

Mixed Endocervical Adenocarcinoma and Poorly Differentiated Neuroendocrine Carcinoma of the Cervix: A Case Report and Review of the Literature

Oumnia Bouchama^{1*}, Majda Idrissi Bendahhou¹, Chahrazed Bouchikhi¹

¹Department of Gynecology and Obstetrics, Hassan II University Hospital, Fez, Morocco

DOI: <https://doi.org/10.36347/sjmcr.2026.v14i10.028>

| Received: 19.08.2026 | Accepted: 07.10.2026 | Published: 12.10.2026

*Corresponding author: Oumnia Bouchama

Department of Gynecology and Obstetrics, Hassan II University Hospital, Fez, Morocco

Abstract

Case Report

Neuroendocrine carcinoma of the uterine cervix is a rare, aggressive malignancy with a high risk of lymphatic and hematogenous dissemination. Mixed tumors combining neuroendocrine carcinoma with conventional cervical carcinoma are uncommon and diagnostically challenging. We report a 48-year-old multiparous woman with postcoital bleeding and a 2-cm ulcerated cervical mass. Biopsy showed poorly differentiated neuroendocrine carcinoma with diffuse chromogranin and strong synaptophysin expression, marked CK7 and p16 expression, focal p63 expression, and a Ki-67 index of approximately 80%. MRI and CT showed a localized cervical tumor with suspicious subcentimetric pelvic and para-aortic lymph nodes. Radical hysterectomy with bilateral pelvic lymphadenectomy and para-aortic sampling was performed. Histology demonstrated mixed endocervical adenocarcinoma and poorly differentiated neuroendocrine carcinoma, measuring 1.5 × 1 cm, with negative margins and 0/26 lymph nodes. No adjuvant therapy was administered. After 5 years of surveillance, the patient remained disease-free. Accurate morphological and immunohistochemical diagnosis is essential.

Keywords: uterine cervix; neuroendocrine carcinoma; adenocarcinoma; mixed carcinoma; cervical cancer; immunohistochemistry.

Copyright © 2026 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

1. INTRODUCTION

Neuroendocrine carcinoma of the uterine cervix (NECC) is rare, accounting for approximately 1%–2% of invasive cervical carcinomas [1,2]. Most are poorly differentiated small-cell carcinomas, whereas large-cell neuroendocrine carcinoma is less common [1,2]. These tumors have aggressive biological behavior and a propensity for early lymphatic and hematogenous dissemination [1,2,6].

Diagnosis requires correlation of morphology with immunohistochemistry. Synaptophysin and chromogranin A are principal neuroendocrine markers, while high-grade tumors generally show high proliferative activity [2,3]. The 2020 WHO classification recognizes neuroendocrine carcinomas as distinct high-grade epithelial malignancies of the female genital tract [3].

Mixed cervical carcinomas containing neuroendocrine and conventional epithelial components are particularly uncommon and have mainly been

reported in case reports and small series [4,5]. We report a rare mixed endocervical adenocarcinoma and poorly differentiated neuroendocrine carcinoma in a 48-year-old woman with a favorable 5-year outcome.

2. CASE PRESENTATION

A 48-year-old multiparous woman was referred for abnormal vaginal bleeding. She reported 2 months of postcoital bleeding. She was still menstruating, with no significant medical history apart from cholecystectomy 13 years earlier. Her body mass index was 40 kg/m².

Gynecological examination revealed an approximately 2 × 2 cm ulcerated, exophytic mass arising from the anterior cervical lip and bleeding on contact. The vaginal walls and parametria appeared clinically free. Cervical biopsy was performed.

Histological examination showed a malignant epithelial proliferation compatible with poorly differentiated neuroendocrine carcinoma. Immunohistochemistry demonstrated diffuse

Citation: Bouchama, O., Idrissi Bendahhou, M., & Bouchikhi, C. (2026). Mixed Endocervical Adenocarcinoma and Poorly Differentiated Neuroendocrine Carcinoma of the Cervix: A Case Report and Review of the Literature. *Sch J Med Case Rep*, 14(10), 2237-2239. <https://doi.org/10.36347/sjmcr.2026.v14i10.028>

chromogranin and strong synaptophysin expression, marked CK7 expression, focal p63 expression, negative estrogen receptors, moderate-to-marked p16 expression, and a Ki-67 index of approximately 80%. These findings supported poorly differentiated neuroendocrine carcinoma of the cervix. The precise small-cell versus large-cell subtype was not specified in the available pathological report.

