

# Adenosquamous carcinoma of the uterine cervix - adjuvant chemotherapeutic treatment with paclitaxel and carboplatin; a case report

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## Summary

Adenosquamous carcinoma of the uterine cervix is a rare mixture of malignant glandular and squamous epithelial elements. We present a case of a 56-year-old woman with Stage IV cervical carcinoma treated with paclitaxel and carboplatin chemotherapy after cytoreductive surgery. Solitary liver metastases were treated by ultrasound guided percutaneous sclerotherapy with 95% ethanol. For ten months the patient showed an objective response to the treatment with a good quality of life during that time.

A year after the first, the second cytoreductive operation was performed and chemotherapy (paclitaxel, carboplatin, and epirubicin) followed. The patient died 20 months after establishing the diagnosis.

Paclitaxel in combination with carboplatin as adjuvant chemotherapeutic treatment could be another promising agent for patients with advanced metastatic cervical adenocarcinoma.

*Key words:* Cervical adenosquamous cancer; Adjuvant chemotherapy; Paclitaxel, Carboplatin.

## Introduction

Adenosquamous carcinomas of the uterine cervix are uncommon, rare carcinomas composed of a mixture of malignant glandular and squamous epithelial elements. The therapy of advanced stages of this carcinoma as well as recurrent disease and metastases is still doubtful. Effective treatment is yet to be determined as various therapies are being evaluated, and results of different options have been presented in the literature.

Adjuvant chemotherapy has been newly introduced in the treatment of the advanced or metastatic cervical carcinoma by itself or in combination with radiotherapy. Advanced stages of the disease are treated with chemotherapeutic agents in various combinations with varying success as well. The use of these agents for non-squamous cell carcinoma of the cervix has not been extensively studied. Cisplatin, bleomycin and vincristin are mostly used for squamous type tumours and the effect of this chemotherapy protocol is considered as satisfactory but not ideal. Paclitaxel and carboplatin are used in gynaecological oncology treatments for the systemic therapy of ovarian and breast carcinoma. New reports have introduced paclitaxel in the chemotherapy regimens for advanced, metastatic or recurrent cervical nonsquamous carcinomas.

Adenosquamous cervical carcinomas with a poorly differentiated squamous component are in general considered and treated like adenocarcinomas of the cervix.

## Case report

In October 2000, a 56-year-old woman was admitted in our tertiary clinic with a suspicion of advanced stage genital neo-

plasia from the local hospital where cytological evaluation of the evacuated ascites was performed and showed malignant cells. The value of CA125 was 4518 kIU/l at that time. The patient visited her gynaecologist after more than ten years because she had been bleeding vaginally since June of that year. She did not have any other related symptoms that she complained of. In her medical history she mentioned cured tuberculosis in her 20's and that she had been menopausal for five years without problems until June of that year. She had never used hormonal replacement therapy.

Clinical examination showed a necrotic tumour, 3 cm in diameter, protruding from the cervix and bleeding, a slightly enlarged uterus and a certain amount of intraabdominal fluid with positive undulation. Transvaginal ultrasound examination revealed an omental "cake" and uterus floating in a large amount of abdominal ascites. The pathohistology of the punch biopsy of the tumour showed adenosquamous carcinoma with poorly differentiated squamous cells. Abdominal ultrasound examination also revealed two suspicious solitary hepatic lesions 13 and 33 mm diameter. Urography and irigography showed no pathological findings. Computed tomography (CT) of the abdomen showed the mentioned metastatic lesions of the liver, peritoneal surface metastases and ascites.

Total abdominal hysterectomy with bilateral salpingo-oophorectomy and supra-colic omentectomy was performed. During the operation a large amount of ascites was evacuated and a few tumorous knots were found palpable on the surface of the liver. The pathohistology confirmed adenosquamous carcinoma of the cervix with a very low differentiated squamous component and metastatic carcinoma of both ovaries and the omentum as well.

