Case Report

A rare variant of carcinoma of the cervix: neuroendocrine tumour

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ABSTRACT

Neuroendocrine neoplasm that occurs in the uterine cervix is rare. It accounts for 0.5-1% of all malignant tumours of the uterine cervix. A 55 years old female patient complained of postmenopausal bleeding and history of foul smelling discharge per vagina since 1 month. On examination cervix appeared bulky, both lips indurated, bleeds on touch, both parametrium involved but not up to pelvic wall with bulky uterus. Vagina and per rectal mucosa was free. Clinical diagnosis of carcinoma cervix, stage 2B was made. Cervix biopsy with HPE revealed squamous epithelium of cervix showing neoplastic cells arranged in nests and prominent perivascular pattern, small round cells with minimal cytoplasm and hyperchromatic nucleus, abundant mitosis, cells showed rosette pattern and isolated foci of cell debris and necrosis. Diagnosis of neuroendocrine tumour of cervix was considered. Immunohistochemistry for cytokeratin, neuron specific enolase, chromogranin and synaptophysin was positive, confirming the final diagnosis of neuroendocrine carcinoma cervix (High grade of small cell type). Recognition of Neuroendocrine carcinoma cervix is important for appropriate therapy & management since these patients have worse clinical outcomes when compared with conventional squamous /adeno carcinoma of cervix. Immunohistochemistry should be supplemented with ultrastructural studies for confirmation and correct categorisation of carcinoma cervix for appropriate management.

Keywords: Carcinoma cervix, Immunohistochemistry, Neuroendocrine tumour

INTRODUCTION

Neuroendocrine neoplasm may occur in uterine cervix. It accounts for 0.5-1% of all malignant tumours of the uterine cervix.^{1,2} It is generally accepted that the integration of HPV into the host genome is the single most important event in evolution of cervical cancer.³ Neuroendocrine carcinoma of cervix is associated with HPV18 and seldom HPV16.⁴ It develops from neuroendocrine cells in the normal endocervix or from stimulated multipotent reserve cells of endocervical epithelium undergoing neuroendocrine metaplasia & hyperplasia.⁵ Neuroendocrine tumours is divided into well differentiated (carcinoid and atypical carcinoid) and poorly differentiated (small cell & large cell).³ tumours. Small cell neuroendocrine tumour of cervix is rare with highly aggressive clinical course & poor prognosis due to

high frequency of lymphnode involvement at an early stage.^{4,6} It is important to differentiate small cell from other malignant tumours of the cervix. Morphological features, cytopathology, histopathology & immunocytochemistry play an important role in accurate diagnosis.

CASE REPORT

A 55 years old female patient P7L7 reported to ESIC medical college and PGIMS on June 2013 complained of postmenopausal bleeding and history of foul smelling discharge per vagina since 1 month. Clinically cervix appeared bulky, both lips indurated, bled on touch, bulky uterus with both parametrium involved but not up to pelvic wall. Vagina and per rectal mucosa was free. Clinical diagnosis carcinoma cervix stage IIB.

Ultrasonogram revealed bulky uterus with haematometra, cervical mass and both ovaries appeared normal. On cervical dilatation 50-60 ml of pus was drained. Ectocervical biopsy was done and sent for HPE which revealed tumour cells arranged as undifferentiated cells showing neoplastic cells arranged in nests with rosette pattern (Figure 1). The tumour cells presented pleomorphic nuclei with hyperchromatism, hyperchromatic granular chromatin & scanty cytoplasm. Moreover, the nuclear cytoplasmic ratio was high & there was an evidence of increased mitosis as well as apoptotic changes (Isolated foci of cell debris & necrosis surrounding the tumour) (Figure 2). Immunohistochemical study was done aiming to recognise neuroendocrine differentiation of tumour with cytokeratin, neuron specific enolase, chromogranin & synaptophysin & the cervical tumour demonstrated positivity (Figure 4). CT Whole Abdomen done shows paraaortic nodal involvement (Figure 5).

