

# Utility of Immunohistochemical Markers in the Diagnosis of Small Cell Neuroendocrine Carcinoma Cervix - A Case Report

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**Abstract:** Neuroendocrine carcinoma (NEC) of cervix is an aggressive histological variant of cervical cancer accounting for about 1-1.5% of all cervical cancers. High grade (G3) neuroendocrine carcinoma is highly aggressive tumours and frequently present at an advanced stage. Immunohistochemical staining for neuroendocrine markers provide support for diagnosis. The 5 year survival for small cell neuroendocrine carcinoma (SCNEC) of all stages reported to be 14-39% with poorer survival in higher stage disease. The management of high grade neuroendocrine carcinoma may include specific neuroendocrine based systemic chemotherapy and radiotherapy including axial sites.

**Keywords:** SCNEC, aggressive, immunohistochemistry.

## 1. Introduction

Cervical neuroendocrine tumours are extremely rare and are primarily defined by the same architectural and cytological features used at other sites. High grade neuroendocrine carcinomas are composed of high grade malignant cells and may be of either small cell or large cell type. Both types are considered grade 3. High grade NEC of small cell type is far the most common of these tumours<sup>1</sup>.

## 2. Case Report

Our case is of a 47 year old female who presented with h/o postmenopausal bleeding, loin pain and increased frequency of urination of about 4 months duration. Perspeculum examination revealed an ulceroproliferative nodular growth

in cervix from 11 'o clock to 3' o clocks anteriorly extending in to vagina involving anterior fornix, posterior fornix is free. A pap smear examination showed malignant small round cells arranged singly scattered and rosette like fashion (Figure 1)

Then a cervical biopsy done and histopathology showed ectocervical epithelium with focal CIN II change (Figure 2) and sub epithelial region showed an infiltrative neoplasm arranged in nests, sheets, rosettes and focal glandular pattern. (Figure 3) The cells are small with high N/C ratio and pleomorphic hyperchromatic nuclei. (Figure 4) Stroma is fibrocollagenous. No lymphovascular or perineural invasion seen. No necrosis. IHC markers synaptophysin (Figure 5) and chromogranin were positive.

