



Superficial Spreading, Microinvasive CIN 3 of Cervix: Report of an Unusual Pattern of Endometrial Involvement

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Abstract

Microinvasive squamous cell carcinoma (SCC) of the cervix is labeled by the lower anogenital squamous terminology as superficial invasive squamous cell carcinoma (SISSCA). This currently conforms to the T1a1/FIGO IA1 stage, which is defined with a stromal invasion of less than 3 mm in depth (Darragh et al. in Arch Pathol Lab Med 136(10):1266–1297, 2012). Under rare circumstances, these carcinomas can spread laterally to involve the endometrium, which increases the tumor volume and is a significant predictor of outcome. We present a case report of a 60-year-old post-menopausal woman who presented with persistent bleeding and absence of an overt cervical mass on magnetic resonance imaging. She underwent a Wertheim's hysterectomy, and on pathological examination, the cervix revealed a diffuse CIN 3 (Cervical Intraepithelial Neoplasia) with focal microinvasion. In addition, there was extensive superficial spread to the entire endometrium along with focal invasion and lymphovascular space invasion. This presentation is extremely rare, with less than 50 cases reported worldwide (Bagde et al. in J Fam Med Prim Care 10(9):3505, 2021).

Keywords CIN 3 cervix · CIN 3 endometrium · Superficial spreading SCC · Microinvasive SCC

Introduction

Cervical cancer is the second most common cancer in India, with around 14% prevalence among all cancers (NCRP, 2015). The high-risk HPV types 16 and 18 are responsible for about 70% of cases. With the advent of modern vaccines, cervical carcinoma is preventable, which can be achieved

by vaccination and secondary prevention by screening for high-risk HPV infection.

The diagnosis of microinvasive squamous cell carcinoma is primarily histopathological. The currently accepted College of American Pathologist (CAP) guidelines acknowledges the definition given by the lower anogenital squamous terminology (LAST) as superficial invasive squamous cell carcinoma (SISSCA), currently conforming to AJCC pT1a1 (2020) or FIGO IA1 (2018) stage which are defined with a stromal invasion of less than 3 mm depth [1]. Cervical carcinomas usually spread laterally to involve the stroma and parametrium by a path of least resistance and through lymphatic invasion of the uterine wall. Under rare circumstances, the tumor cells spread laterally and cause secondary involvement of the endometrium, increasing the tumor volume, a major predictor of lymph node metastasis contributing to an adverse prognosis. The current CAP guidelines and AJCC staging system does not include the horizontal extent in their sub-staging. Also, vascular space invasion, either lymphatic or venous, does not alter the staging [2, 3].

Given the extreme rarity of diffuse CIN 3 of the cervix with focal microinvasion and diffuse lateral spread to the entire endometrial lining, with glandular involvement and focal lymphovascular space invasion (LVSI), we report an

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exceptional case of microinvasive squamous cell carcinoma of the cervix with lateral superficial spread to entire endometrium with due consideration to the staging of such peculiar malignancy.

Materials and Methods

A 60-year-old female of Indian ethnicity presented with persistent post-menopausal vaginal discharge and bleeding for three months. She was initially evaluated at another institute, where her cervical biopsy revealed moderately differentiated SCC, following which she was referred to the All India Institute of Medical Sciences (AIIMS), Jodhpur. The MRI pelvis showed a distended endometrial cavity with pyometra; however, no overt cervical mass was identified (Fig. 1). Pyometra was drained at the time of cervical biopsy. The

patient underwent a Wertheim's hysterectomy, intraoperatively uterus and bilateral ovaries were of senile size, and cervix was firm; however, no overt growth was identified. There was mild parametrial fibrosis and bilaterally enlarged obturator lymph nodes. The postoperative course has been uneventful for two months.

The total hysterectomy specimen was received for histopathological evaluation. The specimen was fixed in 10% neutral buffered formalin. Grossly, the endocervix showed an irregular firm, gray-white area. The endometrial surface appeared irregular; however, no overt growth was identified (Fig. 1). The entire cervix and uterus were processed in 31 blocks. The paraffin-embedded tissue blocks were cut into 2.5- μ m-thick sections, processed, deparaffinized, rehydrated, and stained with hematoxylin and eosin stain. Immunohistochemical analysis was performed using Ventana autostainer according to the manufacturer's instructions.