The histopathology report of small cell type of neuroendocrine cancer of uterine cervix made. Patient referred for chemoradiotherapy and is on regular follow up with no recurrence.

Figure 1: Perivascular rosette like arrangement of tumour cells with frequent mitosis.

Figure 2: Isolated foci of cell debris & necrosis surrounded by the tumour cells - 400x.

Figure 3: Perivascular rosette like arrangement of tumour cells - 100x.

Figure 4: Immunohistochemistry.

Figure 5: CT whole abdomen - paraaortic node.

DISCUSSION

Cervical cancer encompasses various histologic types, squamous cell (70%), adenocarcinoma (25%), neuroendocrine mainly small cell tumour represent (2%) of all cervical malignancies.⁶ Small cell neuroendocrine

carcinoma was first described in 1957 by Reagan et al. Later in 1997, College of American Pathologists and National Cancer Institute proposed the classification of neuroendocrine carcinoma identical to that used for pulmonary neuroendocrine neoplasm. Pap smear is not sensitive for diagnosis of neuroendocrine cancer hence cervix biopsy is mandatory for diagnosis.

Small cell cancer of neuroendocrine origin are considered to be poorly differentiated variety. It is a rare tumour with a highly aggressive clinical course & poor prognosis due to high frequency of lymphnode involvement at an early stage.⁷ The normal endocervix contains as many as 20% of argyophilic cells resembling endocrine cells, cervical neuroendocrine tumour formation can arise from these cells.⁹ Savargaonkar et al. reported that neuroendocrine differentiation was present in 20.9% of his series study of cervical cancer.⁵ Clinically, abnormal vaginal bleeding is the most commonly reported symptom.

The distinction of squamous, glandular & neuroendocrine cancer of the cervix is clinically significant for at least 2 reasons. First, a poorly differentiated cancer of glandular origin, even with early invasion is likely to have a worse prognosis than a similar squamous tumour.¹¹ Second, neuroendocrine cancer are inherently more aggressive than their squamous counter parts & are managed with different protocols.¹² Staging of neuroendocrine tumour of the cervix follows that for traditional cervical cancer.¹⁶ Early lymphatic spread to the regional lymph nodes was noted in 40% of stage 1B small cell cancers <3 cm in diameter and 60% of small cell cancer demonstrated lymphovascular invasion at the time of diagnosis. Bone, supraclavicular lymphnode & lungs are common sites of extrapelvic disease spread. Radiographic evaluation include CT/PETCT.¹⁵ Expression of cytokeration, neuron specific enolase, chromogranin & synaptophysin are used as markers of neuroendocrine cancer. Neuroendocrine cancer of the cervix is regarded as highly aggressive tumours with subclinical haematogenous & lymphatic metastases even in early disease. Neuroendocrine features in poorly differentiated carcinomas of the cervix indicate a poor outcome.¹³ In a recent study, the 5 year survival rate of patients with FIGO stage I B1 disease was between 50% and 60%, which was poorer than 90% rate for patients with stage I B1 squamous cell carcinoma.¹⁴

CONCLUSION

It is important to differentiate small cell neuroendocrine tumour from other malignant tumours of uterine cervix. The diagnosis depends on combination of light microscopy & immunohistochemistry. Morphological features play an important role in making a diagnosis and Immunohistochemistry studies offer an additional useful assistance. Early stage disease is associated with lymphnode metastasis, multimodality treatment approach, surgery with adjuvant chemotherapy. In late stage disease, primary chemoradiation is the treatment of choice followed by regular follow up. The goal of this

manuscript is to provide an insight into neuroendocrine tumour of the cervix.

