

MODERATELY DIFFERENTIATED CERVICAL SQUAMOUS CELL CARCINOMA WITH SUPERFICIAL SPREAD TO THE ENDOMETRIUM AND FALLOPIAN TUBE: A CASE REPORT AND REVIEW OF THE LITERATURE

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Abstract

Squamous cell carcinoma (SCC) is the fourth most common malignancy in women worldwide, accounting for approximately 80% of all cervical cancers. Although SCC typically spreads to adjacent tissues through lymphatic or direct invasion, superficial spread to the endometrium and fallopian tubes is an uncommon and underreported phenomenon. This case report presents a 63-year-old multiparous postmenopausal woman who experienced abnormal vaginal bleeding and pelvic pain for three months. Clinical examination, imaging, and histopathological analysis revealed moderately differentiated squamous cell carcinoma of the cervix with superficial extension to the endometrium and right fallopian tube, without stromal invasion or lymphatic spread. The patient underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy followed by adjuvant chemotherapy, resulting in complete remission at one-year follow-up. This case underscores the importance of recognizing superficial spreading SCC in postmenopausal women with unexplained vaginal bleeding and highlights the need for thorough diagnostic evaluation to distinguish it from primary endometrial malignancies, ensuring accurate treatment and improved patient outcomes.

Keywords: Squamous cell carcinoma, cervix, superficial spread, endometrium, fallopian tube, case report.

INTRODUCTION

Squamous cell carcinoma (SCC) of the cervix is the most prevalent gynecological malignancy, constituting approximately 80% of cervical cancer cases globally. Recent epidemiological data indicate that SCC accounts for about 82.72% of cervical cancers, with the highest incidence observed in Sub-Saharan Africa, reaching 29.79 per 100,000 women (1). Cervical cancer is the second most common cancer among women in India, with approximately 123,907 new cases reported annually, accounting for about 18.3% of all cancers in women (2). In specific regions, such as Mumbai, the ASR reaches 19 per 100,000, while Bengaluru reports an ASR of 15.3 per 100,000. Notably, cervical cancer represents between 6% to 29% of all female cancers across various Indian states (2,3). The proportion of cervical cancer cases attributed to SCC is substantial, with studies indicating that SCC accounts for approximately 83.2% of invasive cervical cancers linked to HPV types 16 and 18 (4). This high correlation underscores the importance of HPV vaccination and screening

initiatives. Despite advancements in screening and HPV vaccination, cervical SCC remains a significant cause of cancer-related mortality, particularly in low-resource settings(5).

Cervical SCC typically spreads through direct extension to adjacent tissues, lymphatic dissemination, or hematogenous routes. However, superficial spread to the endometrium and fallopian tubes is an uncommon phenomenon characterized by tumor growth along epithelial surfaces without deep stromal invasion. This atypical spread can pose substantial diagnostic challenges, as it may mimic primary endometrial or fallopian tube malignancies, leading to misdiagnosis and potentially suboptimal treatment(6).

Distinguishing superficial cervical SCC from other gynecological cancers necessitates meticulous histopathological examination, often enhanced by immunohistochemical staining and HPV DNA analysis. Recent studies emphasize the importance of these diagnostic advancements in improving recognition and management of superficial spreading SCC(7). Increased clinical awareness is crucial for timely and accurate diagnosis, which can significantly impact treatment outcomes for patients presenting with this rare manifestation of cervical SCC(8).

This report discusses a case involving a 63-year-old postmenopausal woman with moderately differentiated SCC of the cervix, highlighting the clinical and diagnostic complexities associated with superficial spread to the endometrium and fallopian tube.

Case report

A 63-year-old multiparous woman presented with a three-month history of abnormal vaginal bleeding and pelvic pain. Her medical history was largely uneventful, with no previous surgeries or significant medical conditions. She had been postmenopausal for 15 years but recalled experiencing irregular menstrual cycles before the onset of menopause. A notable factor in her history was a longstanding smoking habit, which is a recognized risk factor for cervical malignancies. Despite this, she had not undergone routine cervical cancer screening, nor had she been diagnosed with cervical dysplasia or HPV infection. The absence of prior screening or HPV vaccination contributed to a delayed diagnosis, highlighting the importance of regular gynecological examinations in postmenopausal women.

On physical examination (image ?), an ulceroproliferative growth approximately 4 cm in diameter was detected on the cervix, extending into the upper vagina. Palpation of the parametrium and pelvic sidewalls revealed no abnormalities, suggesting that there was no deep tissue invasion at the time of assessment. A speculum examination showed a friable mass that bled on contact, raising concerns about malignancy. A bimanual examination confirmed that the lesion was confined to the cervix and upper vagina without evidence of parametrial involvement, indicating a localized process. This initial examination provided crucial clinical insights and directed further diagnostic efforts to confirm the suspected malignancy.

