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RESEARCH ARTICLE **OPEN ACCESS**

NEURO ENDOCRINE TYPE OF CARCINOMA CERVIX: LONG TERM SURVIVAL AND REVIEW OF LITERATURE

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ABSTRACT

Neuroendocrine carcinomas of the cervix are rare, and account for only 2% of all cervical cancers. the diagnostic and therapeutic management of these tumors is challenging and is extrapolated from other locations of neuroendocrine tumors. Rare cases of neuroendocrine tumors of the cervix have been reported in the literature and were associated with aggressive behavior and poor prognosis. We report the case of a 46 years old woman, diagnosed with locall advanced cervical neuroendocrine carcinoma who received neo ajuvant chemotherapy followed by radical radical radiotherapy with concurrent chemotherapy with good control of her disease even at the end of 30 months.

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INTRODUCTION

Neuroendocrine neoplasias (NENs) are aggressive malignancies derived from neuroendocrine cells. The term neuroendocrine refers to the fact that the tumor cells originate from the embryonic neuroectoderm and display an immunohistochemical profile consistent with endocrine glandular cells (1). They may or may not secrete peptide hormones. In humans, NENs are typically located in the gastrointestinal tract, the pancreas, and the lungs and are subdivided in well-differentiated NENs and poorly differentiated NENs (2). Well-differentiated NENs include neuroendocrine tumors (NET) G1 (also known as typical carcinoid), NET G2 (also known as atypical carcinoid), and NET G3. Poorly differentiated neuroendocrine carcinomas (NECs) include small cell NEC and large cell NEC (Table 1). Rarely, NENs may also occur in other organs such as the female genital tract (3). Neuroendocrine carcinoma of the cervix (NECC) is an aggressive histological variant of cervical cancer accounting for about 1–1.5% of all cervical cancers (1, 4). Small cell NEC is the most common type of NECC, whereas well-differentiated NETs, especially NET G1 (typical carcinoid) and NET G2 (atypical carcinoid), are very rare at this location (5). Grading of NECC is similar to NEN of other locations like lung or the digestive system (Table 1). Due to the rarity of this malignancy, the management of NECC is difficult and associated with uncertainty. An interdisciplinary approach is necessary, because most studies investigating the treatment of neuroendocrine tumors have been performed in patients with tumors in organs other than the cervix, mostly the lung and pancreas (4, 6). Specifically, neuroendocrine tumors mainly occur in the lungs, and thus treatment schedules for neuroendocrine tumors originating in other organs are similar to those. A 46 year old post menopausal female presented with history of bleeding per vaginum since 1 month,white discharge pv since 1month.she is a known diabetic and on regular medication since 3years.on examination :A 4*3 cms ulceroproliferative growth arising from both lips of cervix protruding in upper 2/3rds of vagina left parametrium involved right parametrium free ,rectal mucosa soft .

MRI WITH CONTRAST: Cervix is bulkywith lobulated lesion which is relatively homogenous and well defined and is

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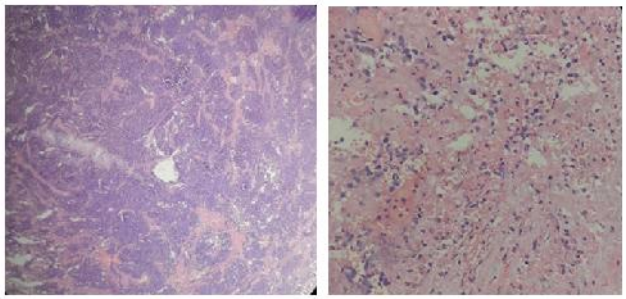
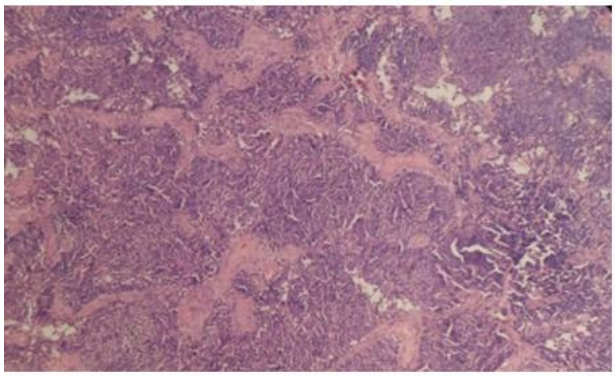
iso-hypo on T1hyper on T2showing restriction on diffusion and showing enhancement on contrast administration .It is measuring approximately 60*39*59 mm(AP*TR*CC),and is seen extending superiorly into lower uterine segment and inferiorly into upper part of vagina .There is suspicious breach of cervical stroma on left side with parametrial invasion abutting parametrial vessels.

BIOPSY: small cell carcinoma of cervix – neuro endocrine type

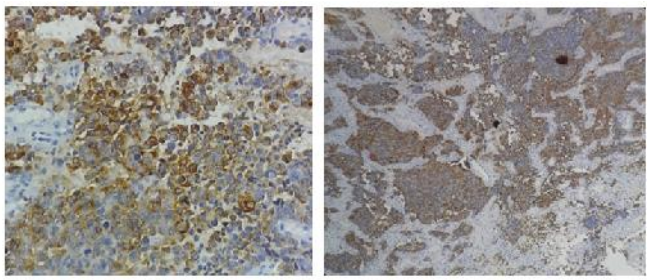
IHC: Chromogranin positive in majority of the cells – neuroendocrine type of a cervix.