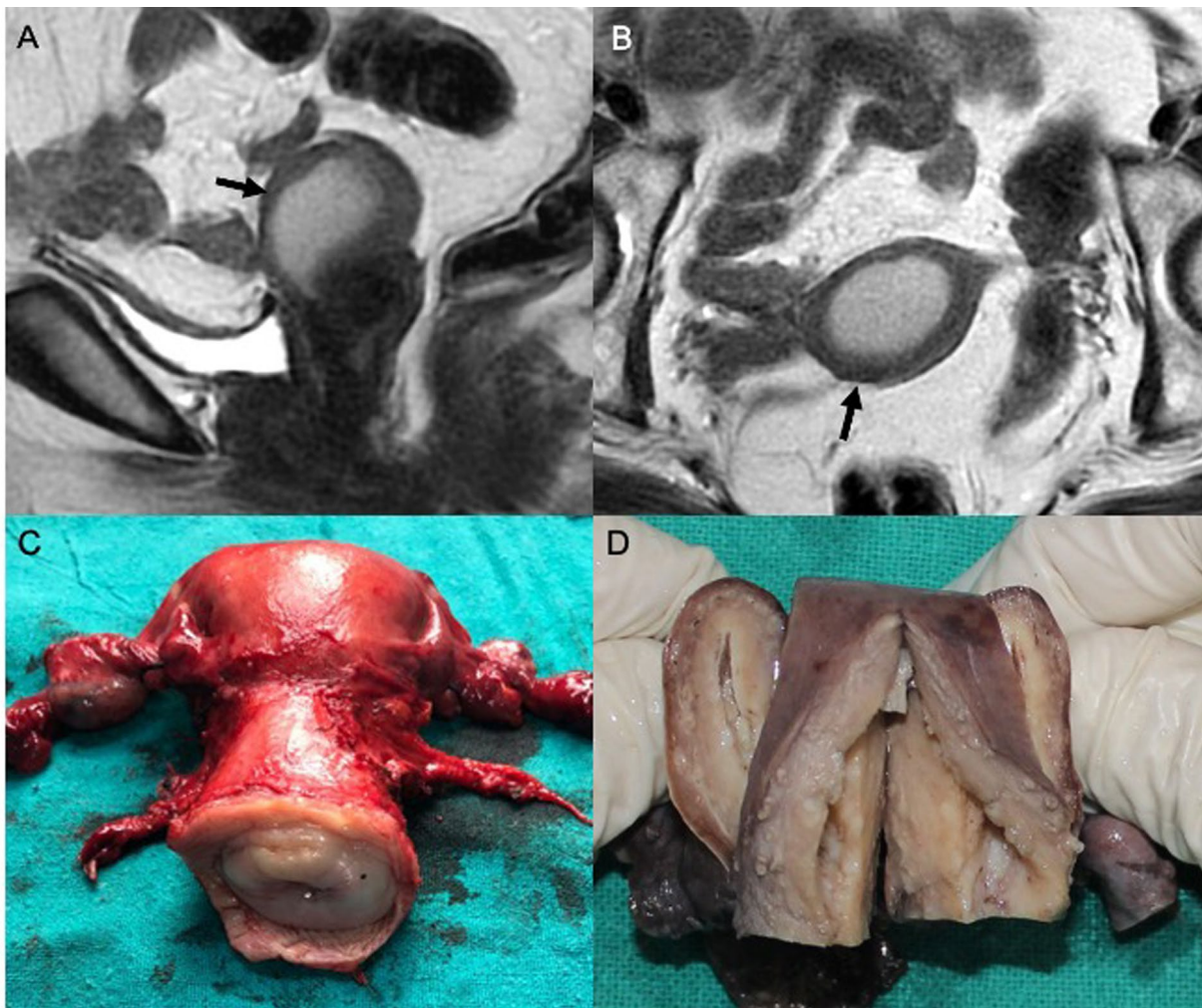


Fig. 1 MRI of pelvis. **A** Sagittal, **B** Axial T2 weighted images show distended endometrial cavity (black arrows). No overt cervical mass is seen. **C** Immediate postoperative image showing uterus and cervix.

D Gross image after formalin fixation showing irregular appearance of endometrial cavity. No overt growth was identified in the cervix

Results

The cervix showed a cervical intraepithelial neoplasia (CIN 3) or HSIL with a focal invasion of less than 1 mm. The squamous intraepithelial neoplasia (SIL) was seen spreading superficially into the lower uterine segment and the entire endometrial cavity replacing the lining. There was the presence of endometrial gland involvement and few foci of microinvasion less than 1 mm into the endometrial stroma. Lymphovascular space invasion was present (Fig. 2). However, no retroperitoneal lymph node metastasis was seen. In addition, there were features of adenomyosis. Bilateral ovaries and fallopian tubes were free of tumor. Immunohistochemical analysis showed block-like positivity with p16 in the tumor cells. The patient was diagnosed with microinvasive squamous cell carcinoma with HSIL.