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REFERENCES

1. Gilks CB, Young RH, Gersell DJ, Clement PB. Large cell carcinoma of uterine cervix: a clinicopathologic study of 12 cases. *Am J Surg Pathol.* 1997;21(8):905-14.
2. Huang L, Li C, Chen C, Lee C, Chu P. Small cell carcinoma of the uterine cervix: a case report with emphasis on cytopathological finding. *Tzu Chi Med J.* 2006;18(6):456-61.
3. Mannion C, Park WS, Man YG, Zhuang Z, Saavedra AJ, Tavassoli FA. Endocrine tumors of the cervix: morphologic assessment expression of human papilloma virus, and evaluation for loss of heterozygosity on 1p, 3p, 11q, and 17p. *Cancer.* 1998;83:1391-400.
4. Conner MG, Richter H, Moran CA, Hameed A, Saavedra AJ. Small cell carcinoma of the cervix: a clinicopathologic and immunohistochemical study of 23 cases. *Ann Diagn Pathol.* 2002;6:345-8.
5. Savargaonkar PR, Hale RJ, Mutton A, Manning V, Buckley CH. Neuroendocrine differentiation in cervical carcinoma. *J Clin Pathol.* 1996;49:139-41.
6. Saavedra AJ, Gersell D, Gilks CB, Henson DE, Lindberg G, Santiago H, et al. Terminology of endocrine tumours of uterine cervix: results of a workshop sponsored by the college of American pathologists and the national cancer institute. *Arch Pathol Lab Med.* 1997;121(1):34-9.
7. Bermudez A, Vighi S, Garcia A, Sardi J. Neuroendocrine cervical carcinoma: a diagnostic and therapeutic challenge. *Gynaecol Oncol.* 2001;82(1):32-9.
8. Koch CA, Azumi N, Furlong MA, Jha RC, Kehoe TE, Trowbridge CH, et al. Carcinoid syndrome caused by an atypical carcinoid of the uterine cervix. *J Clin Endocrinol Metab.* 1999;84(11):4209-13.
9. Stockdale AD, Leader M, Philips RH, Henry K. The carcinoid syndrome and multiple hormone secretion associated with a carcinoid tumour of the uterine cervix Case report. *Br J Obstet Gynaecol.* 1986;93(4):397-401.
10. Benda JA. Histopathologic prognostic factors in early stage cervical carcinoma. *J Natl Cancer Inst Monogr.* 1996;(21):27-34.
11. Ambros RA, Park JS, Shah KV, Kurman RJ. Evaluation of histologic, morphometric and immunohistochemical criteria in the differential diagnosis of small cell carcinoma of the cervix with particular reference to human papillomavirus types 16 and 18. *Mod Pathol.* 1991;4:586-93.

12. Hellweg DG, Doeberitz M, Trunk MJ. Malignant tumour, neuroendocrine types. In: Hellweg DG, Doeberitz M, Trunk MJ, eds. *Colour Atlas of Histopathology of the Cervix Uteri*. 2nd ed. New York: Springer Science & Business Media; 2005: 165-166.
13. O Hanlan KA, Goldberg GL, Jones JG, Runowicz CD, Ehrlich L, Rodriguez RL. Adjuvant therapy for neuroendocrine small cell carcinoma of the cervix: review of the literature. *Gynaecol Oncol.* 1991;43:167-72.
14. Viswanathan AN, Deavers MT, Ihingran A. Small cell neuroendocrine carcinoma of the cervix outcome and patterns of recurrence. *Gynaecol Oncol.* 2004;93:27-33.
15. Baum RP, Swietaszczyk C, Prasad V. FDG-PET/CT in lung cancer: an update. *Front Radiat Ther Oncol.* 2010;42:15-45.
16. Pecorelli S, Zigliani I, Odicino F. Revised FIGO staging for carcinoma of the cervix. *Int J Gynaecol Obstet.* 2009;105:107-8.
17. Chen J, Macdonald OK, Gaffney DK. Incidence, mortality, and factors of small cell carcinoma of the cervix. *Obstet Gynaecol.* 2008;111:1394.
18. Zivanovic O, Leitao MM Jr, Park KJ, Zhao H, Diaz JP, Konner J, et al. Small cell neuroendocrine carcinoma of the cervix: analysis of outcome, recurrence pattern and the impact of platinum-based combination chemotherapy. *Gynaecol Oncol.* 2009;112:590-3.

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