Small-cell carcinoma of the uterine cervix with long-term survival obtained with multimodal treatment: A case report

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ABSTRACT

Introduction: Small-cell carcinoma of the uterine cervix is a rare aggressive tumor accounting for less than 5% of all cervical carcinomas. It is associated with a poor prognosis. Case Report: We report a case in a 37-year-old female revealed by vaginal bleeding. The patient underwent a radical hysterectomy with pelvic and paraaortic lymphadenectomy with advanced stage. An adjuvant chemotherapy using etoposide and cisplatin for six courses was given and followed by adjuvant pelvic radiotherapy and vaginal brachytherapy. After six years of follow-up, the patient is free of disease. Conclusion: The purpose of this case is to report the successful results with a multimodal treatment in small-cell carcinoma of the uterine cervix including surgery, chemotherapy platinum based and radiotherapy.

INTRODUCTION

Squamous cell carcinoma is the most common malignant neoplasm of the uterine cervix. Neuroendocrine carcinoma frequently arises in the bronchial tree, but it is very rare in the genital tract. Small-cell carcinoma of the uterine cervix (SCCC) is the most common and aggressive subtype of cervical neuroendocrine tumors [1]. Reagan described this entity at first in 1957 [2]. The SCCC is a very rare tumor that usually discovered at an advanced stage with a very poor prognosis [3]. There is a great therapeutic heterogeneity in the management of this entity. We report a new case detected in a young patient with a long survival and a literature review.

CASE REPORT

A 37-year-old female, mother of four children, was presented without a past medical history suffering from vaginal bleeding with fetid vaginal discharge and pelvic pain for more than six months. Gynecological examination showed cervical mass measuring about 5 cm in diameter.
without the involvement of parametrium. A biopsy of the tumor had been performed. Histopathological examination of the cervical mass revealed an undifferentiated carcinoma. A computed tomography (CT) scan of the pelvic had objectified a large cervical tumor without pelvic lymph nodes. A chest radiograph and abdominal ultrasound were normal. The patient underwent radical hysterectomy with pelvic and paraortic lymphadenectomy. Microscopic finding showed a cervical localized tumor measuring 5.5 cm in long axis. Histopathological examination of the cervical mass revealed an infiltrative carcinomatous proliferation poorly differentiated, composed of small cells monomorphic and cohesive, with moderately abundant cytoplasm. The cells were arranged in clusters, with the presence of many vascular emboli (Figure 1 and Figure 2). Vaginal section was 2 cm without invasion. We did not observed parametrial, myometrial or vaginal invasion, but we observe metastases to the left pelvic lymph nodes (2N+/42N) and we objectified cancerous cells in the peritoneal fluid. Immunohistochemical staining was positive for chromogranin A (Figure 3), cytokeratine AE1/AE3 and CD56 (Figure 4). The specimen did not stain for synaptophysin. The diagnosis of small-cell carcinoma of the uterine cervix was established. The tumor was classified as IB2 (FIGO classification) and the case was discussed at multidisciplinary consultation meeting. The patient received adjuvant chemotherapy using cisplatin (60 mg/m²) and etoposide (120 mg/m²) daily for three days every three weeks for six cycles. An external pelvic irradiation was delivered after chemotherapy with a dose of 2 Gy per day to a total of 46 Gy in 23 fractions, 5 fractions per week, followed by vaginal brachytherapy with two fractions of 6 Gy weekly. The patient was alive and free of disease six years after the surgery.

DISCUSSION

Small-cell carcinoma of the uterine cervix (SCCC) is a rare disease classified as a neuroendocrine tumor. It represents less than 5% of all uterine cervical carcinomas. It is the most aggressive subtype of uterine cervical cancer, characterized by rapid progression and poor outcomes [3]. The SCCC is characterized by a high frequency of lymph node metastases and lymphovascular invasion more than squamous cell carcinoma of cervix [1, 3]. Distant metastases are frequent to the bone, lung, liver, brain, and bone marrow [3, 4].

Due to its rarity, there are no randomized studies to establish a standardized treatment strategy for SCCC. In case of localized tumors (stage I-IIA) and in the absence of comparative studies between radiotherapy and surgery, most of gynecologic oncologists in China are in favor of surgery; and several authors recommend a radical hysterectomy [5].

Despite the local treatment of the primary tumor, the majority of patients develop distant metastases. Consequently, recent studies require systemic
chemotherapy as part of the initial treatment, along with surgery or radiation, dealing with early-stage disease. In a multicenter study, including 102 patients who with SCCC at five different institutes, chemotherapy was identified as independent prognostic factors and survival was the most unfavorable in patients with early-stage SCCC who had never received chemotherapy [3].

Most clinicians use platinum-based combination chemotherapy in the treatment of patients with SCCC because of its similarities to small-cell lung cancer. In a multicenter, retrospective trial comprising 72 Chinese women diagnosed with SCCC, two protocols of chemotherapy was used; etoposide and cisplatin (EP) or paclitaxel and cisplatin (TP). Platinum-based combination chemotherapy (with EP or TP) can improve the three-year survival outcomes compared to other chemotherapy techniques or no chemotherapy (overall survival: 95%, \( p = 0.001 \); DFS: 95%, \( p = 0.001 \)) [6].

Instead of adjuvant radiotherapy in localized tumors remains controversial, Boruta et al. did not observe a survival advantage for early-stage SCCC treated with adjuvant radiotherapy in addition to radical surgery and chemotherapy. However, the small number of patients in this study limits the ability to comment on any possible benefit of radiation therapy [7]. Other authors have preferred to integrate radiotherapy as part of a multimodal treatment. By combining surgery, radiotherapy and chemotherapy, Chan et al. have succeeded in obtaining a survival rate at five years of 32%, which is significantly higher than those reported in the different series [8].

For locally advanced tumors (stage IIb-IV) and for inoperable patients, chemoradiation is in generally recommended. In a Taiwanese Gynecologic Oncology Group study, concurrent chemoradiation with etoposide and cisplatin was associated with better five-year failure-free survival (62.5% versus 13.1%, \( p = 0.025 \)) and cancer-specific survival (75.0% versus 16.9%, \( p = 0.016 \)). The authors concluded that the chemoradiation might be the treatment of choice for locally advanced tumors, and for earlier stages [9].

Small-cell carcinoma of the uterine cervix is the most aggressive type of cervical cancer, the five-year survival rates vary from 0–30% [3]. Several studies have reported that disease stage was the strongest predictor of outcome [6, 9]. In the Wang et al. study, lesion size and FIGO stage were significant prognostic factors (\( p < 0.01 \)), while age, deep invasion in cervical stromal, pelvic and (or) para-aortic lymph nodes involvement, neoadjuvant chemotherapy, adjuvant radiotherapy were not significantly associated with prognosis (all \( p > 0.05 \)) [10].

CONCLUSION

Small-cell carcinoma of the uterine cervix is a rare cancer and this makes it difficult to derive standard treatment from prospective trials. Based on the review of literature and the presented case report, an aggressive multimodal treatment remains primordial for local disease control and for reducing distant relapses.

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Figure 4: Immunohistochemistry analysis showing a strong membrane staining with anti-CD56 (magnification: x200).
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