



Case Report

Uterine corpus metastasis in stage IA1 squamous carcinoma of the cervix[☆]

A. McCormick^a, P. Cross^b, R.J. Edmondson^{a,b,*}^a Northern Institute for Cancer Research, Newcastle University, UK^b Northern Gynaecological Oncology Centre, Queen Elizabeth Hospital, Gateshead, UK

ARTICLE INFO

Article history:

Received 26 April 2013

Accepted 23 July 2013

Available online 27 July 2013

Keywords:

Cervix cancer

Metastasis

Microinvasive disease

Introduction

The International Federation of Gynecology and Obstetrics (FIGO) defines microinvasive squamous cell carcinoma of the uterine cervix as a microscopic lesion that invades below the basement membrane to a maximum depth of 5 mm, with a horizontal spread not exceeding 7 mm with two subcategories: stage IA1 is a tumour that invades to a depth of 3 mm or less, whereas IA2 is defined as a tumour which invades to a depth of 3 to 5 mm. The purpose of defining microinvasive carcinoma is to identify a group of patients who are not at risk for lymph node metastases or tumour recurrence and who, therefore, may be treated conservatively. With women delaying pregnancy, conservative treatment for microinvasive carcinoma of the cervix is increasingly important for preservation of fertility. We report here a case of uterine corpus metastasis in a patient with FIGO stage IA1 squamous cervical carcinoma of the cervix.

Case report

The patient is a 32-year-old Para 4, who had undergone laparoscopic sterilisation. She was referred to colposcopy due to a finding of severe dyskaryosis on a first abnormal smear. Loop biopsy in June 2009 (25 × 20 × 15 mm in size) showed 2 foci of invasive disease and incompletely excised CIN3. The total dimensions of the invasive foci

were <1 mm deep and 3.5 mm in width and were completely excised. There was no evidence of LVSI. The tumour was therefore graded as a FIGO stage IA1 squamous cell carcinoma. A second loop biopsy was performed in July 2009 in view of the incompletely excised CIN3, and this showed no residual invasive or pre-invasive disease. The case was reviewed by a multidisciplinary team, and no further treatment was recommended, in line with current UK practice.

The patient, however, chose to undergo a hysterectomy for menorrhagia and a laparoscopically assisted hysterectomy was performed in September 2009. Histological examination of the cervix showed no residual pre-invasive or invasive disease. The endocervix and paracervical tissues appeared normal. Given the history, all of the cervix was processed for histology, and the uterine body elsewhere was sampled. The cervix was processed as consecutive parallel blocks. The cervix appeared distorted to the naked eye, but no gross abnormality was seen in the uterus otherwise. However sampling of the endometrium found a single small focus of squamous epithelial dysplasia, giving rise to minimally invasive keratinising squamous carcinoma. The focus of tumour was found in the body of the uterus in the right lateral position and had no direct continuity with the cervix. The focus was entirely superficial and measured 1 mm in transverse dimension and less than 1 mm deep. There was no LVSI and the myometrium appeared normal. Following discussion the attending physicians recommended no further treatment. The patient is undergoing follow up in our unit after the hysterectomy and remains well after four years of follow up (Fig. 1).

Discussion

The purpose of defining stage IA1 cervical cancer is to identify those cancer patients who may safely be managed more conservatively and who have an excellent prognosis. It is generally accepted that FIGO stage IA1 disease can be managed conservatively (Lee et al., 2009).

The incidence of microinvasive cervical cancer has increased over the past few decades and the numbers of patients undergoing conservative treatment are also increasing in response to the apparent low recurrent and metastasis rates in microinvasive disease. However, review of the literature demonstrates emerging evidence for metastasis in stage IA1 cervical cancer. Nagarsheth et al. (2000) described a case of stage IA1 cervical adenocarcinoma with bilateral pelvic lymph node metastases and Elliott et al. (2000) described a case where the tumour had stromal invasion of 0.1 mm with less than 7 mm lateral spread and no capillary space involvement. The patient did however have lymph node metastases and ultimately succumbed to the disease. Argenta

[☆] This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial-No Derivative Works License, which permits non-commercial use, distribution, and reproduction in any medium, provided the original author and source are credited.