SOLID NESTS AND ISLANDS IN LOW POWER VIEWSTROMA –NECROSIS AND NEUTOPHILSIN LOW POWER VIEW



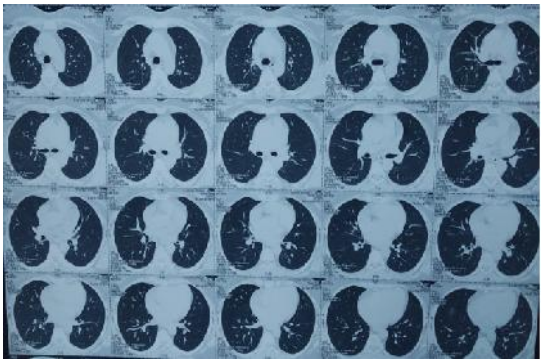
HIGH POWER VIEW



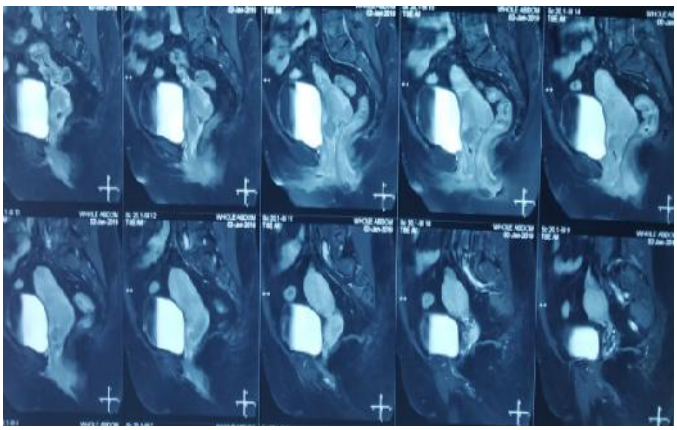
CHROMOGRANIN POSITIVE HIGH POWERCHROMOGRANIN POSITIVE LOW POWER

The patient received 2 cycles of neoadjuvant chemotherapy cisplatin 75 mg / m2 on D1and etoposide 100mg / m2 (D1,D2,D3) 3 weeks apart followed by radical radiotherapy with EBRT to a dose of 5400 cGy along with 2 cycles of concurrent cisplatin and etoposide followed by 3 fractions of HDR brachytherapy ,7Gy /fraction. Patient was on follow up for 30 months and is still with good with clinical and radiological control.

HRCT CHEST – NO LUNG METS AT PRESENTATION



MRI PELVIS SHOWING CERVICAL GROWTH



MRI PELVIS SHOWING CERVICAL GROWTH

DISCUSSION

Neuroendocrine tumors originate from Kulchitsky cells which can be found in all parts of the body, cervical localization is rare and represents only 3% of cervical tumors which are predominantly squamous cell carcinomas (7). During the last two decades, and unlike squamous cell carcinoma of the cervix, an increase in the incidence of small cell neuroendocrine carcinomas has been observed. These tumors occur at a median age of 40 years (20-87) (8), which appears younger than for squamous cell carcinoma of the cervix. The clinical symptomatology is nonspecific it is most often metrorrhagia, recurrent leucorrhea or pelvic mass. The diagnosis is based on the histological study, neuroendocrine differentiation can be shown by many methods. The most important of all these methods is immunohistochemical study with chromogranin A, which was implemented in this study. Chromogranin A is a more specific stain on this issue. In the literature, there are studies that have been conducted to show the presence and significance of neuroendocrine differentiation in a specific tumor, especially on gastrointestinal tract and lungs, and these studies have concluded that this differentiation is related with poor prognosis and survival (9).Race, age and stage of the tumor seem to be the prognostic factors also smoking and advanced stage are reported to be poor prognostic factors for survival in patients with NE small cell carcinoma of the cervix . Of all these, the most important prognostic factor is lymph node metastasis. While the lymph node invasion in neuroendocrine tumors is more than 30% (10). Given the strong trend towards regional and remote dissemination, the assessment should include abdomino-pelvic imaging, preferably magnetic resonance imaging. In order to improve

ganglion staging FDG-PET is significantly more accurate than computed tomography (CT) and is recommended for loco-regional lymph node and extra pelvic staging. The metabolic dimension of the technique provides additional prognostic information, allowing a good follow-up of the target lesions, it becomes the tool of choice when one wishes to appreciate at best effectiveness of a treatment (10). The treatment of cervical neuro endocrine carcinomas is modeled after squamous cell carcinoma, taking into account the characteristics of neuroendocrine tumors of the lung. In the case of locally advanced disease, neo adjuvant chemotherapy with cisplatin and etoposide for 2 cycles followed by concurrent chemoradiation with cisplatin and etposide followed by 3 fracrions of HDR brachytherapy, 700cGy per fraction .After 30months of follow-up the patient is still with good clinical and radiological control.

CONCLUSION

We found that NECC is a rare form of cervical cancer with a poor prognosis, but multimodality treatment with radical surgery and adjuvant or neoadjuvant chemotherapy with etoposide and cisplatin is the mainstay of treatment for early stage disease while combined radiochemotherapy and chemotherapy are appropriate for women with locally advanced or recurrent NECC. In light of the poor prognosis of women with NECC despite aggressive treatment, novel therapeutics such as immune check-point inhibitors and targeted agents should be incorporated into the management even without controlled evidence.

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