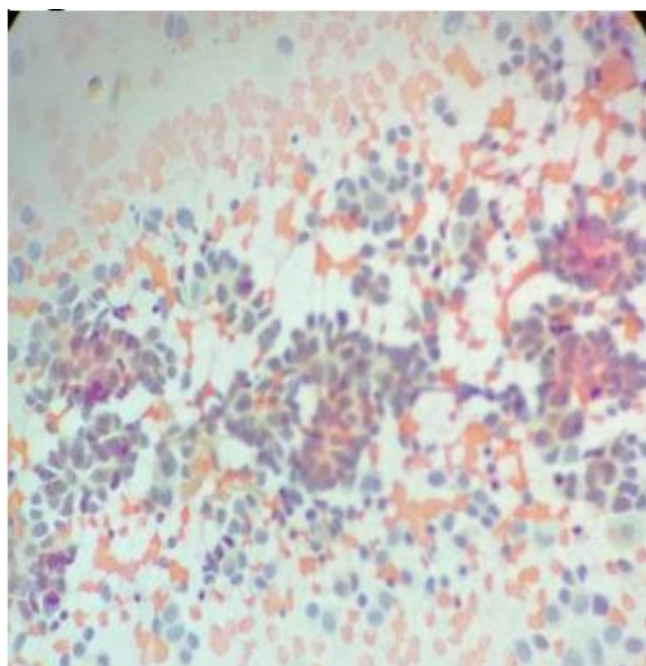


Figure 1

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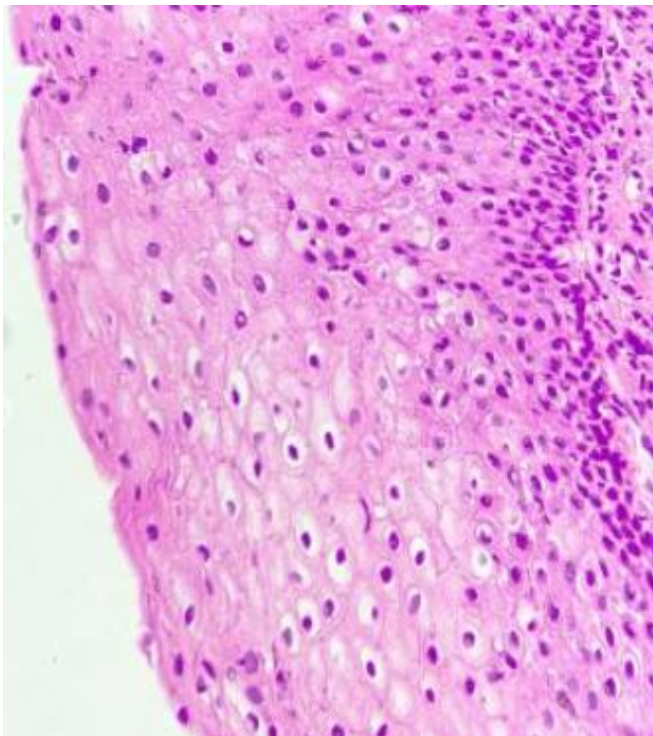