* Corresponding author at: NICR, Paul O'Gorman Building, Newcastle University, Framlington Place, Newcastle upon Tyne, NE2 4HH, UK.

E-mail address: richard.edmondson@ncl.ac.uk (R.J. Edmondson).

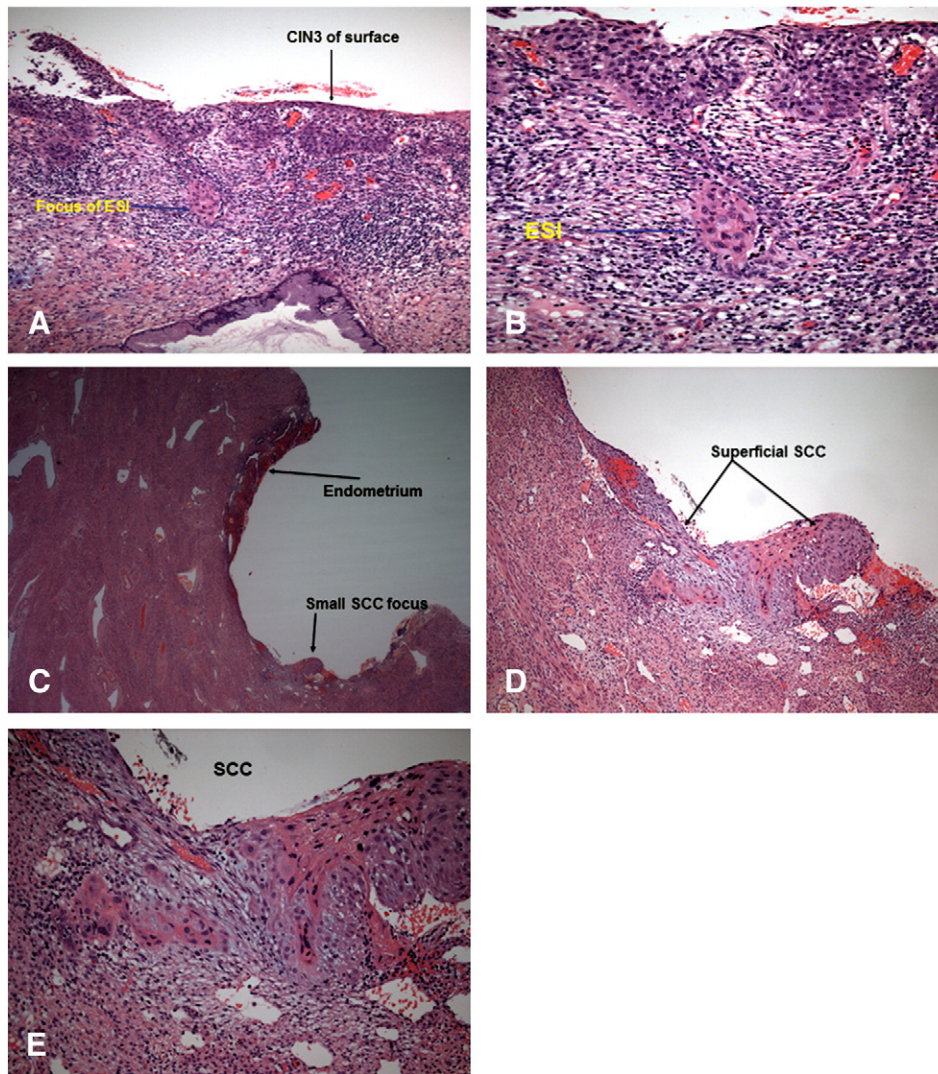


Fig. 1. H&E stained cervical images (A&B) from LLETZ specimen and endometrial (C,D,E) sections of the specimen from hysterectomy. **A** - Cervical epithelium demonstrating CIN3 (black arrow) and a focus of early stromal invasion (blue arrow) (100× magnification). **B** - Early stromal invasion (blue arrow) (400× magnification). **C** - Endometrial section demonstrating small focus of squamous cell carcinoma (SCC) (40× magnification). **D** - Superficial SCC (200× magnification) and **E** (400× magnification).

