

# Rare cervical malignancy: a case of small cell neuroendocrine tumour of the cervix

## Abstract

**Objective:** To describe a case of a small cell neuroendocrine tumour of the cervix.

**Case report:** a 46 year old lady was diagnosed with an infiltrative high grade small cell neuroendocrine adenocarcinoma which was infiltrating the uterus, after she presented with unprovoked vaginal bleeding. Surgery was done successfully, after which she was referred for chemotherapy.

**Discussion:** MR imaging was essential in staging the tumour. It is also important to appreciate the rarity of such a diagnosis and the intricacies of its management

**Conclusion:** A multidisciplinary approach in such cases is essential, as well as appropriate counselling of the patient.

Volume 10 Issue 2 - 2019

Silvaine Marie Dalli, Karl Cutajar, Tatyana Kenkovski, Mark Formosa  
Mater Dei Hospital, University of Malta, Malta

**Correspondence:** Silvaine Marie Dalli, Mater Dei Hospital, University of Malta, Malta, Tel 0035679254376, Email silvaine.dalli@gmail.com

**Received:** June 12, 2018 | **Published:** March 07, 2019

## Introduction

Cervical malignancy is the fifth deadliest malignancy and the second most common worldwide killing 9 per 100,000 per year.<sup>1</sup> Neuroendocrine tumours of the cervix account for a mere 2% of the total cervical malignancies,<sup>2</sup> exhibiting features of endocrine and neural tissue. Usually they follow a rapid progression and poor prognosis.

## Case report

A 46 year old patient with 2 previous normal vaginal deliveries presented with unprovoked vaginal bleeding. On examination an erythematous cervix was noted and the cervix was adherent to the posterior wall of the vagina. The patient was scheduled for an urgent colposcopy and hysteroscopy.

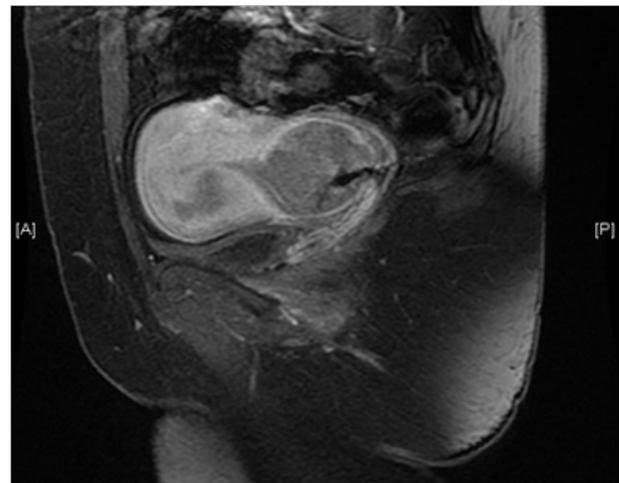
Hysteroscopy was attempted yet failed due to a highly stenosed and deformed cervical os. Colposcopic histology showed an extensive necrotic invasive small cell neuroendocrine carcinoma with extensive synaptophysin expression. MRI imaging illustrated a 4cm in diameter mass within the cervix (Figure 1) which extended partially to the lumen of the uterine body. There was no evidence of extension outside the uterine corpus or to the lower third of the vaginal wall. No pelvic lymphadenopathy was noted. The patient was scheduled for surgery and a radical hysterectomy with internal iliac node sampling was performed. This was done after discussion with the oncologists since unusual cell types are more likely to disseminate directly into surrounding tissues, as happened in this case as the cervix was adherent to the posterior wall of the vagina, and via lymphatic pathways, with the commonest route being via the internal iliac nodes. It can also spread haematogenously, which did not happen in this case<sup>3-5</sup>

Histology showed an infiltrative high grade small cell neuroendocrine adenocarcinoma infiltrating the endocervix and isthmic zones of uterine body perforating the cervix, pT2Nx Figo stage 2. The patient was discharged from hospital in good health following surgery with subsequent oncology follow-up for chemotherapy.

## Discussion

Neuroendocrine tumors of the cervix are extremely rare and rapidly progressing accounting for only 2% of cervical carcinomas.<sup>2</sup> They usually arise from the diffuse neuroendocrine cell system within

the cervix. The site of origin and histologic subtype determine the prognosis. There are four types of neuroendocrine tumours: carcinoid and atypical carcinoid include the well differentiated subtypes whilst small cell and large cell tumours are the poorly differentiated groups. The latter having a poorer prognosis because of the poor differentiation. Most of such tumours express synaptophysin and chromogranin A by immunochemistry thus well and poorly differentiated tumours are grouped together due to such marker expression.<sup>2,6</sup> This makes the degree of expression not correlate with the severity of the malignancy.



