

## Small Cell Neuroendocrine Cervical Carcinoma: A Case Report

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### Abstract

**Objective:** Small cell neuroendocrine cervical carcinoma is a neuroendocrine tumor with the great aggravation that comprises 0.5 to 3 percent of cervical tumors and progresses rapidly with early lymphogenous and hematogenous metastases.

**Case report:** We reported a 40 years old woman with cervical cancer in stage IB2 that had radical hysterectomy with mistaken diagnosis of squamous cervical cancer. The disease has progressed after 50 days of surgery with a 6 cm tumor in vaginal cuff; review of pathology demonstrated small cell neuroendocrine cervical carcinoma.

**Conclusion:** Recognition of this separate histopathological entity with IHC analysis is important. Chemoradiotherapy and multimodality therapeutic approaches could improve the survival rates.

**Keywords:** Small Cell Neuroendocrine Tumor; Cervical Carcinoma; Chemoradiotherapy; Chemotherapy

### Introduction

Small cell neuroendocrine cervical carcinoma is a neuroendocrine tumor with great aggravation that comprises 0.5 to 3% of cervical tumors and progresses rapidly with early lymphogenous and hematogenous metastases (1). Small cell neuroendocrine cervical carcinoma has clinical and biological characteristics of both cervical neoplasm that means local aggressiveness of the squamous tumor and early dissemination of the neuroendocrine tumor (2).

Although chemoradiation is a treatment that

improves survival in non-small cell carcinoma of cervix, the standard therapeutic approach has not been clear in Small cell neuroendocrine cervical carcinoma (2). Standard chemotherapy regimens such as cisplatin and etoposide are the best management of small cell lung cancer. The five-year survival rate for this type of cervical cancer is between 0 and 30% (3). These tumors show a worse prognosis compared with other histological types of cervical cancers (4).

In this study, we reported a case of small cell neuroendocrine cervical carcinoma.

### Case report

A 40-year-old woman, para 3 was admitted with abnormal uterine bleeding. The patient had a 4-month history of spotting after menses. She had no

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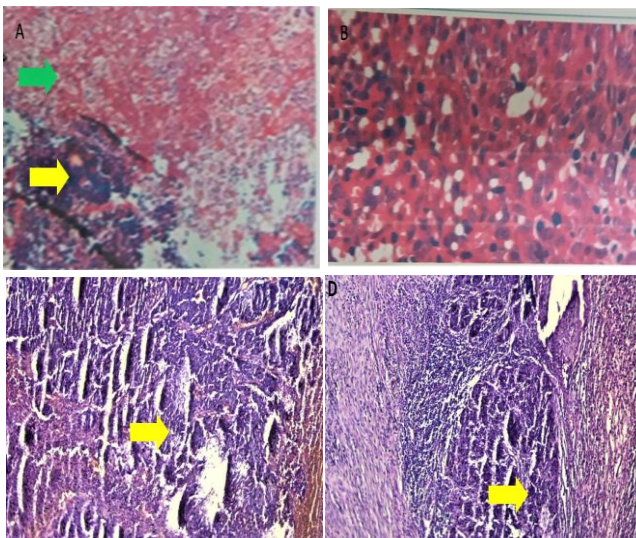
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partner and had no coitus for a long time. A 4 cm mass was identified in the uterine cervix upon gynecological examination. It was confined to the cervix and left parametrium was shortened but released (stage IB2 in FIGO staging system). Ultrasound and MRI were performed. On ultrasound examination, the uterine cervix appeared as a bulging with a diameter of 42 mm and a heterogeneous echo structure compared with the surrounding cervical stroma. Pelvic MRI was unremarkable. The result of Papanicolaou smear was P1 (negative for intraepithelial lesion or malignancy) with severe inflammation. Tissue specimens were obtained using cervical biopsy. The report of the biopsy was high grade malignant tumor without lymphovascular invasion. The second biopsy was performed one month later and reported extensive necrosis and poorly differentiated squamous cervical cancer, grade 3 (Figure 1).



