Primary Endometrial Squamous Cell Carcinoma
In Situ
Report of a rare disease

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ABSTRACT: Squamous cell carcinoma (SCC) of the endometrium, whether primary or secondary to cervical cancer, is a rare entity. Primary endometrial squamous cell carcinoma in situ is even more uncommon; it usually occurs in postmenopausal women and has a strong association with pyometra. We report a 60-year-old multiparous postmenopausal woman who presented to the Hakeem Abdul Hameed Centenary Hospital, New Delhi, India, in May 2014 with a lower abdominal swelling corresponding in size to a pregnancy of 26 gestational weeks and vaginal discharge of one year’s duration. A total abdominal hysterectomy with a bilateral salpingo-oophorectomy was performed, which revealed an enlarged uterus with pyometra. Histopathology showed that the entire endometrial lining had been replaced with malignant squamous cells without invasion of the myometrium. Immunohistochemistry revealed that the tumour cells were positive for p63 with a high Ki-67 labelling index. No adjuvant therapy was required and the patient was disease-free at a seven-month follow-up.

Keywords: Squamous Cell Carcinoma; Endometrium; Pyometra; Case Report; India.

Cancer of the endometrium is a common gynaecological malignancy in the developed world and is second only to cervical cancer in the developing world. Most endometrial cancers are adenocarcinomas. Primary endometrial squamous cell carcinomas (PESCCs) are extremely rare although the exact prevalence is not yet known. The majority of squamous cell carcinoma (SCC) cases represent an extension from the cervix, where SCC spreads superficially to the inner surface of the uterus and replaces the endometrium with carcinoma cells. However, whether primary or secondary, endometrial SCC is rare and PESCC in situ even rarer.

Case Report
A 60-year-old multiparous postmenopausal woman presented to Hakeem Abdul Hameed Centenary Hospital, New Delhi, India, in May 2014 with abdominal swelling and vaginal discharge which had been occurring for the past year. There was no history of vaginal bleeding, the obstetric history was uneventful and the patient had been postmenopausal for 16 years. An abdominal examination revealed a soft and nontender lump corresponding to the size of a pregnancy of 26 gestational weeks. A speculum examination showed a healthy cervix. Ultrasonography revealed a mass in the pelvic region measuring 14.2 x 10.8 cm, suggestive of a postmenopausal simple ovarian cyst. Contrast-enhanced computed tomography of the lower abdomen showed a large pelvic-abdominal cystic lesion, likely of left adnexal origin. A Papanicolaou smear of the cervix was suggestive of atrophy and was negative for intraepithelial lesions or invasive cancers.

An exploratory laparotomy and total abdominal hysterectomy with bilateral salpingo-oophorectomy...
was performed. On gross examination, the uterus was enlarged and the uterine cavity was filled with approximately 1,500 mL of pus. The inner surface of the cavity had a slightly irregular appearance [Figure 1]. The cervix had thinned but showed no growth.

Microscopy of multiple sections from different areas of the uterine wall revealed that the entire endometrial lining had been replaced by sheets of atypical squamous cells with marked pleomorphism and bizarre forms [Figure 2]. The changes were limited to the epithelial lining and extensive sampling did not reveal any invasion into the myometrium. In view of the chronic pyometra, the presence of ichthyosis uteri was suspected but samples taken from multiple sections did not yield evidence of the condition. Despite extensive sampling, no evidence of normal endometrial glandular epithelium was found. Sections from the cervix did not show any abnormalities and there was no evidence of atypia or dysplasia. Both ovaries and the myometrium were unremarkable. Positive immunohistochemical staining for p63 confirmed the squamous nature of the lesion and a high Ki-67 labelling index was noted [Figure 3]. A diagnosis of PESCC in situ was made. The patient was not given any adjuvant therapy and was disease-free during the seven-month follow-up period.

Discussion

Endometrial SCC usually occurs in postmenopausal women (mean age: 67 years). The condition has been strongly associated with pyometra, cervical stenosis, multiparity and chronic inflammation. Clinically, the majority of patients present with vaginal bleeding. Endometrial SCC usually originates from the uterine cervix and extends in a superficial spreading pattern. An extensive review of the literature by Marwah et al. revealed 26 cases of cervical carcinoma with endometrial surface involvement; Ishida et al. reported two more cases the following year. In all of these cases, the women were over the age of 50 years and presented with vaginal bleeding.

PESCC is defined as a primary carcinoma of the endometrium composed of squamous cells with varying degrees of differentiation. Although a few reports of PESCC are available in the literature, the prevalence of this condition is unknown. While the exact pathogenesis is unclear, the cellular origin of PESCC has been proposed to be “reserve or stem cells located between the glandular basement membrane and the endometrial columnar cell layer, squamous metaplasia of the normal endometrium, or heterotopic cervical tissue.” Further research supports this finding. Human papilloma virus is known to have a definite role in the pathogenesis of SCC of the uterine cervix; however, its role in endometrial SCC is still to be determined.

In cases of PESCC, it is important to exclude cervical SCC extension into the endometrium and squamous differentiation of an endometrioid adenocarcinoma. It is also essential to differentiate PESCC from endometrial SCC involvement based on the following strict pathological criteria recommended by Fluhmann: (1) no evidence of a coexisting endometrial adenocarcinoma or primary cervical SCC; (2) no connection between the endometrial tumour and squamous epithelium of the cervix; or

**Figure 1:** Cut-open hysterectomy specimen showing the greyish-yellow irregular uterine cavity of a patient with primary endometrial squamous cell carcinoma *in situ*. No cervical growth was seen.

**Figure 2A & B:** Haematoxylin and eosin stains at (A) x40 and (B) x400 magnification showing extensive replacement of the entire endometrial lining by sheets of atypical squamoid cells with marked pleomorphism in a patient with primary endometrial squamous cell carcinoma *in situ*. No invasion of the myometrium was seen.

**Figure 3A & B:** Immunohistochemistry stains at x100 magnification showing (A) tumour cells positive for p63 and (B) a high Ki-67 labelling index in a patient with primary endometrial squamous cell carcinoma *in situ*.
The labelling index has also been reported, demonstrating the aggressive and malignant nature of the lesion. Lee et al. found a positive immunoreactivity for the cytokeratin 7, p63 and p16INK4a proteins, but not for cytokeratin 20 or the oestrogen and progesterone receptors. As a prognostic indicator of PESCC, the role of these receptors is still uncertain; however, lack of oestrogen cannot be completely ruled out as an aetiologcal factor since most patients diagnosed with PESCC are postmenopausal.

The prognosis for patients with SCC depends mainly on the stage of the tumour. PESCC has been reported to show a poorer prognosis than endometrioid carcinomas. Management for this condition usually consists of a surgical hysterectomy with adnexectomy and radiotherapy.

**Conclusion**

Few cases of PESCC have been reported in the literature. As the disease usually presents with vaginal bleeding and is most commonly seen in postmenopausal women, PESCC should be considered...
in the differential diagnosis for these patients, despite its rarity. The exact pathogenesis is unclear and diagnosis is based on strict pathological criteria. This report presents a case of PESCC in situ in a 60-year-old multiparous postmenopausal woman with pyometra and without invasion of the myometrium.

References