

# Squamous cell carcinoma in situ lining the uterine cavity

J. Anthuenis, J. Baekelandt, C. Bourgain, C. De Rop

*AZ Imelda Hospital, Bonheiden (Belgium)*

## Summary

Cervical intra-epithelial neoplasia is a very common and well-known pathology. However superficial spreading of this lesion is very rare. The authors present a case of a 72-year-old woman with an abdominal mass, who had previously undergone a cervical conisation for a high-grade cervical intra-epithelial neoplasia. Anatomic-pathological examination of the mass showed a large distended fluid-filled uterus with the entire endometrium replaced by a high-grade squamous cell lesion. There were only micro-invasive foci found. The authors performed a literature search in PubMed with the following MeSH-terms: "squamous cell carcinoma" and "endometrium". Other articles were selected out of the references of previously found articles. Only 31 similar cases were found. The presentation of the cases varies extremely and a long-term prognosis is not yet known.

*Key words:* Squamous cell carcinoma; Endometrium; Cervical intra-epithelial neoplasia; Superficial spreading.

## Introduction

Cervical intra-epithelial neoplasia and squamous carcinoma of the cervix are common. Normally squamous carcinoma of the cervix spreads by direct invasion into the parametria. Superficial spreading squamous carcinoma is very rare. In this condition the normal endometrium is replaced by intraepithelial squamous cell carcinoma with or without invasive foci. These lesions are difficult to stage within the FIGO-classification because of the wide spread to the uterus with sometimes only micro-invasive foci.

## Case Report

A 72-year-old woman presented with a distended abdomen. She had been experiencing abdominal discomfort for three to four months. She had no vaginal bleeding or abnormal discharge. Twelve years earlier she had undergone a cervical conisation for a high-grade cervical intra-epithelial neoplasia. This neoplasia had reached the surgical margins. A PAP smear two months after conisation had shown atrophic cells with mild atypia. The patient had neglected follow-up after that.

An abdominal ultrasound showed the presence of an abdominal mass of approximately 17 cm, probably of uterine origin. The CA 125 level was 74 (normal 0-35) kU/L. A CT-scan could not clearly identify the origin of the mass. The preoperative differential diagnosis was a subserosal cystic degenerated uterine fibroma, a proliferative endometrial disorder, or an ovarian cystadenoma. An abdominal hysterectomy with bilateral salpingo-oophorectomy was performed. The mass was confined to the uterus. No cervix was visualized during the surgery. There were only a few fibrotic strands connecting the uterus with the vagina. The vagina was opened and there were no lesions found in the vaginal mucosa.

Pathologic investigation revealed a large distended uterine body with an obliterated isthmus. The myometrial thickness was reduced to a few millimeters. The uterine cavity was filled with a pale brownish clear fluid. Histologically, the endometrium was completely replaced by a high-grade squamous cell lesion, compatible with a cervical intra-epithelial neoplasia with micro-invasive growth (Figures 1-4). Most likely a cervical or isthmus stenosis occurred after the conisation. The cervical intra-epithelial dysplasia spread superficially into the endometrium. The ovaria and fallopian tubes were free of tumor. The patient did not receive any adjuvant therapy after the surgery. Two years after the surgery the patient is still disease-free. Regular follow-up with vaginal cytology shows normal results.

## Discussion

Cervical intra-epithelial neoplasia of the cervix is a well-known entity. Squamous carcinoma of the endometrium is also widely described. The aforementioned case shows a superficial spreading of the cervical intra-epithelial neoplasia to the endometrium. A literature review shows only 31 cases with the same spreading mechanism (Table 1). In the cases where information about the age was described, the patients were all older than 48 years. The most common presenting symptoms were vaginal bleeding or discharge, pyometra or an abdominal mass with abdominal discomfort. Some cases were incidental findings during hysterectomy because of cervical intra-epithelial carcinoma (in situ or invasive). Cervical stenosis was often described. The cervical component could be carcinoma in situ, micro-invasive carcinoma, or invasive cervical carcinoma [1]. Extension of

Revised manuscript accepted for publication October 20, 2014

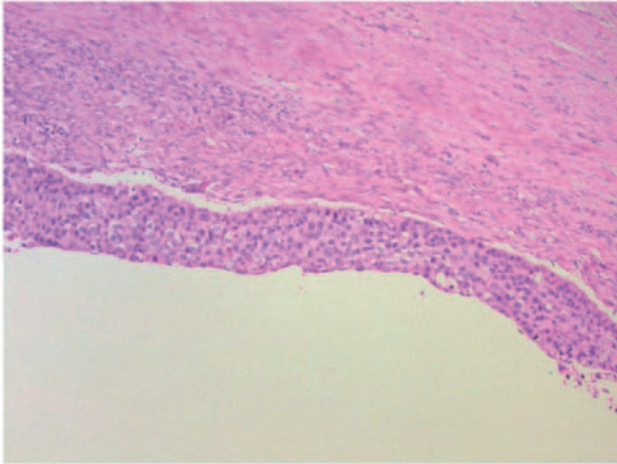


Figure 1. — The lining of the endometrium is completely replaced by squamous epithelium with high-grade cervical intraepithelial neoplasia, resting directly on the myometrium. There is no residual endometrium (HE, x10).