**Figure 1:** A and B; Cervical lesion biopsy demonstrates SCC (yellow arrow) with abundant necrosis (green arrow). C and D, Small round cell tumor of cervix (yellow arrows)

The patient underwent radical hysterectomy, pelvic lymphadenectomy, and transposition of both ovaries above the pelvic brim using firm sutures to the peritoneum. After 50 days, she came back with severe vaginal bleeding. Gynecological examination revealed 6 cm vegetative and necrotic mass in the vaginal cuff. The tissue was friable with hemorrhage. Review of pathology reported small cell neuroendocrine cervical carcinoma with deep stromal and lymphovascular invasion. An

Immunohistochemistry (IHC) test was performed for the tumor markers and was positive for pan cytokeratin, synaptophysin, and chromogranin A, indicating a neuroendocrine carcinoma. The patient subsequently underwent radiotherapy (25 sessions external 5000 gray, internal 1000 gray) and chemotherapy (4 courses with cisplatin and etoposide). The disease controlled well and she had regularly followed up by pelvic examination and Pap smear. She is in good health condition and has no recurrence after 3 years.

## Discussion

Neuroendocrine cervical carcinoma (NECC) is a rare variant of cervical cancer that carries a poor prognosis with a mean overall survival of 40 months and a 5-year overall survival rate of 34% (5). Also, local and distant relapses occur more often in NECC, and the 5-year overall survival is significantly poorer with around 30% compared to >65% for squamous cell carcinoma and adenocarcinoma of the cervix (6-9).

The biology of neuroendocrine carcinoma of the cervix is different from squamous cell carcinoma or adenocarcinoma of the cervix regarding several characteristics. For example, NECC is more likely to invade the lymph-vascular space and to spread to the regional lymph node basin at the time of diagnosis (5). Radical surgery should be suggested for early-stage of small cell neuroendocrine cervical carcinoma and combining radiation therapy with brachytherapy should be suitable for the advanced-stage (10). Our patient had localized disease and received multimodality treatment including chemotherapy, surgery, and radiotherapy.

Different studies demonstrated that pelvic control by radical hysterectomy is not beneficial for patients with small cell neuroendocrine cervical carcinoma, and should be limited to those with an early invasive lesion without obvious lymph node metastasis. On the contrary, non-radical hysterectomy followed by new and aggressive adjuvant chemotherapy should be administered (11). In the presented case, radical surgery was performed because of the misdiagnosis of squamous cell carcinoma at the beginning.

It is important to differentiate this tumor (using IHC analysis) from lymphomas, poorly-differentiated squamous cell carcinomas, and sarcomas or melanomas that can arise in the cervix and mimic small cell-like features (2, 5). Differential diagnosis of NECC includes metastasis of extra-cervical NEC (e.g.

lung NEC) and extra-cervical NEC with local wide tumor spread (e.g. urinary bladder) (5). IHC studies such as synaptophysin, CD56, and chromogranin A, detect neuroendocrine differentiation, and strong Ki-67/MIB-1 labeling shows the malignant characteristics of neuroendocrine tumors (4). In the current case, IHC analysis was positive for pan cytokeratin, synaptophysin, and chromogranin A, indicating a neuroendocrine carcinoma.

Effective treatments of neuroendocrine cervical tumors remain inconclusive (12). A multicenter study conducted by Kuji et al. reported that postoperative chemotherapy compared with non-chemotherapy improved overall survival and progression-free survival (13). Multimodality treatment with radical surgery and neoadjuvant/adjuvant chemotherapy with cisplatin and etoposide with or without radiotherapy is the mainstay of treatment for early stage disease while chemotherapy with cisplatin and etoposide or topotecan, paclitaxel, and bevacizumab are appropriate for women with locally advanced or recurrent NECC (5).

## Conclusion

Small cell neuroendocrine cervical carcinoma is a rare malignancy with aggressive behavior. Recognition of this separate histopathological entity with IHC analysis is important. Chemoradiotherapy and multimodality therapeutic approaches could improve the survival rates.

## Acknowledgments

Authors have no conflict of interests.

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