Figure 2

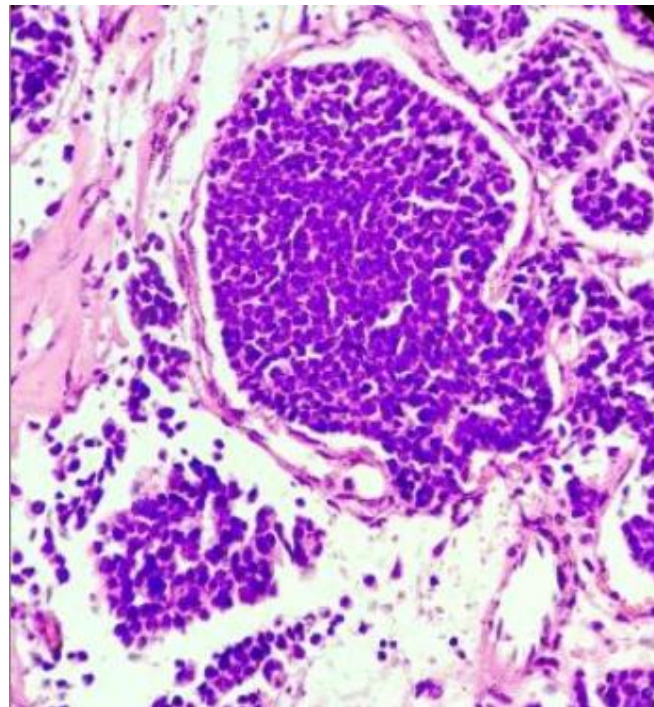


Figure 4

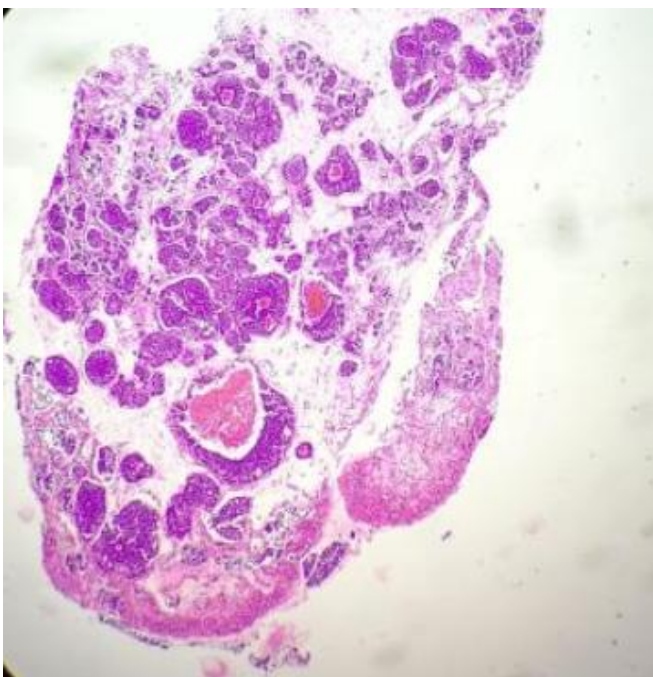


Figure 3

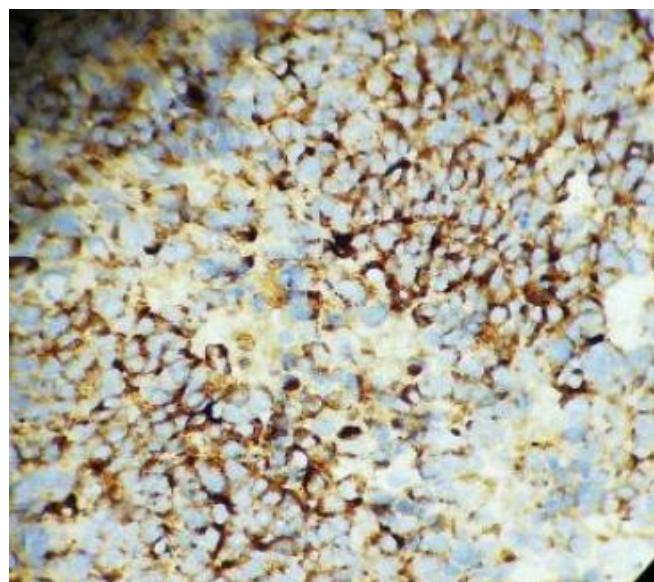


Figure 5

### 3. Discussion

Neuroendocrine differentiation occurs within neoplasms arising from cervical epithelium. Cells that express neuroendocrine markers are present in some cases of cervical adenocarcinoma insitu and could be the precursor of cervical neuroendocrine tumours.<sup>2</sup> Grade 1 neuroendocrine tumours (carcinoid) generally follow an indolent course. Grade 2 neuroendocrine tumours (atypical carcinoid) are more aggressive neoplasms.<sup>3</sup> High grade neuroendocrine carcinomas (grade 3) are composed of high grade malignant cells and may be of either small cell or large cell type.<sup>4</sup> SCNEC are rare, extremely aggressive even at low stage.

<sup>5</sup>Initially small cell neuroendocrine carcinomas of the cervix may be misdiagnosed as cervical myomas<sup>(6, 7)</sup> such as the case in our study or rapidly growing polyps in the cervix. Abnormal vaginal bleeding is the most common presentation and some have pelvic pain and pressure-like discomfort.<sup>(7, 8)</sup>

SCNEC is characterised by monotonous population of small cells with ovoid hyperchromatic nuclei, often exhibits moulding and IHC for neuroendocrine markers provide support for diagnosis.<sup>4</sup> Cervical SCNEC is reliably associated with high risk HPV, HPV -18 is identified more frequently than in cervical squamous cell carcinomas.<sup>6</sup> SCNEC usually accompanied by insitu or invasive

carcinoma. In our case ectocervix showed a focus of CIN II with koilocytic change. The pap smear cytology showed malignant small round cells and rosettes however proceeded with biopsy and immunohistochemistry for accurate diagnosis. It's very important to differentiate these small blue round cell tumours from lymphoms, small cell squamous cell carcinomas, basaloid squamous cell carcinomas, embryonal rhabdomyosarcomas, and metastasis.<sup>(9, 10)</sup> Immunohistochemical markers synaptophysin and chromogranin A can detect neuroendocrine differentiation.<sup>9</sup> Our case showed positivity for synaptophysin and chromogranin suggestive of neuroendocrine carcinoma. 5 year survival for SCNEC of all stages is reported to be 14-39%, with poorer survival in higher stage disease.<sup>1</sup>

#### 4. Conclusion

SCNEC is rare, aggressive tumour prone for local distant metastasis even at low stage. The management of this tumour include specific neuroendocrine based systemic chemotherapy and radiation therapy including axial sites. Hence identification by thorough investigations and histopathology with immunohistochemistry is necessary for accurate diagnosis.

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