et al. (2005) reported another case of lymph node metastasis in the setting of multifocal microinvasive squamous cell cervical carcinoma. More recently Yeasmin reported another stage IA1 squamous cell carcinoma with widespread bilateral pelvic lymph node metastases. (Yeasmin et al., 2009) Lee et al. (2006) also reported a case of a 63 year old with <1 mm invasion depth of disease but with supraclavicular lymph node metastasis and Kang et al. (2009) reported a case of stage IA1 squamous cervical carcinoma with invasion of less than 1 mm without lymphovascular involvement but with unilateral ovarian metastasis.

Young et al. (1993) also reported a case of unilateral ovarian Stage IA1 squamous cell carcinoma metastasis in 1993.

This case demonstrates that when the uterus is preserved we must also consider the possibility of a recurrence involving the corpus of the uterus. Such recurrences were previously not seen because all radical treatments treat or remove the uterus. Our case of uterine metastasis of stage IA1 cervical squamous carcinoma adds to the debate about the optimal management of very early cervical cancer. In conservatively managed patients, the risk of uterine corpus metastases and recurrence has

Table 1
Summary of previous reports of metastasis in microscopic cervical cancer.

Cervical cancer diagnosis	Reported metastasis	Reference
IA1 cervical adenocarcinoma	Bilateral pelvic lymph node	Dhingra et al. (2008)
IA1, no capillary space involvement	Lymph node	Elliott et al. (2000)
Multifocal microinvasive squamous cell cervical carcinoma	Lymph node	Gadducci et al. (2013)
IA1 squamous cell carcinoma	Bilateral pelvic lymph node	Kang et al. (2009)
IA1 squamous cervical carcinoma with negative LVSI	Supraclavicular lymph node and lung	Lee et al. (2006)
IA1 squamous cervical carcinoma	Unilateral ovarian	Lee et al. (2009, 1988)
IA2 cervical adeno-squamous carcinoma	Myometrium just underneath the peritoneum and ovarian	Nagarsheth et al. (2000)
IB1	Benign endometrial polyp.	Utsugi et al. (2001)
IA1 cervical adenocarcinoma	vaginal stump recurrence	Young et al. (1993)
IA	GI recurrence	Zenatta et al. (2000)

to be considered. Despite this evidence the outcome significance of endometrial metastasis for a stage IA1 squamous cervical carcinoma is unclear. Other cases of cervical carcinoma metastasis to the uterine corpus have been reported. Zenatta et al. (2000) reported a case of IA2 cervical adenosquamous carcinoma which was treated conservatively with cone biopsy and pelvic lymphadenectomy and presented 3 years later with recurrence of carcinoma involving the myometrium just underneath the peritoneum and ovarian metastases. Another case of metastasis of cervical carcinoma to the uterine corpus was reported by Dhingra et al. (2008) in 2008. Dhingra et al. described a metastasis of stage IB1 cervical squamous cell carcinoma to a benign endometrial polyp (Table 1).

We believe this case also raises the question of the mechanism of cervical carcinoma metastasis to the uterine corpus. There is no evidence to suggest that multifocal disease is associated with any higher risk of metastasis compared to unifocal lesions. Given that the disease was superficial we question whether cervical carcinoma dispersion into the uterus could be caused by the previous local excision.

Conservative treatment of microinvasive cervical carcinoma is extremely important for patients in whom fertility preservation is required. However a small number of cases of extracervical metastasis have now been described and this must be considered. This small number of cases must be offset however by the large numbers of women who present with microinvasive disease each year, and clearly treatment must be appropriate and commensurate with risk. A recent review¹¹ evaluated the various tissue biomarkers to predict the clinical outcome of patients with cervical carcinoma; this included studies which assessed DNA ploidy, cell-cycle and apoptosis-regulatory proteins, epidermal growth factor receptor, vascular endothelial growth factor [VEGF], cyclooxygenase-2, signal transducer and activator of transcription, human papilloma virus [HPV] status, tumour hypoxia, tumour infiltrating lymphocytes [TIL], microarray technology and microRNA.

