Neuroendocrine Carcinoma of the Cervix (NECC)

WHAT SHOULD I KNOW?

Foundation for Women's Cancer

DESCRIPTION OF THE TUMOR/CANCER TYPE

Neuroendocrine carcinoma of the cervix (NECC) is a rare tumor category, accounting for 1-1.5% of all cervical cancers. NECC consists of different subtypes of neuroendocrine tumors (NET) – typical carcinoid (NET G1), atypical carcinoid (NET G2), and poorly differentiated neuroendocrine tumors including small cell and large cell (NET G3). Small cell carcinoma of the cervix is the most common subtype. Neuroendocrine tumors are more often found in the lungs or the pancreas, and the majority of treatment strategies are due to investigation in these other tumor locations.

NECC tumors are more aggressive than other cervical cancers. NECC is more likely to have metastasized at the time of diagnosis to regional lymph nodes and involve the lymphovascular spaces. Given the rarity of this tumor, expert pathologic review is key. Immunohistochemical (IHC) staining of the tumor with at least two of the neuroendocrine markers on IHC is usually necessary to make the diagnosis of NECC. These markers include chromogranin, synaptophysin, CD-56, and neuron-specific enolase (NSE). It is important to distinguish between NECC and other NET which may have metastasized to the cervix.

SIGNS & SYMPTOMS

Patients with neuroendocrine carcinoma of the cervix have symptoms similar to women with other subtypes of cervical cancer. These symptoms include irregular vaginal bleeding, bleeding after sex, or bleeding after menopause. A pap smear may show abnormal findings including atypical glandular cells. Other symptoms include abnormal vaginal discharge, pelvic pain, urinary or stool changes, blood in the urine or stool, unexplained weight loss, decreased appetite, abdominal bloating/pain, or pain with sexual activity.

SCREENING

While pap smears are effective in screening for cervical dysplasia and more common forms of cervical cancer (squamous cell carcinoma and adenocarcinoma), NECC is a rare aggressive variant that may not be detected early with a pap smear. If a patient develops abnormal vaginal bleeding or has other concerning symptoms or exam findings, a pap smear and cervical biopsy in the office may be needed to make the diagnosis.

TREATMENT & FOLLOW-UP

This section is intended to clarify basics and showcase how treatment and follow-up may be different for these rare types of cancer.

Role of Surgery

Similar to other types of cervical cancer, surgical removal of the uterus and cervix with evaluation of lymph nodes is often the first step in treatment for suspected early-stage disease.
Radical hysterectomy is usually performed over standard extrafascial hysterectomy for patients which NECC; however, a detailed evaluation with physical exam and imaging are necessary to determine the approach and type of hysterectomy. The role of removal of the ovaries and tubes should be discussed with the treating team prior to surgery.

Role of Chemotherapy and Radiation

For patients who are not surgical candidates, the role of chemosensitizing radiation (chemotherapy given at the time of radiation) may be an important component of treatment. For patients who can undergo hysterectomy, adjuvant chemotherapy or chemosensitizing radiation is often recommended due to the aggressive nature of NECC. Radiation after surgery may be in the form of external beam radiation (EBRT), vaginal brachytherapy (VBT), or both.

The two most common chemotherapy drugs used for the initial treatment of NECC are cisplatin and etoposide in combination. There is not a standard regimen to treat these tumors. Platinum agents such as cisplatin or carboplatin are often used. Other options, especially in the recurrent setting, may include taxol and/or topotecan.

For advanced stage disease (stage III or IV), chemotherapy is the mainstay of treatment with consideration of surgery and/or the addition of radiation (vaginal brachytherapy, EBRT, or both).

Targeted Therapy Options

For patients with advanced stage or recurrent disease, testing the DNA of the tumor for different molecular markers with next-generation sequencing may open the possibility for treatment with targeted therapies outside of standard chemotherapy. The addition of

Neuroendocrine Carcinoma of the Cervix (NECC)

WHAT SHOULD I KNOW?

Foundation for Women's Cancer

bevacizumab, a monoclonal antibody which targets new blood vessel growth, may be recommended in the setting of advanced stage or recurrent disease.

Immunotherapy Options

If the tumor has spread beyond the cervix or has recurred, the addition of immunotherapy to standard chemotherapy may help treat the cancer more effectively. Increasing data supports the use of immunotherapy for those patients undergoing chemosensitizing radiation for cervical cancer. Patients with advanced stage disease or recurrent NECC may be candidates for the use of immunotherapy. Immunotherapies target checkpoints in the immune system including PD-L1, PD-1, and CTLA-4. By blocking these checkpoints, the immune system can more effectively attack cancer cells. Examples of these drugs include pembrolizumab, dostarlimab, atezolizumab, and ipilimumab.

QUESTIONS YOU SHOULD ASK YOUR CARE TEAM ABOUT YOUR TREATMENT PLAN & FOLLOW-UP CARE

If you are not already being treated by a gynecologic oncologist, consider seeking a second opinion.

Has my pathology been reviewed at a comprehensive cancer center?

What imaging has been ordered to assess if the cancer has spread in my body?

Has my case been presented at a multidisciplinary tumor board?

Should immunotherapy be added to my regimen?

If necessary, what type of chemotherapy will be used to treat my cancer?

Are there clinical trials that I am a candidate for?

Has my tumor been sent for next-generation sequencing?

What is the goal of my treatment?

What are the chances my cancer will come back?

How will this affect my sex life?

How will we know if the treatment is working?

SGO
Society of Gynecologic Oncology

The Foundation for Women's Cancer (FWC) is a 501(c)3 nonprofit organization dedicated to supporting research, education, and public awareness of gynecologic cancers. The FWC is the official foundation of the Society of Gynecologic Oncology. Learn more at foundationforwomenscancer.org.