

# Small cell carcinoma of cervix: Rare and enigmatic

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## ABSTRACT

Small cell carcinoma of the cervix is a rare, poorly differentiated neuroendocrine tumor of cervix showing a high propensity to spread to lymph nodes as well as distant metastasis. Earlier considered to be a variant of squamous cell carcinoma, it is now acknowledged as a distinct entity showing markers of neuroendocrine differentiation. Because of the dismal prognosis, it is important to make early diagnosis and to differentiate it from a small cell variant of squamous cell carcinoma and other differentials. We present a case of a 45-year-old female who presented with cervical growth.

**Key words:** Cervix, metastasis, neuroendocrine, small cell

## INTRODUCTION

Small cell carcinoma (SmCC) is a tumor of neuroendocrine origin commonly seen in the lung. Extrapulmonary SmCC accounts for 5% of the total incidence.<sup>[1]</sup> Within a female genital tract, the cervix is one of the rare sites for this tumor. Other sites of SmCC include vulva and vagina.<sup>[2]</sup> SmCC of cervix accounts for approximately 2% of all invasive cervical malignancy.<sup>[3]</sup> Most of the studies have shown a close association of SmCC cervix with human papillomavirus (HPV) infection.<sup>[3-6]</sup>

## CASE REPORT

A 45-year-old perimenopausal female, Para 7, Live 7 birth comes with complain of urinary retention since 15 days. Patient was catheterized for the same in a private hospital. Patient also had foul smelling per vaginal discharge since 15 days along with excessive bleeding since 2 months. Her menstrual history

was uneventful. Her general and systemic examinations were unremarkable. On per vaginal examination, a huge, friable growth was present in the cervix extending into right and left parametrial tissue. Ultrasonography abdomen revealed a well-defined hypoechoic mass of size 10.5 cm × 9.7 cm × 9.4 cm seen arising from the cervix resulting in obstruction of endometrial cavity causing pyometra. The fat planes between the lesion of urinary bladder appeared to be maintained. However, fat planes between the anal canal and the mass cannot be commented upon. Positron emission tomography scan showed metabolically active soft-tissue mass in cervix along with bilateral external and internal iliac lymph nodes and precaval and aortocaval lymph nodes present. Cervical biopsy was performed. On gross examination, multiple fragmented tissue bits totally aggregating to 1cc, grayish white were received. Histopathological examination revealed a tumor arranged in sheets and nests in a background of dense inflammatory infiltrate [Figure 1]. The individual tumor cells showed salt and pepper chromatin with inconspicuous nucleoli [Figure 2]. Immunohistochemistry revealed leukocyte common antigen (LCA) negativity along with positivity for synaptophysin [Figure 3] favoring the diagnosis of SmCC of the cervix. HPV testing was negative ruling out the association of this tumor with it. The patient had underwent a radical hysterectomy and bilateral pelvic lymphadenectomy. Postoperative phase of the patient was uneventful. She was given three cycles of chemotherapy. She is followed up and is still under treatment.

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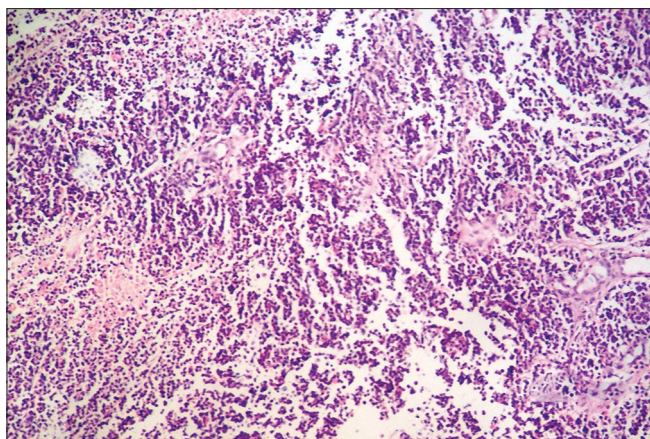
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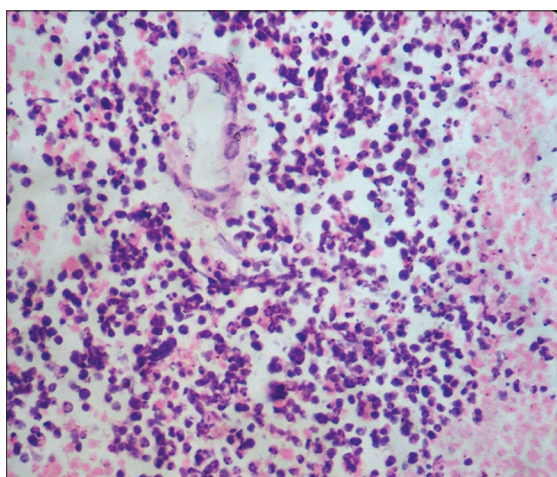
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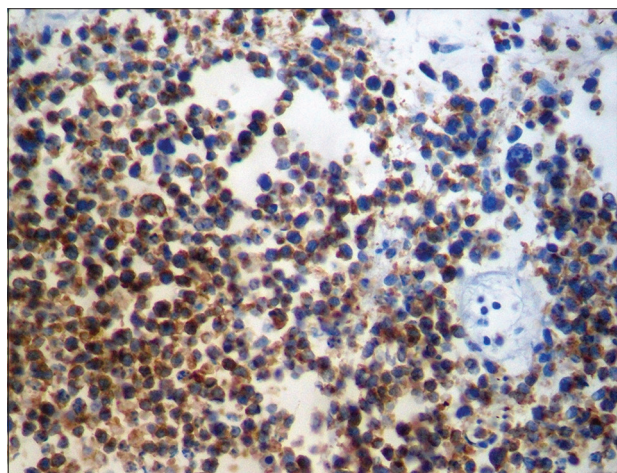
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**Figure 1:** Photomicrograph showing an infiltrative small round cell tumour arranged in diffuse sheets admixed with inflammatory cells (H and E, ×40)