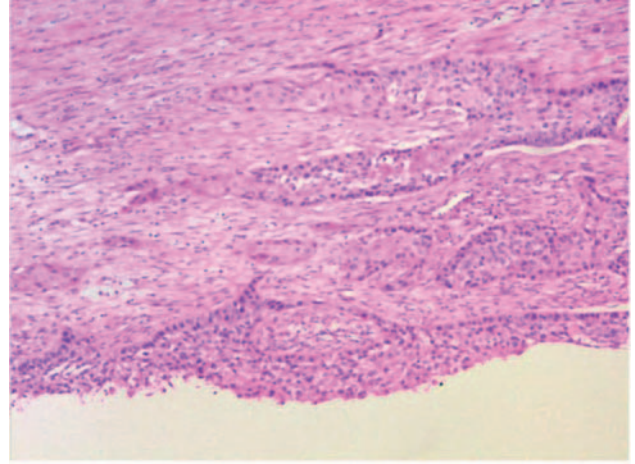


Figure 2. — Minute foci of invasive squamous carcinoma, less than two-mm invasion depth (HE, x10).

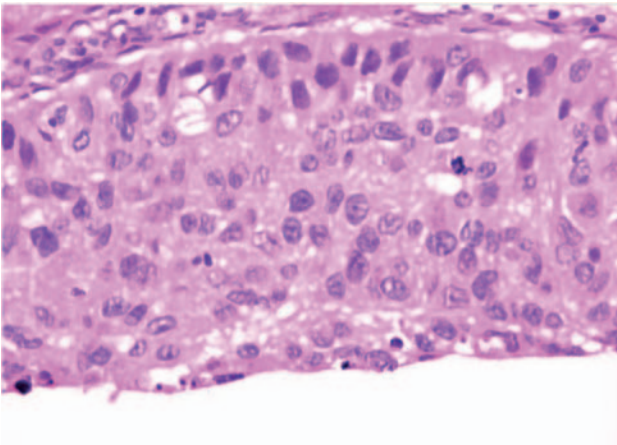


Figure 3. — Severe cytological atypia and mitotic figures are visible throughout the epithelium (HE, x40).

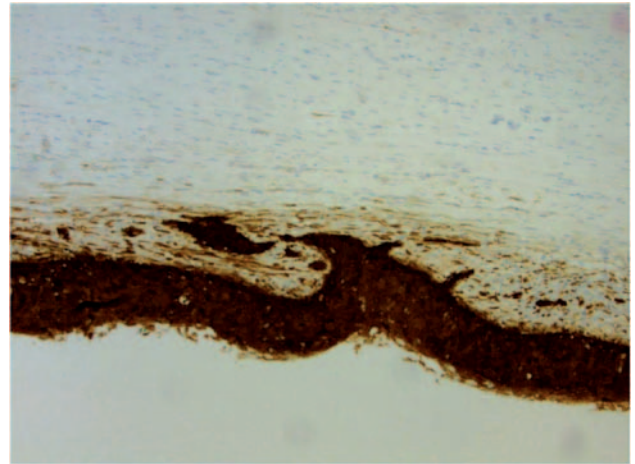


Figure 4. — P16Ink staining: intense homogenous staining in the CIN and micro-invasive component of the tumor.

the cervical intra-epithelial neoplasia involves the endometrium in all cases but can extend further to the fallopian tubes and even the ovaries in a continuous manner [2].

Ishida *et al.* presented two cases of superficial spreading squamous cell carcinoma of the cervix to the endometrium [3]. In those cases there was no invasive growth observed in the endometrium. In addition, a role for CD138 is suggested in the superficial spread by regulating cell-cell interactions.

Radiation therapy of the pelvis was present in the case presented by Gupta *et al.* [4] Another report of superficial spreading cervical squamous carcinoma in situ after pelvic

cobalt therapy was described by Razquin *et al.* [5]. The etiologic role of radiation therapy in superficial spreading of squamous cervical neoplasia has not yet been determined.

