



Small cell neuroendocrine carcinoma of the uterine cervix (SCNEC): a case report and review

ABSTRACT

Tujuan: Meningkatkan pengetahuan dan kemampuan untuk mendiagnosis dan menangani kasus jarang tumor neuroendokrin sel kecil pada kanker serviks uteri

Metode: Laporan kasus

Hasil: Seorang perempuan Indonesia berusia 51 tahun paritas 2 dengan keluhan utama perdarahan dari kemaluan pasca hubungan seksual. Pemeriksaan ginekologi pada serviks ditemukan massa eksofitik yang rapuh dan mudah berdarah dengan bagian nekrotik berukuran 3x3x3,5 cm, menginfiltrasi kedua parametrium namun belum mencapai dinding panggul sesuai dengan stadium IIB. Hasil pemeriksaan histopatologi dari biopsi massa adalah adeno karsinoma berdiferensiasi baik, tidak terdapat invasi limfovaskuler DD/ adenoskuamosa, tumor neuroendocrine. Kami melakukan review histopatologi dan dilanjutkan pemeriksaan immunohistokimia. Hasil pemeriksaan immunohistokimia menunjukkan meskipun sampel tidak tipikal, pola immunohistokimia bisa mendukung tampilan morfologi dari karsinoma neuroendokrin, tipe sel kecil. Pasien selanjutnya menjalani proses terapi kemoradiasi.

Kesimpulan: Karsinoma neuroendokrin sel kecil pada serviks uteri merupakan kasus yang langka. Pemeriksaan histopatologi dan immunohistokimia mempunyai peranan penting dalam penegakan diagnosis. Meskipun prognosinya buruk, kemoterapi adjuvant atau kemoradiasi pada stadium lanjut dihubungkan dengan meningkatnya angka keberlangsungan hidup.

Kata kunci: SCNEC, immunohistokimia, kemoradiasi

Apa yang sudah diketahui tentang topik ini?

Kasus tumor neuroendokrin sel kecil pada kanker serviks uteri

Objective: Improving skill and knowledge to diagnose and manage a rare case of small cell neuroendocrine uterine cervical cancer

Method: a Case report

Result: A 51 years old, para 2, Indonesian woman with chief complaint post-coital vaginal bleeding. Gynecology examination revealed cervical exophytic fragile mass size 3x3x3,5 cm, easily bleeding, with a necrotic part, infiltrated both parametria but not reach the pelvic wall correspond to stage IIB. Initially, the histopathology result from punch biopsy was an adenocarcinoma well-differentiated, with no lymph vascular invasion, DD/ adenosquamous, neuroendocrine tumor. We did the histopathology review continued with immunohistochemistry examination. Immunohistochemistry result showed that although all the sample was not typical, immunohistochemical outward patterns can support morphological features of high-grade neuroendocrine carcinoma, small cell type. We proceed here for chemoradiation therapy.

Conclusion: Small cell neuroendocrine carcinoma of the uterine cervix is a rare case. Histopathology and immunohistochemistry examination has an important role to develop the diagnosis. Although the prognosis is poor, adjuvant chemotherapy or chemoradiation was associated with improved survival in patients with advance staged.

Keywords: SCNEC, immunohistochemistry, chemoradiation

Apa yang ditambahkan pada studi ini?

Diagnosis dan penanganan kasus jarang tumor neuroendokrin sel kecil pada kanker serviks uteri

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Introduction

Neuroendocrine small cell cervical carcinoma is an aggressive histological variant of cervical cancer accounting for 1-3% of all cervical cancers.⁴

Earlier reports have shown that the majority of patients present with advanced-stage disease, have lymph node metastasis, and are at high risk for recurrence and disease progression. Due to the rarity of this malignancy, the management of NECC is difficult and associated with uncertainty.²

Case Illustration

History, Examination, and Management

We report a case, 51 years old, para 2, an Indonesian woman who came to our hospital with chief complaint post-coital vaginal bleeding for 9 months before admission. Initially, she went to a district public hospital that found a cervical bulky mass and then performed punch biopsy, the histopathology result was an adenocarcinoma well-differentiated, no lymph vascular invasion, DD/ adenosquamous, neuroendocrine tumor. Then she was referred to our hospital.

Our gynecology examination revealed a cervical exophytic fragile mass, easily bleeding, with necrotic part size 3x3x3,5 cm, already infiltrated both parametrium but not reach the pelvic wall correspond to stage IIB cervical cancer. A chest x-ray examination showed no radiological abnormalities in the lung and heart.



Picture 1. Cervical appearance

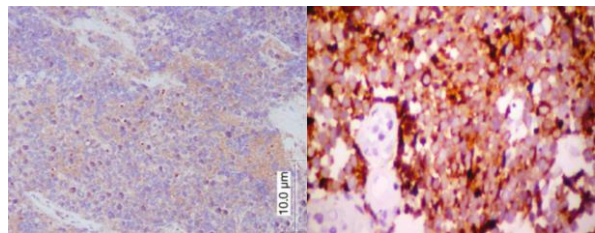
The transvaginal ultrasound found cervical mass size 3,28x2,65x4,17cm with active vascularization correspond to cervical malignancy. No pelvic or paraaortic lymph node enlargement.



Picture 2. Transvaginal Ultrasound

We did histopathology examination review and the result was histologically suitable for epithelial malignant tumors, DD/ poorly differentiated squamous cell carcinoma, high-grade neuroendocrine carcinoma, small cell type. The pathologist suggests to proceed for immunohistochemistry examination.