Pelvic MRI demonstrated an endocervical tumor measuring 25 × 23 mm without obvious parametrial or vaginal extension. Several bilateral common and external iliac lymph nodes were subcentimetric. Thoraco-abdomino-pelvic CT showed the cervical mass and several subcentimetric pelvic and para-aortic lymph nodes considered potentially suspicious; no visceral metastases were identified.

The patient underwent radical hysterectomy (Wertheim procedure) with bilateral pelvic lymphadenectomy and para-aortic lymph-node sampling. Intraoperative exploration showed no peritoneal effusion, carcinomatosis, or macroscopic abnormalities of the liver, spleen, omentum, or diaphragm.

Definitive histopathology revealed a mixed cervical carcinoma composed of a well-differentiated invasive adenocarcinoma and a minor component of poorly differentiated neuroendocrine carcinoma. The tumor was circumferential and measured 1.5 × 1 cm, infiltrating approximately 50% of the cervical wall. No lymphovascular space invasion was identified. Vaginal margins, parametria, adnexa, and endometrium were free of tumor.

Twenty-six lymph nodes were examined: 14 right pelvic, 5 left pelvic, and 7 para-aortic; all were negative for metastasis (0/26). The final pathological classification was pT1b1N0, corresponding to FIGO stage IB1 according to the 2018 FIGO classification [8].

The case was discussed at a multidisciplinary tumor board. Given the small tumor size, confinement to the cervix, absence of lymphovascular invasion, negative margins, and negative lymph nodes, no adjuvant chemotherapy or radiotherapy was administered. The patient underwent close clinical and radiological surveillance. At 5 years, she remained in complete remission without documented local, nodal, or distant recurrence.

3. DISCUSSION

NECC represents approximately 0.9%–1.5% of invasive cervical cancers. In the systematic review by Salvo *et al.*, 3,538 cases were identified across 112 studies, with a pooled prevalence of approximately 1.41% [1]. Small-cell carcinoma accounts for most cases, while large-cell carcinoma is less common [1]. High-grade neuroendocrine carcinomas are characterized by a

marked tendency toward lymphatic and hematogenous dissemination, including distant metastasis despite a small primary tumor [1,2,6].

The present case was unusual because the definitive specimen demonstrated two components: well-differentiated endocervical adenocarcinoma and a minor poorly differentiated neuroendocrine component. Ramalingam *et al.*, reported two cases of mixed endocervical adenocarcinoma and high-grade neuroendocrine carcinoma [4], while Teoman and Ersoz described a similar mixed tumor [5]. These reports, together with the present case, emphasize the importance of examining the complete surgical specimen because the preoperative biopsy may sample only the neuroendocrine component.

The diagnosis of cervical neuroendocrine carcinoma requires integration of morphology and immunohistochemistry. In our patient, diffuse chromogranin and strong synaptophysin expression supported neuroendocrine differentiation, while the Ki-67 index of approximately 80% reflected high proliferative activity. Neuroendocrine markers should nevertheless be interpreted with morphology because focal neuroendocrine marker expression may occur in conventional cervical carcinomas [2,3]. The mixed nature of the tumor was established only on the hysterectomy specimen.

High-risk HPV infection is strongly associated with cervical neuroendocrine carcinoma, particularly HPV18 and HPV16 [9]. HPV testing was not available in this case; therefore, the HPV status remains unknown. Moderate-to-marked p16 expression provides supportive information but is not equivalent to direct HPV detection [9].

Imaging showed several subcentimetric pelvic and para-aortic lymph nodes considered potentially suspicious, but all 26 surgically examined nodes were negative. This illustrates the limitations of imaging in characterizing small lymph nodes and the value of pathological nodal assessment in selected patients. The tumor was confined to the cervix, measured 1.5 cm, and was classified as pT1b1N0, FIGO IB1 [8].

There is no universally accepted treatment strategy for cervical neuroendocrine carcinoma because of its rarity and the lack of randomized trials [1,6,7]. Radical surgery followed by chemotherapy, often using platinum-etoposide regimens, has been reported in early-stage disease [1]. Retrospective studies have evaluated radical hysterectomy in early-stage high-grade neuroendocrine carcinoma, although treatment recommendations remain limited by selection bias and the absence of prospective evidence [6,7]. In the present case, the multidisciplinary team chose surveillance after radical surgery because of the small, localized tumor, absence of lymphovascular invasion, negative margins,

and negative lymph nodes. This individualized decision should not be interpreted as evidence that surgery alone is a standard treatment for poorly differentiated cervical neuroendocrine carcinoma.