The review concluded that the presence of HPV-18 genotype and an elevated VEGF expression are poor prognostic factors in women with early disease treated with primary surgery, however the prognostic relevance of biological tissue factors is still unclear in view of the limitations and heterogeneity of studies.

Therefore identifying which group of women with microinvasive disease are at risk of either lymph node or uterine corpus metastasis which would thus allow greater stratification of treatment remains a high priority

Conflict of interest

The authors declare that they have no conflict of interest.

References

- Argenta, P.A., Kubicek, G.J., Dusenberry, K.E., et al., 2005. Widespread lymph node metastases in a young woman with FIGO stage IA1 squamous cervical cancer. *Gynecol. Oncol.* 97, 659–661.
- Dhingra, K.K., Saroha, V., Khurana, N., 2008. Metastasis of cervical carcinoma to endometrial polyp: an interesting case report. *Malays. J. Pathol.* 30 (2), 125–127.
- Elliott, P., Coppleson, M., Russell, P., et al., 2000. Early invasive (FIGO stage IA) carcinoma of the cervix: a clinico-pathologic study of 476 cases. *Int. J. Gynecol. Cancer* 10, 42–52.
- Gadducci, A., Guerrieri, M.E., Greco, C., 2013. Tissue biomarkers as prognostic variables of cervical cancer. *Crit. Rev. Oncol. Hematol.* 86 (2), 104–129.
- Kang, W., Kim, C., Cho, M., et al., 2009. Unilateral ovarian metastasis in a case of squamous cervical carcinoma IA1. *J. Obstet. Gynaecol. Res.* 35 (4), 824–826.
- Lee, K.B., Lee, J.M., Park, C.Y., et al., 2006. Lymph node metastasis and lymph vascular space invasion in microinvasive squamous cell carcinoma of the uterine cervix. *Int. J. Gynecol. Cancer* 16, 1184–1187.
- Lee, S.W., Kim, Y.M., et al., 2009. The efficacy of conservative management after conization in patients with stage IA1 microinvasive cervical carcinoma. *Acta Obstet. Gynecol. Scand.* 88 (2), 209–215.
- Misonou, J., et al., 1988. stage (Ia) cervical cancer recurring 13 years after hysterectomy and causing small intestinal perforation. A case report with a review of literature. *Acta Pathol. Jpn.* 38 (2), 225–234.
- Nagarsheth, N.P., Maxwell, G.L., Bentley, R.C., et al., 2000. Bilateral pelvic lymph node metastases in a case of FIGO stage IA(1) adenocarcinoma of the cervix. *Gynecol. Oncol.* 77, 467–470.
- Utsugi, K., Shimizu, Y., Akiyama, F., et al., 2001. Is the invasion depth in millimeters valid to determine the prognosis of early invasive cervical adenocarcinoma? A case of recurrent FIGO stage IA1 cervical adenocarcinoma. *Gynecol. Oncol.* 82 (1), 205–207.
- Yeasmin, S., Nakayama, K., Ishikawa, M., et al., 2009. A case of bilateral pelvic lymph node involvement in stage IA1 squamous cell carcinoma of cervix and a review of the literature. *Int. J. Clin. Oncol.* 14, 564–567.
- Young, R.H., Gersell, D.J., Roth, L.M., Scully, R.E., 1993. Ovarian metastases from cervical carcinoma other than pure adenocarcinoma. A report of 12 cases. *Cancer* 71, 407–417.
- Zenatta, G., Gabriele, A., et al., 2000. Unusual recurrence of cervical adenosquamous carcinoma after conservative surgery. *Gynecol. Oncol.* 76, 409–412.