

# Primary Endometrial Squamous Cell Carcinoma *In Situ*

## Report of a rare disease

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### سرطان الخلايا الحرفية الأولي في موقع بطانة الرحم تقرير تشخيص نادر

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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.

**المخلص:** سرطان الخلايا الحرفية (SCC) لبطانة الرحم، سواء كان أولي أو ثانوي لسرطان عنق الرحم، نادر الحدوث. وسرطان الخلايا الحرفية الأساسي الناشيء في موقع بطانة الرحم نفسه أكثر ندرة. وعادة ما يحدث في النساء بعد سن اليأس، وله علاقة قوية مع تقيح الرحم. نعرض حالة امرأة في سن اليأس، متعددة الولادات تبلغ من العمر 60 عاما قدمت إلى مستشفى الذكرى المئوية لحكيم عبد الحميد، نيودلهي، الهند، مايو 2014 ومعها تورم أسفل البطن يشابه حمل 26 أسبوعا وإفرازات مهبلية لمدة سنة واحدة. تم إجراء استئصال كلي للرحم مع قناتي فالوب والمبيضين، وكان الرحم متضخما مع تقيح وأظهر التشريح أنه قد تم استبدال خلايا بطانة الرحم بأكملها بخلايا حرفية خبيثة دون انتشار إلى النسيج العضلي. وكشف فحص النسيج المناعي أن الخلايا السرطانية كانت ايجابية لـ p63 مع ارتفاع قياس مؤشر Ki-67. لم يكن العلاج المساعد مطلوباً وأصبحت المريضة خالية من الأمراض عند متابعتها بعد سبعة أشهر.

**مفتاح الكلمات:** خلايا السرطان الحرفية؛ بطانة الرحم؛ تقيح الرحم؛ تقرير حالة؛ الهند.

CANCER OF THE ENDOMETRIUM IS A common gynaecological malignancy in the developed world and is second only to cervical cancer in the developing world.<sup>1</sup> 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.<sup>2</sup> 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 non-tender 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



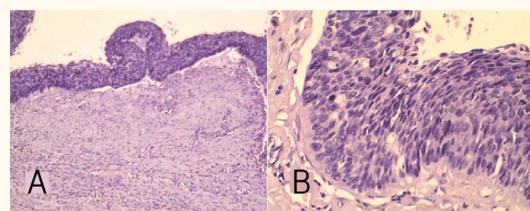
**Figure 1:** Cut-open hysterectomy specimen showing the greyish-yellow irregular uterine cavity of a patient with primary endometrial squamous cell carcinoma *in situ*. No cervical growth was seen.

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).<sup>2</sup> The condition has been strongly associated with *pyometra*, cervical *stenosis*, multiparity and chronic inflammation.<sup>2</sup> Clinically, the majority of patients present with vaginal bleeding. Endometrial SCC usually originates from the uterine cervix and extends in a superficial spreading pattern.<sup>3</sup> An extensive review of the literature by Marwah *et al.* revealed 26 cases of cervical carcinoma with

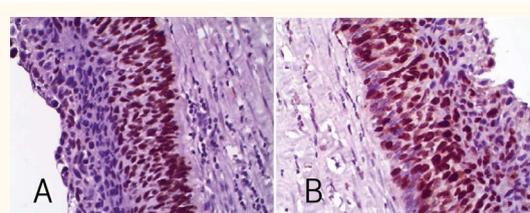


**Figure 2A & B:** Haematoxylin and eosin stains at (A) x40 and (B) x400 magnification showing extensive replacement of the entire endometrial lining by sheets of atypical squamoid cells with marked pleomorphism in a patient with primary endometrial squamous cell carcinoma *in situ*. No invasion of the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

endometrial surface involvement; Ishida *et al.* reported two more cases the following year.<sup>3,4</sup> In all of these cases, the women were over the age of 50 years and presented with vaginal bleeding.<sup>3,4</sup>

PESCC is defined as a primary carcinoma of the endometrium composed of squamous cells with varying degrees of differentiation.<sup>5</sup> 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.”<sup>6</sup> Further research supports this finding.<sup>7-9</sup> 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.<sup>6</sup>

In cases of PESCC, it is important to exclude cervical SCC extension into the endometrium and squamous differentiation of an endometrioid adenocarcinoma.<sup>6,10</sup> 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 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*.