Liver metastases were treated with sclerotherapy – ultrasound guided percutaneous injection of 95% ethanol.

Laboratory evaluation before chemotherapy showed normal values of the complete blood cell count and differential, bilirubin, aspartate aminotransferase (AST), alkaline phosphatase, creatinin, chest X-ray, creatinin clearance and no abnormalities of the EKG and cardiac ultrasound examination.

Postoperatively the patient received six cycles of the TC protocol - paclitaxel (175mg/m<sup>2</sup>) plus carboplatin (Calvert formula,

AUC 5) in the regimen: 1-day therapy/ 3-week rest period. The patient received pretreatment medications intravenously 30 min before chemotherapy to avoid allergic reactions. No complications during or after the therapy were observed.

The value of CA125 postoperatively was 1200 kIU/l, after three cycles of systemic therapy and 98 and after six cycles of 18 kIU/l.

In September 2001 the patient was admitted to the clinic dyspnoic with ascites and liquid in the thorax. A second cytoreductive operation was performed and it showed carcinosis of the peritoneal surface, multiple hepatic solitary metastases with a large amount of ascites. Preoperative evacuation of liquid in the thorax showed adeno-malignant cells.

The patient received another three cycles of chemotherapy: TEC protocol - paclitaxel (175 mg/m<sup>2</sup>), plus carboplatin (Calvert formula, AUC 5), plus epirubicin (75 mg/m<sup>2</sup>) in the regimen: 1-day therapy/3-week rest period.

The patient died 20 months after establishing the diagnosis.

## Discussion

Cervical carcinoma is the third most frequent neoplasia in women with a high level of curability of early phase lesions. Several studies have shown a certain sensitivity of advanced stages of cervical carcinoma, metastatic or recurrent disease to systemic therapy. It is evident by now that adjuvant chemotherapy improves the prognosis of advanced stages of the disease. As mentioned before, reported randomised trials have mostly assessed activity of the cisplatin, bleomycin and vincristin (PVB) protocol for advanced stages of squamous cervical cancer [1, 2]. It has been reported that paclitaxel has a certain action in the treatment of advanced cancer of the cervix comparable with the action of the above-mentioned agents [3-7]. In progress are evaluations of the effectiveness of anti-neoplastic drugs already in use or new ones, in particular for the treatment of advanced stages of adenocarcinoma of the cervix [8-10]. The latest phase II trial has determined a good chemosensitivity of the tumour to paclitaxel and cisplatin systemic therapy as preoperative treatment of cervical cancer patients with Stage IB2 to IIB by the International Federation of Gynaecology and Obstetrics (FIGO) on a small group of patients [11]. It was also reported that the same protocol could be an active treatment in advanced stages of cervical carcinoma in addition to pelvic radiotherapy [12]. Unfortunately all of the results achieved until now, confirm that systemic therapy is still being considered insufficient but it increases survival rates.

There is still lack of large prospective trials reporting on response to paclitaxel alone or in combination with other antineoplastic drugs in the treatment of squamous or nonsquamous cervical carcinoma. Several small studies with paclitaxel alone or with carboplatin (TC protocol) in patients with recurrent or persisting adenocarcinoma of the cervix confirmed chemosensitivity of this type of the tumour [13, 14].

Nevertheless, all of these reports concluded that protocols with paclitaxel were well tolerated by patients with an acceptable toxicity profile and that the action in nonsquamous cancer of the cervix is comparable with other reported agents [7, 11, 14].

The motivation to treat our patient with paclitaxel and carboplatin with the addition of epirubicin after the second operation, were the pathohistologic type of the tumour and the advanced stage of the disease.

We conclude that our patient tolerated the therapy well with a progression-free period after postoperative TC protocol treatment of ten months and a good quality of life during that time.

We believe that paclitaxel in combination with carboplatin could be an active agent for patients with advanced and/or metastatic adenocarcinoma of the cervix. Nevertheless a greater number of cases have to be studied to confirm the efficacy of the treatment.

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