Immunohistochemistry result showed that although all the sample was not typical, immunohistochemistry outward patterns can support morphological features of high-grade neuroendocrine carcinoma, small cell type. We decided to treat her with chemoradiation therapy.



Picture 3. NSE and chromogranin positive

Table.1 Immunohistochemistry result

Variables	Result
P63,p16	Negative
CEA	Positive in some tumor cell
Chromogranin	Weak positive
Synaptophysin,CD 56	Negative
NSE	Weak moderate positive

Discussion

The biology of NECC (neuroendocrine carcinoma) is different from squamous cell carcinoma or adenocarcinoma of the cervix regarding several characteristics. For example, NECC is more likely to invade the lymphovascular space and to spread to the regional lymph node basin at the time of diagnosis. 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. ⁴

Immunohistochemistry for neuroendocrine markers including chromogranin, synaptophysin, CD56, and neuron-specific enolase may aid in making the diagnosis. For establishing the diagnosis, positive staining of at least two neuroendocrine markers is recommended. SYN and CD56 are the most sensitive markers. ⁴

Several small case series have evaluated other immunohistochemistry stains in an attempt to determine additional markers that may help distinguish both between neuroendocrine and non-neuroendocrine tumors of the cervix, as well as between cervical neuroendocrine primaries versus metastatic neuroendocrine disease to the cervix. Some of the markers that have been evaluated include thyroid transcription factor-1, p16, and p63. Neuroendocrine cervical carcinomas are frequently but not always positive for thyroid transcription factor-1 and p16, but negative for p63. ²

Neuroendocrine carcinomas of the cervix have been classified into four distinct histologic types: small cell, large cell, and carcinoid (typical and atypical). While large cell carcinomas are rarer and have a distinctly different histologic appearance, they appear to behave similar to their more common counterpart, small cell carcinoma and therefore are managed the same way clinically ²

The Gynecologic Cancer InterGroup (GCIG), in 2014, also published a consensus review on the treatment of small cell NECC. They recommend radical surgery for early-stage disease, either primarily or after neoadjuvant chemotherapy. For patients with advanced-stage disease, the GCIG recommends chemoradiation or systemic chemotherapy consisting of etoposide and cisplatin. In line with the SCG and GCIG recommendations, treatment schemes for patients with NECC in the literature usually consist of radical hysterectomy followed by adjuvant chemotherapy for early-stage disease. For locally advanced and metastatic disease, definitive concurrent chemoradiation, neoadjuvant chemotherapy followed by surgery, or chemotherapy alone have been described. Various chemotherapy regimens have been reported in women with NECC and they usually differ from those typically used in squamous cell carcinoma

and adenocarcinoma of the cervix. A combination of cisplatin and etoposide are common to be used. Other chemotherapy regimens described in the literature are cisplatin/irinotecan, carboplatin/paclitaxel, and cisplatin/vincristine/bleomycin. ^{4,5}

Additionally, a few studies have suggested more interesting variables; chromogranin positivity and smoking may be associated with a poorer prognosis, while the incorporation of radical hysterectomy for the treatment of early-stage disease and use of adjuvant chemotherapy in later stages is associated with improved survival. ²

In a retrospective study of 21 patients with small cell cervical cancer, the 2- and 5-year survival rates were only 43% and 29%, respectively. In fact, of the patients with greater than IB1 disease, there were no survivors beyond 30 months. Compared with patients with squamous cell carcinomas, women with small cell tumors have 1.84 times greater risk of death ¹

Intraraphet et al (2014) study over 130 patients SCNEC patients. Five-year CSS for patients with the early-stage disease was 62.6% and for patients with advanced-stage disease was 18.1% (PG 0.001). Among the patients with advanced-stage disease, decreased survival was associated with age at diagnosis (older than 60 years: HR, 9.9; PG 0.001 and younger than 45 years: HR, 3.4; P = 0.035) and International Federation of Gynecology and Obstetrics stage IV (HR, 7.4; P = 0.024). ³

A study by Cohen et al (2010) over 188 patients, 135 had stages I-IIA, 45 stages IIB-IVA, and 8 stage IVB disease. Of those with stage IIB-IVA disease, 26.7% had surgery, 35.6% underwent chemoradiation, 24.4% had radiation therapy, 6.7% underwent chemotherapy alone, and 6.6% had other or no treatment. The 5-year disease-specific survival in stage I-IIA, IIB-IVA, and IVB disease was 36.8%, 9.8%, and 0%, respectively (P<.001). Adjuvant chemotherapy or chemoradiation was associated with improved survival in patients with stages IIB-IVA disease compared with those who did not receive chemotherapy (17.8% vs 6.0%; P < .04). On multivariable analysis, early-stage disease and use of chemotherapy or chemoradiation were independent prognostic factors for improved survival.²

Conclusion

Small cell neuroendocrine carcinoma of the uterine cervix is a rare case. The cellular behavior of the cell made diagnosis and treatment of this disease are quite difficult and associated with uncertainty. Histopathology examination accompanied by immunohistochemistry has an important role to establish the diagnosis. The treatment for early-stage is radical surgery either primarily or after neoadjuvant chemotherapy. For patients with advanced-stage disease, chemoradiation or systemic chemotherapy are the options.

References

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