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Primary Synchronous Neuroendocrine, Adenocarcinoma and Squamous Cell Carcinoma of Cervix- A Case Report

Manisha Vernekar[1*], Amit Mandal[2], Gaurav Singh[3], Dipanwita Banerjee[1] and Ranajit Mandal[4]

[1]Specialist, Department of Gynaecological Oncology, Chittaranjan National Cancer Institute, 37 S. P. Mukherjee Road, Kolkata, West Bengal, India
[2]Senior Resident, Department of Gynaecological Oncology, Chittaranjan National Cancer Institute, 37 S. P. Mukherjee Road, Kolkata, West Bengal, India
[3]DNB Trainee, Department of Pathology, Chittaranjan National Cancer Institute, 37 S. P. Mukherjee Road, Kolkata, West Bengal, India
[4]Specialist and Head, Department of Gynaecological Oncology, Chittaranjan National Cancer Institute, 37 S. P. Mukherjee Road, Kolkata, West Bengal, India

***Corresponding author:** Manisha Vernekar, Specialist, Department of Gynaecological Oncology, Chittaranjan National Cancer Institute, 37 S. P. Mukherjee Road, Kolkata, West Bengal, India, Tel: 9051239019, E-mail: manu_1486@yahoo.co.in

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Abstract

It is rare to have the simultaneous presence of three neoplasm including neuroendocrine carcinoma, glandular and squamous cell carcinoma in a uterine cervix. The etiologies of cervical epithelial neoplasms are associated with various types of Human Papilloma Virus and are well known to be associated with squamous cell carcinoma and other types of epithelial neoplasms of the uterine cervix. We present a case of a 45-year-old woman with synchronous neuroendocrine, adenocarcinoma and squamous cell carcinoma of cervix.

Keywords: Squamous Carcinoma Cervix; Adencarcinoma Cancer Cervix; Neuroendocrine Carcinoma; Human Papilloma Virus

Introduction

It is rare to have three synchronous neoplasms including neuroendocrine carcinoma, squamous cell and glandular neoplasia in a uterine cervix [1]. Neuroendocrine carcinoma of the cervix (NECC) is a rare variant of cervical cancer. The prognosis of women with neuroendocrine cancer cervix is poor and there is no standardized therapy for this type of malignancy based on controlled trials [2]. Here we report a case of triple cervical neoplasms: Neuroendocrine carcinoma and moderately differentiated infiltrating adenosquamous carcinoma of cervix. The etiologies of cervical epithelial neoplasms are associated with various types of Human Papilloma Virus (HPV). HPV types 16 and 18 are well known to be associated with squamous cell carcinoma and other types of epithelial neoplasms of the uterine cervix [3].

Case report

A 45-year-old female, married for 25 years with one living issue coming from urban areas of West Bengal, came with pain abdomen in our institute on 7/11/2017. She consulted the private doctor for post-menopausal bleeding following menopause for 3 years in September 2017 and diagnosed with uterine polyp on hysteroscopy. She underwent hysteroscopic polypectomy in private nursing home on 5/10/2017 for the same. Histopathology report suggested poorly differentiated adenocarcinoma.

On examination her general condition was good with no pallor, icterus, pedal edema. Her systemic examinations did not show any abnormalities. Per abdominally, on palpation was soft and no obvious mass felt. On per speculum there was an irregular growth around 1.5x1.5cm in size over cervix, vaginal wall free. Pelvic examination revealed a hard, irregular nodular growth over cervix. Vaginal wall, bilateral fornices were free. Uterus was free and normal size. Rectum mucosa and bilateral parametrium were free on per rectum examination. Clinically, cervical cancer stage Ib1. Laboratory and radiological test results were within normal limit.

Radical hysterectomy and bilateral pelvic node dissection were performed in our institute on 17/11/17.

Grossly, cervix showed a 2cm tumors along with the small cervical polyp. Microscopically, tumors composed of nests, trabeculae and islands of uniform cells with round to oval nuclei and eosinophilic cytoplasm. Tumor cells at places formed small acini (Neuroendocrine carcinoma). Mitotic igures were seen. Focal areas showed moderately differentiated infiltrating adenosquamous carcinoma with metastasis in pelvic lymph nodes. Carcinoma has invaded >2/3rd of the total thickness of the cervix. Vaginal resection margin involved. Radial resection margin, body of uterus and parametria were free of lesion, pTNM staging was pT1b1N1Mx.

Immunohistochemistry showed the lesional cells in which the majority of the tumor was positive for synaptophysin and chromogranin. The Ki67 (Mibi) labeling index was 65%. P63 highlights the squamous cell carcinoma component. CEA stains the glandular component. The IHC studies were suggestive of combination of neuroendocrine carcinoma and moderately differentiated infiltrating adenosquamous carcinoma.

Following radical hysterectomy, patient received concurrent chemoradiotherapy in the department of radiation oncology. She completed 25#/50Gy of External Beam Radiation (EBRT) and 7Gy/3 cycles of Brachytherapy. Patient is on regular follow up without any symptoms.

Discussion

The simultaneous presence of three neoplasms, including neuroendocrine, squamous cell, and glandular neoplasms, in a uterine cervix is also rare, although two different neoplasms occasionally may be seen simultaneously [1].

The etiologies of cervical epithelial neoplasms are associated with various types of Human Papilloma Virus (HPV). HPV types 16 and 18 are well known to be associated with squamous cell carcinoma and other types of epithelial neoplasms of the uterine cervix.

Almost all neuroendocrine carcinomas of the cervix are associated with HPV 18 or seldom HPV 16 [3].

Neuroendocrine neoplasms may occur in the uterine cervix, although rarely; it accounts for 0.5-1% of all malignant tumors of the uterine cervix [1].

Adenosquamous carcinoma of cervix is also an occasionally found form of cancer having malignant squamous cells and malignant glandular cells, and accounts for ~10% of cervical carcinomas. May arise from sub columnar reserve cells in basal layer of endocervix [2].

Neuroendocrine carcinomas most likely develop from neuroendocrine cells occurring in the normal endocervix or from stimulated multipotential reserve cells of the endocervical epithelium undergoing neuroendocrine metaplasia and hyperplasia [3].

Neuroendocrine tumors of uterine cervix are divided into small and large cell type as well as carcinoid and atypical carcinoid [4]. Small cell neuroendocrine carcinoma of the uterine cervix is a rare tumor with a highly aggressive clinical course and poor prognosis due to the high frequency of lymph node involvement at an early stage [5].

The definitive diagnosis of neuroendocrine tumors can be achieved through immunohistochemical staining. Epithelial membrane antigen (EMA), cytokeratin 7 (CK7), cytokeratin 19 (CK19), chromogranin, and synaptophysin staining are diagnostic. Polymerase chain reaction (PCR) study of these viruses is also crucial because of the strong relationship with human papillomavirus (HPV) type 16 and 18 [2].

Nagao, et al. [5] suggested that patients with an early-stage disease of neuroendocrine carcinoma might achieve a significant survival if treated by a definitive operation, followed by platinum-based combination chemotherapy. These findings indicated that patients with FIGO stage Ib to IIa SCNEC who received adjuvant platinum-based chemotherapy were likely to have a better survival than patients who received adjuvant CCRT (The 5-year OS, 52.5% vs. 45.5%).

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