Primary Small Cell Neuroendocrine Carcinoma of the Vagina

Presenting in 36-year-old: Case Report

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1. Abstract

Purpose: Primary small cell neuroendocrine carcinoma of the vagina is an extremely rare malignant epithelial tumor with an aggressive behavior. Little is known about this entity since very few cases have been published. Current treatment modalities are extrapolated from small cell carcinoma of the lung, which is the most common primary site.

Case Description: We present a case of a 36-year-old G4P2A2 female with no prior history of malignancy who presented with discomfort associated to a mass in the posterior vaginal wall.

Clinical Approach: Gynecologic evaluation and surgery revealed an 8-cm friable pedunculated mass with irregular contours arising from the posterior vaginal wall. Pathologic evaluation revealed a submucosal tumor consisting of small, round cells with scant cytoplasm, fine granular nuclear chromatin, and nuclear molding. These morphologic features, along with a neuroendocrine immunophenotype are diagnostic for small cell neuroendocrine carcinoma. High-Dose Rate Brachytherapy was given to the upper vagina, as well as a chemotherapy regimen with Cisplatin and Etoposide.

Clinical Findings: Whole body bone scan performed after treatment revealed findings consistent with metastatic disease to the skull and femur. The patient was admitted to the hospital with intractable pain and pancytopenia. Bone marrow biopsy revealed tumor infiltration, for which therapy with Etoposide was restarted.

Hypothesis: Accurate diagnosis of small cell neuroendocrine carcinoma and its distinction from other carcinomas is of paramount importance, since it will determine the patient’s management and prognosis.

2. Case Report

This is the case of a 36-year-old G4P2A2 female with no prior history of systemic illness or malignancy who presented with a bulging mass of increasing size in her vagina associated to discomfort. Her past medical history was unremarkable including regular menstrual periods since menarche at age 11, no history of sexually transmitted disease or cigarette smoking. Physical examination revealed a pedunculated friable mass arising from the posterior vaginal wall. Pap smear was negative for intraepithelial lesion or malignancy. Excisional biopsy was performed for pathologic diagnosis. Various hematoxylin and eosin (H & E) stained slides were evaluated and immunohistochemistry was performed on formalin fixed paraffin embedded tissue. A submucosal malignant neoplasm (Figure 1), was identified consisting of closely packed cells with round to oval hyperchromatic nuclei showing fine stippled chromatin and inconspicuous nucleoli (Figure 2). Cytoplasm was scant and cell borders were indistinct (Figure 3). Areas of comedo-type necrosis were identified. Immunohistochemistry (IHC) showed a high proliferation index (Figure 4), cells positive for chromogranin, synaptophysin (Figure 5), neuron specific enolase, and CD56 (Figure 6). This is consistent with a neuroendocrine phenotype. Tumor cells were focally positive for CK 8/18 and negative for TTF-1. Initial PET CT showed no evidence of metastatic disease. The patient was treated with combination radiotherapy and chemotherapy. The clinical course was complicated with metastatic disease involving bone marrow, skull, and femur associated to intractable pain and pancytopenia. Despite additional chemotherapy, the patient developed bilateral pleural effusions and died 8 months after diagnosis.

3. Discussion

Small cell neuroendocrine carcinoma is a malignant epithelial tumor with an aggressive behavior. It is most commonly diagnosed in lung as a primary site. However, it has been described in many other sites, including the female genital tract (cervix, ovary, endometrium, vagina, vulva). Primary small cell neuroendocrine carcinoma of the vagina is extremely rare, with less than 30 cases reported. Little is known about this entity and current treatment modalities are extrapolated from small cell carcinoma of the lung. The mean age at diagnosis is 59 years and women typically present with post-menopausal bleeding. Lesions have a propensity for early widespread dissemination and one year survival after diagnosis is less than 15%.

Accurate diagnosis of small cell neuroendocrine carcinoma and its distinction from other carcinomas is of paramount importance, since it will determine the patient’s management and prognosis. The differential diagnosis includes small cell variant of squamous cell carcinoma (SCC), basaloid carcinoma, metastatic disease, and other small cell blue tumors like lymphoma and sarcoma. Classic morphologic findings that suggest a neuroendocrine differentiation are tightly packed, small round to oval and spindle cells with scant cytoplasm, ill-defined borders, fine granular nuclear chromatin, nuclear molding and no definitive epithelial differentiation. Electron microscopy showing scattered dense-core neurosecretory granules confirm the neurosecretory nature of these rare tumors. However this practice has greatly been replaced by the use of immunohistochemistry (synaptophysin, chromogranin, NSE, CD56). TTF-1 positivity would favor a lung primary, but has been described in primary vaginal cases, as well as other non-pulmonary sites. There is no consensus regarding optimal therapy and current therapies have resulted in poor outcomes. For small localized lesions surgical resection followed by chemoradiation can be considered. Small cell carcinomas are clinically aggressive, with rapid recurrences and distant metastases. This entity, although rare, should be included in the differential diagnosis of poorly differentiated vaginal lesions to ensure prompt diagnosis and treatment.

4. References