix, associated with squamous cell carcinoma *in situ* in the endometrium, suggests a superficial spread or a concomitant carcinoma in the endometrium. Primary squamous cell carcinoma may arise through the process of squamous metaplasia, as proposed by Baggish and Woodruff.^[3]

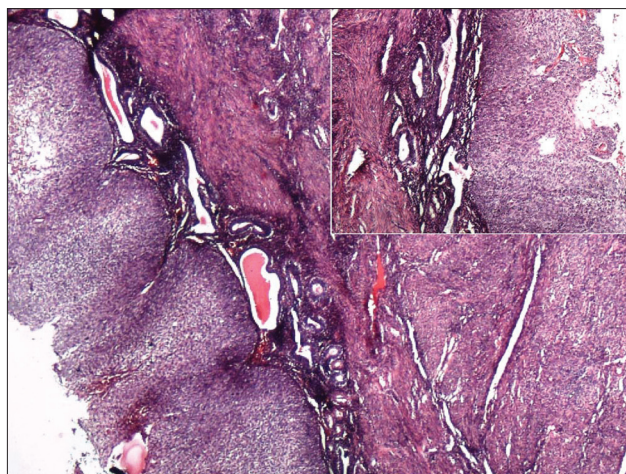


Figure 1: A photomicrograph of the endometrium showing total replacement by intraepithelial squamous cell carcinoma (H and E; x40). Inset shows superficial carcinoma *in situ* covering the normal endometrial glands, without myometrial invasion (H and E; x100)

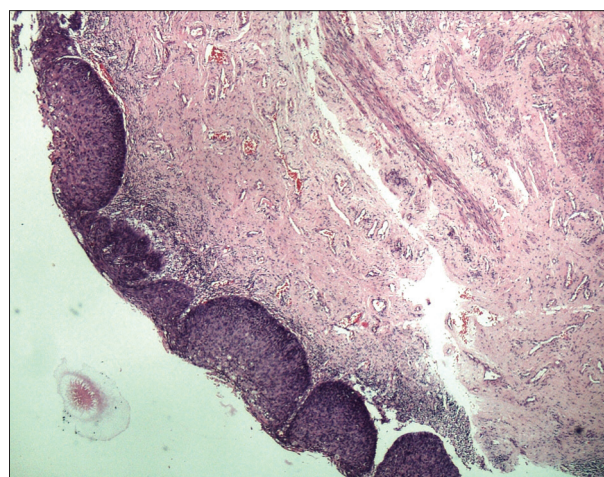


Figure 2: A photomicrograph showing squamous cell carcinoma *in situ* involving the entire vagina (H and E; x40)

To be accepted as primary carcinoma of the endometrium, the tumor must satisfy the criteria established by Fluhmann and modified by Kay.^[4,5] These criteria are: No coexistent endometrial adenocarcinoma, no demonstrable connection between the endometrial tumor and the stratified squamous epithelium of the cervix, and no primary cervical carcinoma. Pyometra, non-specific and specific endometritis, tuberculosis, syphilis, vitamin A deficiency, irradiation, foreign body, including intrauterine devices (IUDs), chemical agents, and exogenous and endogenous estrogens have been mentioned as being associated with or as precursors of this type of lesion.

More commonly squamous cell carcinoma of the endometrium can occur by direct extension from carcinoma of the cervix. The common pattern of uterine corpus involvement by cervical cancer is through deep myometrial penetration or via lymphatic dissemination. However, the superficial spread of *in situ* or invasive squamous cell carcinoma of

the cervix over the contiguous endometrial surface may occur in rare instances. The intrauterine spread of cervical carcinoma in the endometrium may be evident as whitish patches, on gross inspection, a condition called 'cake icing' or 'Zukerguss' carcinoma, wherein the superficial squamous tumor sweeps over or replaces the entire endometrium.^[1] Such an involvement was seen in all of our cases. Such a lesion may involve the entire endometrial cavity and may extend into the tubal mucosa, fimbria, and ovary.

The tumor appeared more often in the older age group. Various predisposing factors, such as, early marriage, early first sexual intercourse, and multiparity were seen in one of our patients as well. Cervical stenosis and subsequent pyometra could have a promoting effect for surface propagation of cervical cancer.