Three months prior to her presentation, the patient first noticed abnormal vaginal bleeding and pelvic discomfort. At the initial clinical visit, physical examination revealed the cervical lesion (image ?), prompting further diagnostic evaluation. A Pap smear performed during the assessment indicated a high-grade squamous intraepithelial lesion (HSIL) (image ?), raising suspicion for underlying malignancy. This led to a colposcopy-guided biopsy, which subsequently confirmed the diagnosis of moderately differentiated squamous cell carcinoma (image ?). Imaging studies, including pelvic ultrasound and MRI, demonstrated cervical infiltration and superficial extension into the endometrium and the right fallopian tube (image ?). T2-weighted MRI sequences revealed a hyperintense lesion confined to these areas without evidence of distant metastases or lymph node involvement (image ?). This combination of histological and radiological findings confirmed the presence of squamous cell carcinoma with superficial spread, a rare presentation requiring prompt surgical intervention.

Histopathological analysis of the hysterectomy specimen confirmed squamous cell carcinoma with superficial spread to the endometrium and right fallopian tube (image ?). Tumor cells were seen replacing the endometrial epithelium, but no stromal invasion was identified, consistent with a superficial spreading pattern. Immunohistochemical staining for p16 and HPV DNA testing were both positive, confirming the involvement of high-risk HPV infection in the pathogenesis of the malignancy. This histopathological evidence underscored the role of HPV in the development and progression of cervical squamous cell carcinoma, reinforcing the need for preventive HPV vaccination in reducing the incidence of such malignancies.

The patient underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy (image ?). Intraoperatively, an infiltrating cervical lesion was observed, with additional irregularities noted in the right fallopian tube suggestive of pyosalpinx. Postoperative histopathological analysis (image ?) confirmed the

diagnosis of superficial squamous cell carcinoma with spread to the endometrium and right fallopian tube. Surgical margins were free of tumor involvement, and no lymphovascular invasion was detected. The procedure was completed without complications, and the patient's postoperative recovery was uneventful. To minimize the risk of recurrence, she received adjuvant chemotherapy consisting of cisplatin and paclitaxel, a regimen commonly used in the management of advanced or high-risk cervical cancer.

At the six-month follow-up, the patient remained disease-free, with no clinical or radiological evidence of recurrence. Her follow-up plan included regular pelvic examinations, Pap smears, and periodic imaging studies to monitor for any signs of disease progression or recurrence. At the one-year mark, the patient continued to show no signs of disease, with improved quality of life and no significant side effects from the chemotherapy regimen. She expressed satisfaction with her treatment outcomes and reported a return to normal daily activities. The patient remains under close observation as part of her long-term follow-up, which is essential for early detection of any potential recurrence or new lesions. This case highlights the importance of early recognition and comprehensive management of superficial spreading squamous cell carcinoma, emphasizing the need for vigilant postoperative surveillance and adherence to follow-up care.

DISCUSSION

Despite advances in prevention, cervical cancer continues to be a major concern in developing countries like India, where screening and vaccination programs are less established. The introduction of HPV vaccination has dramatically reduced the incidence of cervical cancers in various populations. For instance, a study from England reported an 83.9% reduction in cervical cancer rates among women who received routine vaccinations compared to those who did not (9). This underscores the critical role of vaccination and regular screening in combating cervical SCC, particularly in high-burden regions.

Traditionally, SCC spreads through lymphatic dissemination, direct invasion into adjacent tissues, or hematogenous routes. However, superficial spread to the endometrium and fallopian tubes is rare and poses unique diagnostic challenges. Recent findings suggest that this superficial spread may occur via intraepithelial migration, where tumor cells migrate along the epithelial layer without significant stromal invasion (8). This theory aligns with observations from other malignancies that exhibit similar superficial extension patterns. Moreover, microinvasion of the basal layer could allow cancer cells to proliferate superficially while bypassing typical invasive pathways, further complicating the understanding of SCC spread mechanisms.

Distinguishing superficially spreading SCC from primary endometrial or tubal malignancies is particularly challenging due to overlapping clinical presentations. In postmenopausal women presenting with abnormal uterine bleeding, the differential diagnosis can be complex. Histopathological evaluation remains crucial; immunohistochemical staining for p16 and HPV DNA testing are essential tools for confirming the cervical origin of the tumor(10). Recent advancements in imaging techniques, such as diffusion-weighted imaging (DWI) on MRI, have shown promise in identifying superficial spread by revealing high signal intensity areas corresponding to tumor locations (8). These advanced diagnostic modalities enhance our ability to accurately characterize cervical lesions and differentiate them from other gynecological cancers.

Superficially spreading squamous cell carcinoma (SCC) of the cervix presents unique challenges in treatment and prognosis due to its uncommon pattern of spread.

Radical hysterectomy combined with bilateral salpingo-oophorectomy is a cornerstone in treating such cases. This approach involves the removal of the uterus, cervix, fallopian tubes, and ovaries, aiming to eradicate the primary tumor and any potential microscopic spread. The significance of achieving clear surgical margins cannot be overstated, as residual disease is a known risk factor for recurrence. In instances where lymphatic dissemination is suspected, lymphadenectomy becomes crucial. A study highlighted that while hysterectomy with bilateral salpingo-oophorectomy is common, the addition of lymphadenectomy in specific cases can provide comprehensive staging and potentially improve outcomes(11). The efficacy of platinum-based chemotherapy, particularly cisplatin and paclitaxel, in reducing recurrence risks in cervical cancer is well-documented. A study demonstrated that the combination of cisplatin and paclitaxel improved survival rates in advanced cervical cancer. Additionally, the combination of gemcitabine and cisplatin has shown promise in certain gynecological malignancies. A phase III trial indicated that adding gemcitabine to cisplatin and radiation therapy improved progression-free and overall survival in locally advanced cervical cancer (12).