**Figure 1** MR image showing the 4cm in diameter neuroendocrine small cell tumour on the cervix with uterine extension.

Small cell malignancy being the most common with 300 cases described is associated with human papilloma virus subtype 18<sup>7</sup> and is divided into hypercalcaemic and pulmonary type making it most sensitive to platinum compounds chemotherapy.<sup>8</sup> Large cell neuroendocrine tumour accounts for only 78 reported cases in the medical literature.<sup>9</sup> The aetiology is poorly understood in view of the low incidence; however, many believe that human papilloma virus and smoking may have a role. Unlike other forms of cervical cancer, this form does not have a pre-invasive lesion that can be detected by screening.<sup>7</sup>

Such tumours generally present like other forms of cervical carcinoma, including post-coital bleeding, increased vaginal discharge

and dyspareunia. If more advanced it can also present with cachexia, weight loss, abdominal pain and symptoms of metastatic disease. If endocrinologically active, it can also lead to hypercalcaemia, Cushing syndrome and syndrome of inappropriate ADH secretion.<sup>10,11</sup>

Magnetic Resonance Imaging (MRI) is a gold-standard imaging modality for such tumours. A tumour of 4cm or less is amenable to surgery followed by chemotherapy. A tumour of >4cm is amenable to neoadjuvant chemotherapy. A late stage or candidates not fit for surgery should have combination chemotherapy and chemo radiation following the Hoskins protocol.<sup>2</sup>

The prognosis varies from 80% 3year survival if grade 1-2 to 38% 3 year survival if grade 3-4.<sup>12,13</sup> However, in cases where the tumour was <4cm there are usually no recurrences.<sup>14</sup> Distant sites of recurrence especially lung and bone (28%) are described being more common than local spread (13%),<sup>15,16</sup> especially if the tumour is mixed and larger than 4cm.

## Conclusion

Counselling and adequate investigations are required for proper management of such rare form of cervical malignancy. A multidisciplinary approach is best advised to give good standards of care.

## Acknowledgments

None.

## Conflicts of interest

The authors declare no conflicts of interest.

## References

1. WHO. Fact sheet No. 297: Cancer. 2017.
2. Gardner G, Reidy-Lagunes D, Gehrig P. Neuroendocrine tumors of the gynecologic tract: A Society of Gynecologic Oncology (SGO) clinical document. *Gynecol Oncol*. 2011;122(1):190–198.
3. Sakuragi N, Satoh C, Takeda N, et al. Incidence and distribution pattern of pelvic and paraaortic lymph node metastasis in patients with stages IB, IIA, and IIB cervical carcinoma treated with radical hysterectomy. *Cancer*. 1999;85(7):1547–1554.
4. Gallup D. The spread and staging of cervical cancer. *Glob libr women's med*. 2008.
5. Dongol S, Tai Y, Shao Y, et al. A retrospective clinicopathological analysis of small-cell carcinoma of the uterine cervix. *Mol Clin Oncol*. 2014;2(1):71–75.
6. Campana D, Nori F, Piscitelli L, et al. Chromogranin A: is it a useful marker of neuroendocrine tumors? *J Clin Oncol*. 2007;25(15):1967–1973.
7. Stoler M, Mills S, Gersell D, et al. Small-cell neuroendocrine carcinoma of the cervix. A human papillomavirus type 18-associated cancer. *Am J Surg Pathol*. 1991;15(1):28–32.
8. Moertel C, Kvols L, O'Connell M, et al. Treatment of neuroendocrine carcinomas with combined etoposide and cisplatin: evidence of major therapeutic activity in the anaplastic variants of these neoplasms. *Cancer*. 1991;68(2):227–232.
9. Yoseph B, Chi M, Truskinovsky A, et al. Large-cell neuroendocrine carcinoma of the cervix. *Rare Tumors*. 2012;4(1):e18.
10. Petignat P, Michel R. Diagnosis and management of cervical cancer. *BMJ*. 2007;335(7623):765–768.
11. Mwaka A, Orach CG, Were EM, et al. Awareness of cervical cancer risk factors and symptoms: cross-sectional community survey in post-conflict northern Uganda. *Health Expect*. 2016;19(4):854–867.
12. Lee S, Nam JH, Kim DY, et al. Unfavorable prognosis of small cell neuroendocrine carcinoma of the uterine cervix: a retrospective matched case-control study. *Int J Gynecol Cancer*. 2010;20(3):411–416.
13. Chan J, Loizzi V, Burger RA, et al. Prognostic factors in neuroendocrine small cell cervical carcinoma: a multivariate analysis. *Cancer*. 2003;97(3):568–574.
14. Vighi S, Ana Garci' A, Juan Sardi J. Neuroendocrine cervical carcinoma: a diagnostic and therapeutic challenge adriana bermúdez. author links open the author workspace. *Gynecologic Oncology*. 2001;82(1):32–39.
15. Sevin B, Method MW, Nadji M, et al. Efficacy of radical hysterectomy as treatment for patients with small cell carcinoma of the cervix. *Cancer*. 1996;77(8):1489–1493.
16. Collinet P, Lanvin D, Declerck D, et al. Neuroendocrine tumors of the uterine cervix. clinicopathologic study of five patients. *Eur J Obstet Gynecol Reprod Biol*. 2000;91(1):51–57.