**Table 1:** Comparative analysis of cases of endometrial squamous cell carcinoma *in situ* in the literature

Author and year of report	Patient age in years	Clinical presentation	Gross findings	Microscopy findings	Associated pathology
Kairys <i>et al.</i> <sup>16</sup> 1964	57	Asymptomatic pelvic mass which appeared 3.5 years after undergoing apparently successful radiation therapy for stage II SCC of the cervix	Multiple myomas with replacement of the endometrium by a pyogenic membrane	Endometrial SCC <i>in situ</i>	Multiple leiomyomas with <i>pyometra</i>
Radhika <i>et al.</i> <sup>13</sup> 1993	50	Complete prolapse of the uterus	Normal uterine cavity with wall thickness of 1.3 cm	PESCC <i>in situ</i>	Squamous metaplasia of the surface mucosal lining and involvement of some of the superficial glands by SCC <i>in situ</i>
Mitchell <i>et al.</i> <sup>14</sup> 1999	65	Vaginal bleeding	Haemorrhagic and granular endometrium	Endometrial SCC <i>in situ</i>	Extensive squamous metaplasia of the endometrium and <i>in situ</i> carcinoma of the cervix uteri
Zidi <i>et al.</i> <sup>15</sup> 2003	75	Pelvic pain and vaginal discharge	Thickened and epidermalised endometrium with <i>pyometra</i>	PESCC <i>in situ</i>	Extensive squamous metaplasia of the endometrium with foci of dysplasia and <i>pyometra</i>
Pailoor <i>et al.</i> <sup>17</sup> 2014	52	Pelvic pain	Widened endometrial cavity lined by irregular, shaggy, membrane-like material	PESCC <i>in situ</i>	Extensive <i>ichthyosis uteri</i>
Present case	60	Abdominal swelling and vaginal discharge	Irregular appearance of the endometrial surface with <i>pyometra</i>	PESCC <i>in situ</i>	<i>Pyometra</i> and replacement of the endometrial lining with atypical squamous cells without invasion of the myometrium

SCC = squamous cell carcinoma; PESCC = primary endometrial squamous cell carcinoma.

(3) no connection between any existing cervical *in situ* carcinoma and the independent endometrial neoplasm.<sup>10</sup> These criteria were later modified by other authors.<sup>11,12</sup> The present case conformed to Fluhmann's criteria and also displayed sequential changes of dysplasia and carcinoma *in situ*, although there were no signs of an invasive carcinoma despite extensive sampling.

To the best of the authors' knowledge, only five cases of PESCC *in situ* have been reported to date [Table 1].<sup>13-17</sup> Radhika *et al.* reported a case of PESCC *in situ* associated with a prolapsed uterus, while Mitchell *et al.* noted an association with the long-term use of intrauterine devices.<sup>13,14</sup> Zidi *et al.* described a case of PESCC *in situ* with extensive squamous metaplasia and dysplasia along with a serous cystadenoma of the right ovary.<sup>15</sup> PESCC *in situ* was also reported by Kairys *et al.*, while a rare case with extensive *ichthyosis uteri* was described by Pailoor *et al.* in a postmenopausal woman with *pyometra*.<sup>16,17</sup>

The role of immunohistochemistry is limited, with most studies demonstrating a mutation of the *p53* tumour suppressor gene.<sup>18,19</sup> A high Ki-67

labelling index has also been reported, demonstrating the aggressive and malignant nature of the lesion.<sup>18</sup> 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.<sup>6</sup> 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 aetiological factor since most patients diagnosed with PESCC are postmenopausal.<sup>6</sup>

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.<sup>18</sup> Management for this condition usually consists of a surgical hysterectomy with adnexectomy and radiotherapy.<sup>2</sup>

## 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.

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