Adjuvant radiotherapy plays a critical role in managing cervical cancer, particularly in cases where surgical margins are close or there is evidence of microscopic parametrial involvement. A retrospective analysis

demonstrated that adjuvant pelvic radiotherapy significantly reduced recurrence rates in patients with high-risk cervical cancer, including those with minimal stromal invasion (13). Despite the established benefits of radiotherapy for invasive cervical cancer, there remains a gap in the literature specifically addressing its efficacy in cases of superficially spreading SCC, emphasizing the need for individualized and case-by-case treatment planning.

Prognosis in cervical squamous cell carcinoma (SCC) is influenced by several key factors, including lymphovascular invasion (LVI), tumor grade, and HPV status. LVI is a well-recognized prognostic marker, with studies consistently linking its presence to higher recurrence rates and reduced disease-free survival. Extensive LVI is associated with significantly worse progression-free survival (PFS) and overall survival (OS) compared to patients without LVI, underscoring the importance of its quantification in treatment planning and risk stratification (14,15). The prognostic impact of LVI necessitates its routine assessment in histopathological evaluations to better tailor adjuvant therapies and improve patient outcomes.

The influence of HPV status and p16 overexpression on cervical SCC prognosis is well-documented. High-risk HPV DNA positivity and p16 overexpression have been shown to correlate with better treatment responses and improved survival rates. Patients with HPV-positive tumors typically exhibit superior overall survival (OS) and disease-free survival (DFS) outcomes, with pooled hazard ratios indicating a notable survival advantage for those with p16-positive tumors(16,17). Furthermore, the combination of high-risk HPV detection and p16 overexpression serves as a surrogate marker for HPV-driven tumors, which are generally associated with favorable prognoses and more effective responses to chemoradiation therapy (18). This evidence highlights the value of incorporating HPV and p16 testing into the diagnostic and prognostic workflow for cervical SCC.

Superficial spread of SCC without stromal invasion presents a distinct clinical course, often with a more favorable prognosis due to the reduced risk of metastatic dissemination. Nevertheless, despite the lower likelihood of distant spread, close surveillance remains essential to monitor for potential progression or recurrence, as even superficially spreading tumors can exhibit aggressive behavior over time (15). Regular follow-up and comprehensive post-treatment care are crucial for maintaining long-term disease control in these patients.

Post-treatment surveillance plays an indispensable role in the early detection of recurrent disease. According to the National Comprehensive Cancer Network (NCCN) guidelines, patients treated for cervical cancer should undergo follow-up every 3-6 months for the first two years and annually thereafter. This structured approach, which involves routine pelvic examinations, Pap smears, and periodic imaging studies, facilitates the prompt identification of recurrence, enhancing the chances of timely intervention and successful management. Adherence to these surveillance protocols significantly improves patient outcomes by ensuring that recurrences are detected at an early and potentially more treatable stage.

The rarity of superficially spreading SCC contributes to the limited data available on its optimal management, highlighting the pressing need for further research into its molecular underpinnings and clinical behavior. Collaborative multicenter studies and extensive case series are essential to develop standardized treatment protocols and identify prognostic biomarkers that can guide individualized patient care. Expanding the current understanding of this uncommon variant of cervical cancer will not only improve therapeutic strategies but also enhance overall survival and quality of life for affected patients.

CONCLUSION

The case of moderately differentiated squamous cell carcinoma (SCC) of the cervix with superficial spread to the endometrium and fallopian tube highlights the importance of recognizing rare patterns of tumor dissemination in cervical cancer. This unusual presentation underscores the need for comprehensive histopathological evaluation, advanced imaging, and molecular testing to ensure accurate diagnosis and appropriate management. Although superficially spreading SCC may present without significant stromal invasion, its potential for recurrence necessitates vigilant surveillance and long-term follow-up.

The successful management of this case through surgical resection and adjuvant chemotherapy demonstrates the efficacy of a multidisciplinary approach in addressing rare cervical cancer variants. This case also reinforces the prognostic value of HPV status and p16 overexpression in guiding therapeutic decisions and predicting treatment outcomes.

Given the limited data available on superficially spreading SCC, this report contributes valuable insights to the growing body of literature, emphasizing the importance of individualized treatment plans and the role of

ongoing research. Future studies and collaborative efforts are essential to establish evidence-based guidelines, improve patient outcomes, and enhance our understanding of the molecular mechanisms underlying this rare form of cervical cancer.

Patient Perspective

The patient reported satisfaction with treatment and significant improvement in quality of life. She emphasized the importance of regular follow-up and expressed gratitude for the multidisciplinary care received.

Informed Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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