Discussion

Microinvasive squamous cell carcinoma of the cervix spreading superficially into the endometrium is an extremely rare entity. There has been a recent increase in the literature regarding this entity, with 49 cases reported worldwide in 29 published articles. However, currently,

The International Federation of Gynecology and Obstetrics (FIGO) and the World health organization (WHO) have not included the horizontal spread of SCC in their classification and staging systems which remains an optional element in the synoptic reporting protocol [3]. Clinicians strongly agree to collect and assess the data on superficially spreading SCC as there may be a prognostic significance and therapeutic implication in such exceptional cases.

In our current case, a 60-year-old post-menopausal woman was presented with persistent per vaginal bleeding. On histopathological examination, the entire cervix and endometrium showed involvement by HSIL/CIN 3 with extensive replacement of endometrial lining, glandular involvement, and lymphovascular space invasion. The stage of the tumor would require to be pT1a1 and FIGO IA1 according to the current CAP and FIGO guidelines, respectively. However, no staging was done in our particular case, and the rare pathological findings were explicitly described in the histopathology report.

The survival data from previous studies for superficial spreading SCC are poor, as reviewed by Jing Du et al. [4] Our patient was alive on two months of follow-up; however, she requires a prospective vigilance for lymph node metastasis and the requirement of additional chemotherapy or radiotherapy.

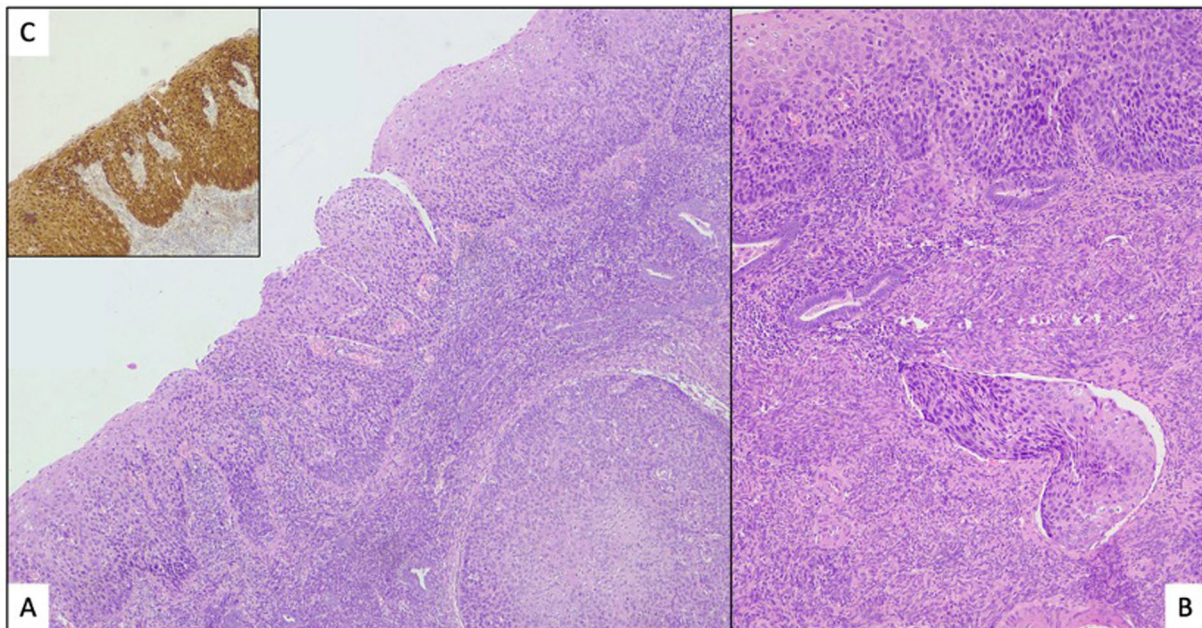


Fig. 2 Histopathological features from the uterus. **A** Endometrial lining replaced by squamous neoplastic cells with involvement of endometrial glands (hematoxylin and eosin, $\times 100$). **B** Lymphovascular

space invasion by atypical squamous cells (hematoxylin and eosin, $\times 400$). **C** p16 immunostain showing block-like positivity in the endometrium (inset)

Conclusion

Patients with CIN 3 and SCC of the cervix should be evaluated for any endometrial abnormalities to detect such superficial spreading squamous lesions. It is necessary to identify such unusual emerging entities and include them in the staging systems for the requirement of other adjuvant therapies after total hysterectomy with or without salpingo-oophorectomy.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval This case report was approved by the Department of Pathology, All India Institute of Medical Sciences, Jodhpur.

Consent to Participate Obtained for the purpose of this study.

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