An extensive survey of the literature revealed 26 reported cases of cervical carcinoma with endometrial surface involvement; of these 26 cases presented by various authors, nine cases were of carcinoma *in situ*,^[1,6-8] two cases of microinvasive carcinoma,^[2,6] and 15 cases were of invasive cervical carcinoma.^[6,9-14] In three cases, the fallopian tube was also involved, in direct continuity with the cervical and endometrial lesions.^[6,10] In four cases, the bilateral ovaries were also involved.^[1,8,11,14] In addition, two cases showed an extensive superficial spread to almost the entire genital tract, with associated endometrial stromal sarcoma.^[11] Gupta *et al.* reported a case of superficial endometrial spread and pointed out that this condition may be followed by radiation therapy.^[7] These studies suggested a need for more cytological and histological studies on patients receiving radiation therapy previously. However, there was no such past medical or surgical history in the present cases. The present cases showed the endometrium lined with malignant squamous epithelium, with foci of microinvasion into the surrounding stroma.

It is still difficult to determine the optimal treatment; whether such lesions can be safely treated by simple hysterectomy or they require radical hysterectomy and pelvic lymphadenectomy, still needs to be resolved. As reports on unusual forms of superficial spreading squamous cell carcinoma of the cervix have been primarily limited to case series, and the data are limited, the prognostic significance is uncertain.

Superficial spreading squamous cell carcinoma of the cervix is a rare phenomenon, with fewer than 30 cases reported in the literature, and guidelines for the management of these cases have not been determined yet. The International Federation of Gynecology and Obstetrics (FIGO) staging system has ignored

such an entity, leading to the fact that all these cases will be in stage IB or higher. It is hoped that the increase in number of cases that have been reported will help in recognition of the pathogenesis of this unusual entity.

REFERENCES

1. Agashe SR, Kulkarni MP, Momin YA, Sulhyan KR. Superficial extension of squamous cell carcinoma *in situ* of cervix involving endometrium, bilateral fallopian tubes and ovaries: A case report. *Indian J Pathol Microbiol* 2007;50:375-7.
2. Tan GC, Isa MR, Ng SP, Jamil YM. Unusual form of superficial spreading microinvasive squamous cell carcinoma of uterine cervix involving the endometrium of uterus. *J Obstet Gynecol Res* 2004;30:363-7.
3. Baggish MS, Woodruff JD. The occurrence of squamous epithelium in the endometrium. *Obstet Gynecol Surv* 1967;22:69-115.
4. Fluhmann CF. Squamous epithelium in the endometrium in benign and malignant conditions. *Surg Gynecol Obstet* 1928;46:309-16.
5. Kay S. Squamous-cell carcinoma of the endometrium. *Am J Clin Pathol* 1974;61:264-9.
6. Kanbour AI, Stock RJ. Squamous cell carcinoma *in situ* of the endometrium and fallopian tube as superficial extension of invasive cervical carcinoma. *Cancer* 1978;42:570-80.
7. Gupta S, Gupta IM, Tiwari PV. *In-situ* carcinoma of the uterine cervix showing superficial endometrial spread. *Acta Obstet Gynecol Scand* 1979;58:507-8.
8. Pins MR, Young RH, Crum CP, Leach IH, Scully RE. Cervical squamous cell carcinoma *in situ* with intraepithelial extension to the upper genital tract and invasion of tubes and ovaries: Report of a case with human papilloma virus analysis. *Int J Gynecol Pathol* 1997;16: 272-8.
9. Schmitt K, Schäfer A. Intraepithelial spread of the squamous cell carcinoma of the uterine cervix into the endometrium. A contribution to the question of a surface spread of the cervical carcinoma. *Z KrebsforschKlinOnkol Cancer Res Clin Oncol* 1977;89:45-51.
10. Sandhyamani S, Seth HN, Verma K. Intraepithelial involvement of endometrium, fallopian tube and vagina by cervical carcinoma. *Indian J Pathol Microbiol* 1983;26:299-303.
11. Motoyama T, Watanabe H. Squamous cell carcinoma of the cervix with extensive superficial spreading to almost whole genital tract and associated with endometrial stromal sarcoma. *Acta Pathol Jpn* 1988;38:1445-52.
12. Fadare O. Dysplastic Ichthyosis uteri-like changes of the entire endometrium associated with a squamous cell carcinoma of the uterine cervix. *Diagn Pathol* 2006;1:8.
13. Adler F, Rabban JT, Yeh BM, Qayyum A, Chen L-may, Coakley FV. Superficial endometrial spread of squamous cell cervical carcinoma: A diagnostic challenge at magnetic resonance imaging. *J Comput Assist Tomogr* 2007;31:247-50.
14. Gungor T, Altinkaya SO, Ozat M, Akbay S, Mollamahmutoglu L. Unusual form of superficial spreading squamous cell carcinoma of cervix involving the endometrium, bilateral tubes and ovaries: A case report with literature review. *Arch Gynecol Obstet* 2010;283:323-7.

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