The 5-year disease-free outcome is noteworthy given the generally aggressive behavior of cervical neuroendocrine carcinoma. However, a single case cannot establish prognostic factors or determine optimal treatment. The favorable course may reflect the localized disease and absence of pathological nodal or vascular involvement.

The main strengths of this case are the detailed clinicopathological assessment, including biopsy immunohistochemistry, MRI, CT, definitive histopathology, pelvic and para-aortic nodal assessment, and 5-year follow-up. Limitations include unavailable HPV testing, lack of precise morphological subclassification of the neuroendocrine component, absence of molecular characterization, and the inherent limitation of a single case. The report was prepared in accordance with the CARE guidelines [10].

This case highlights the diagnostic complexity of mixed cervical carcinomas. Comprehensive pathological examination is essential to identify both components, while management should be individualized according to stage, pathological risk factors, and multidisciplinary assessment. The favorable 5-year outcome in this patient should not be generalized to other patients with cervical neuroendocrine carcinoma.

Disclosure: The authors have nothing to disclose.

Ethics Statement: Ethical approval was not required for this case report in accordance with the policies of our institution.

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

Conflicts Of Interest: The authors declare no conflicts of interest.

REFERENCES

1. Salvo G, Gonzalez Martin A, Gonzales NR, Frumovitz M. Neuroendocrine carcinoma of the

cervix: a systematic review of the literature. *Gynecol Oncol.* 2019;153(2):411-418. doi: 10.1016/j.ygyno.2019.01.019. PMID:29728073.

2. Mandic A, Maksimovic T, Nadj GS, Maricic S, Čelebić A. Neuroendocrine cervical cancer: Have we made any steps forward in its management? *Eur J Surg Oncol.* 2025;51(4):108570. doi: 10.1016/j.ejso.2024.108570. PMID:39095302.
3. Höhn AK, Brambs CE, Hiller GGR, May D, Schmoeckel E, Horn LC. 2020 WHO Classification of Female Genital Tumors. *Geburtshilfe Frauenheilkd.* 2021;81(10):1145-1153. doi:10.1055/a-1545-4279. PMID:34629493.
4. Ramalingam P, Malpica A, Deavers MT. Mixed endocervical adenocarcinoma and high-grade neuroendocrine carcinoma of the cervix with ovarian metastasis of the former component: a report of 2 cases. *Int J Gynecol Pathol.* 2012;31(5):490-496. doi:10.1097/PGP.0b013e31824735a5. PMID:22833092.
5. Teoman G, Ersoz S. Mixed endocervical adenocarcinoma and high-grade neuroendocrine carcinoma of the cervix: a case report. *Indian J Pathol Microbiol.* 2021;64(1):174-176. doi: 10.4103/IJPM.IJPM_1006_19. PMID:33433435.
6. Salvo G, Ramalingam P, Flores Legarreta A, Jhingran A, Gonzales NR, Chisholm GB, Frumovitz M. Role of radical hysterectomy in patients with early-stage high-grade neuroendocrine cervical carcinoma: a NeCTuR study. *Int J Gynecol Cancer.* 2021;31(4):495-501. doi:10.1136/ijgc-2020-002213. PMID:33563641.
7. Zhang Y, Li L, Wang Z, Huang Y, Luo S, Peng Y, *et al.*, Preferred method of therapy for patients with early-stage high-grade neuroendocrine carcinoma of the cervix. *Am J Cancer Res.* 2021;11(9):4595-4606. PMID:34659908.
8. Bhatla N, Aoki D, Sharma DN, Sankaranarayanan R. Cancer of the cervix uteri. *Int J Gynaecol Obstet.* 2018;143 Suppl 2:22-36. doi:10.1002/ijgo.12611.
9. Castle PE, Pierz A, Stoler MH. A systematic review and meta-analysis on the attribution of human papillomavirus (HPV) in neuroendocrine cancers of the cervix. *Gynecol Oncol.* 2018;148(2):422-429. doi: 10.1016/j.ygyno.2017.12.001.
10. Gagnier JJ, Kienle G, Altman DG, Moher D, Sox H, Riley D; CARE Group. The CARE guidelines: consensus-based clinical case reporting guideline development. *BMJ Case Rep.* 2013;2013. doi:10.1136/bcr-2013-201554. PMID:24155002.