**Figure 2:** High power view showing tumor cells with salt and pepper chromatin and inconspicuous nucleoli with a foci of necrosis (H and E, ×200)



**Figure 3:** Immunohistochemistry showing synaptophysin positivity (IHC, ×400)

## DISCUSSION

Small cell carcinoma arises from the neuroendocrine cells located within the normal epithelium throughout the female genital tract. In the earlier days, it was considered

to be rare, highly aggressive subtype of squamous cell carcinoma. However, later evidences proved that most of these tumors express one or more markers of neuroendocrine differentiation.<sup>[3,4]</sup> Hence, now labeled as a separate entity. SmCC of the cervix have been related to HPV infection. Studies have demonstrated the presence of HPV virus type 18 DNA or messenger RNA in the majority of SmCC cases.<sup>[3,4]</sup> Our patient, however, did not show infection by HPV. The mean age of presentation, as mentioned in the literature is around fourth to fifth decade.<sup>[2]</sup> Our patient was also in the same age group. The common clinical presentations include abnormal vaginal bleeding and obvious mass in most cases.<sup>[6,7]</sup> Our patient also had similar complaints. Grossly the tumors are usually ulcerative and infiltrative making the cervix barrel shaped.<sup>[6]</sup> On histopathology, SmCC is composed of small blue cells with high nuclear - cytoplasmic ratio, scant cytoplasm, and markedly hyperchromatic nuclei with speckled chromatin. Nuclear molding is present and nucleoli are inconspicuous. It showed increased mitotic activity (>10 mitoses/10 HPF). Furthermore, the tumor shows areas of necrosis and apoptosis.<sup>[2]</sup> The tumor pattern may vary from sheet-like, insular or perivascular and thick trabeculae with serpiginous growth architecture.<sup>[8]</sup> On immunohistochemistry, the tumor shows positivity for at least one neuroendocrine marker (synaptophysin, chromogranin, CD56) and shows negativity for LCA.<sup>[2,3,4,6]</sup> Our case reveal same findings, thus confirming the diagnosis. Electron microscope shows dense core granules in most cases along with tightly packed cells with close apposition of cell membranes.<sup>[2]</sup> The differential diagnosis on histopathology includes poorly differentiated SmCC, or poorly differentiated adenocarcinoma or small cell variant of SmCC, non-Hodgkin's lymphoma.<sup>[2,3,9]</sup> Furthermore, SmCC often develops in concomitance with usual SmCC or adenocarcinoma, hence it becomes very important to do immunohistochemistry.<sup>[9]</sup> It is extremely challenging to establish the diagnosis of this tumor on a small cervical biopsy because of its limited paraffin tissue and by the fact that it can show fragmentation, crush artifacts and streaming effects. The rare occurrence of SmCC of the cervix had made it difficult to define precise treatment guidelines for the management of this tumor.<sup>[7]</sup> Radical hysterectomy with bilateral lymphadenectomy, radiation therapy, and chemotherapy are the treatment modalities for this tumor with the special role of chemotherapy.<sup>[11]</sup> Use of adjuvant chemotherapy or chemoradiation is associated with better survival in such patients.<sup>[10]</sup> Since it has a high propensity to metastasis, it is mandatory to do full body computed tomography scan and magnetic resonance imaging along with bone marrow examination in all patients to know the stage of the tumor.<sup>[2]</sup> McCusker *et al.* had concluded in his studies that the survival was worse with this tumor with short disease-free period and early recurrences.<sup>[9]</sup>

To conclude, SmCC is a rare, poor differentiated neuroendocrine tumor having high propensity to nodal and distant metastasis with dismal prognosis and need early diagnosis with prompt search for metastasis to increase the survival rates of the patient.

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