Kushima *et al.* [6] described five cases of superficial spreading squamous cell carcinoma. Genetic test on these five cases showed loss of heterozygosity in four out of five cases, suggesting that a unique combination of genetic alterations can lead to superficial spreading of squamous cell carcinoma. These genetic alterations seem to be different from those in invasive carcinoma.

Follow-up data were only present in six out of 28 cases with follow-up ranging from six months up to 4.5 years. All of these six patients were disease-free on follow-up

Table 1. — Literature overview.

Author	Cases	Age	Clinical presentation	Extension of lesion	Follow-up
Our case	1	72	abdominal mass	Cervix (in situ), endometrium (in situ)	2 years
Marwah et al. (1)	3	65	abnormal PAP smear	Cervix (invasive), endometrium (in situ)	NA
		60	postmenopausal bleeding	Cervix (invasive), endometrium (in situ)	NA
		49	postmenopausal bleeding	Cervix (invasive), endometrium (in situ), vagina (in situ)	NA
Gungor et al. (2)	1	53	postmenopausal bleeding	Cervix (invasive), endometrium (micro-invasive), bilateral tubes (in situ), ovaries (in situ)	1 year
Ishida and Okabe (3)	2	64	postmenopausal bleeding	Cervix (invasive), endometrium (in situ)	10 months
		59	postmenopausal bleeding	Cervix (invasive), endometrium (in situ), parametrium (invasive)	6 months
Gupta et al. (4)	1	NA	NA	Cervix (in situ), endometrium (in situ)	NA
Razquin et al. (5)	1	52	vaginal stenosis, pyometra	Cervix (in situ), endometrium (in situ)	NA
Kushima et al. (6)	5	68	genital discharge	Cervix (in situ), endometrium (in situ), left tuba (invasive), left ovary (invasive)	4,5 years
		58	NA	Cervix (in situ), endometrium (in situ)	NA
		72	abdominal mass	Cervix (in situ), endometrium (in situ)	2,5 years
		78	postmenopausal bleeding	Cervix (invasive), endometrium (micro-invasive), vagina (in situ)	NA
		59	abdominal mass, postmenopausal bleeding	Cervix (invasive), endometrium (in situ), left fallopian tube (in situ), left ovary (in situ), vagina (in situ)	NA
Tan et al. (7)	1	70	postmenopausal bleeding	Cervix (in situ), endometrium (micro-invasive)	6 months
Agashe et al. (8)	1	NA	NA	Cervix (in situ), endometrium (in situ), both fallopian tubes (in situ), both ovaries (in situ)	NA
Kanbour and Stock (9)	5	NA	pyometra and cervical stenosis (66% of cases)	Cervix, endometrium (in situ), in one case fallopian tube (in situ)	NA
Pins et al. (10)	1	55	abnormal PAP smear	Cervix (in situ), endometrium (in situ), both fallopian tubes (invasive), both ovaries (invasive)	NA
Motoyama and Watanabe (11)	1	NA	NA	Cervix (invasive), endometrium (invasive)	NA
Quizilbash and DePettrillo (12)	1	NA	NA	Cervix, endometrium, both fallopian tubes	NA
Punnonen et al. (13)	1	NA	NA	Cervix (invasive), endometrium (in situ), one fallopian tube (in situ)	NA
				Cervix (invasive), endometrium (2 cases in situ), 2 cases invasive)	NA
Schmitt and Schafer (14)	4	NA	NA	Cervix (invasive), endometrium (in situ)	NA
Kamalian and Ghafoorzdeh (15)	1	55	NA	Cervix (invasive), endometrium (in situ)	NA
Daniele et al. (16)	1	NA	NA	Cervix (in situ), endometrium (in situ)	NA
Teixeira et al. (17)	1	64	pyometra	Cervix (in situ), endometrium (in situ)	NA

consultation. This suggests a good short term outcome. There are no long-term outcome data and there is still doubt about the metastatic potential of superficial spreading squamous carcinoma.

A cervical stenosis after the initial conisation may be responsible for the late detection of the recurrence and the spread into the endometrium.

## Conclusion

Superficial spreading squamous carcinoma of the cervix is a very rare pathology. The authors present a new case with a disease-free survival two years after hysterectomy without adjuvant therapy. There is very little experience with this pathology. There are no evidence-based treatment guidelines or prognosis predictions. The short-term prognosis seems to be good. Further investigation is needed to determine the long-term outcome.

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Address reprint requests to:  
 J. BAEKELANDT, M.D.  
 A.Z. Imelda Hospital  
 Imeldalaan 9  
 2820 Bonheiden (Belgium)  
 e-mail: jan.baekelandt@imelda.be