

Effective combination chemotherapy of taxanes and platinum in advanced uterine cervical cancer: a case report

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Abstract

The prognosis of advanced cervical cancer remains poor. Recently, the significant activity of paclitaxel has been shown in advanced cervical cancers. We report a patient with advanced uterine cervical cancer who responded to neoadjuvant combination chemotherapy with taxanes and platinum.

The patient was a 53-year old woman who presented with pollakisuria, lumbago, and pain in the anus and inguinal lesion, without genital

bleeding. The findings indicated a clinical diagnosis of stage 4b disease with lung metastasis. We performed neoadjuvant combination chemotherapy with 7 courses of TC therapy (paclitaxel and carboplatin) and 7 courses of DP therapy (docetaxel and cisplatin) with a good effect. Key words: advanced uterine cervical cancer, neoadjuvant combination chemotherapy, taxanes, platinum

Introduction

Uterine cervical cancer is the second most common cancer in women worldwide. Many patients present with early stage disease and subsequent treatment results in a high cure rate; however, the prognosis of advanced cervical cancer remains poor, with a 5-year relative survival rate for stage 4 of 17%.1 The treatment of advanced or recurrent cervical cancer has been improved by the introduction of new active chemotherapy agents. Recently, the significant activity of paclitaxel has been shown in gynecological malignancies, such as ovarian and endometrial cancer, and in several squamous cell carcinomas, such as head and neck, lung cancer, and advanced cervical cancers.2 Another report suggested that the combination of docetaxel and carboplatin is an effective and safe treatment for uterine cervix cancer.3 Here, we report a patient

with advanced uterine cervical cancer (stage 4b) who responded to neoadjuvant combination chemotherapy with taxanes and platinum.

Case report

The patient was a 53-year old woman (gravida 4, para 2), who presented with pollakisuria, lumbago, and pain in the anus and inguinal lesion, without genital bleeding. Her family history and past history were unremarkable. An abnormal smear for uterine cervix was detected, leading to her presentation at our hospital for further examination.

On examination, a huge cervical tumor developing in the vagina was detected and a chest X-ray and chest CT showed the multiple lung metastases (Fig. 1). On MRI, a tumor shadow was detected in the uterine cervix to vagina and metastasis to the left femoral bone was found

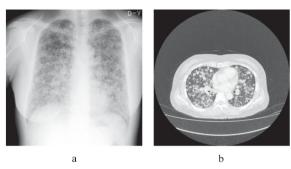


Fig. 1 Multiple lung metastases at the first examination. (a. on chest X-ray; b. on chest CT)

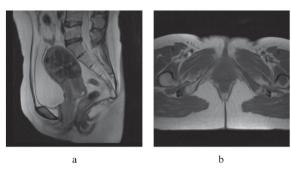


Fig. 2 A tumor shadow was detected in the uterine cervix to vagina (a) and metastasis to the left femoral bone (b) was found on the first MRI.

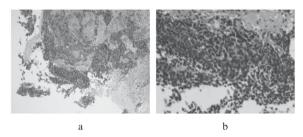


Fig. 3 Histopathological findings: Biopsy of the tumor in the vagina showed non-keratinizing squamous cell carcinoma. (a. $H \cdot E \times 100$ b. $H \cdot E \times 400$)

(Fig. 2). Biopsy of the tumor in the vagina was diagnostic for squamous cell carcinoma, nonkeratinizing (Fig. 3), showing positive for cytokeratin and negative for NSE (neuron-specific enolase) and chromogranin A. These findings indicated a clinical diagnosis of stage 4b disease. Tumor marker levels were as follows: SCC, 0.9 ng/ml; CEA, 1.3 ng/ml; CA125, 13.2 U/ml; CA19-9, 16.7 U/ml; CA 72-4, 0.9 U/ml. Two days after admission to our hospital, she developed dyspnea requiring to O2 and severe lumbago requiring morphine. We immediately started chemotherapy to extend her life after obtaining written informed consent. Neoadiuvant combination chemotherapy with paclitaxel (175 mg/m²) and carboplatin (AUC=5) (TC ther-

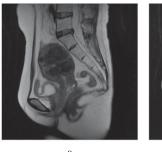




Fig. 4 Tumor volume in the uterine cervix markedly decreased after chemotherapy on MRI. (a. after 2 cycles of TC; b. after 7 cycles of TC and 4 cycles of DP)





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Fig. 5 The tumor volume in lung metastasis markedly decreased after chemotherapy. (a. on chest X-ray after 7 cycles of TC and 4 cycles of DP; b. on chest CT after 7 cycles of TC and 7 cycles of DP)

apy) was performed and repeated every 28 days because of fewer complications. Three cycles were administered and she was discharged from hospital with decreased symptoms of dyspnea and pain. The tumor volume in the uterine cervix was markedly decreased after 2 cycles of chemotherapy (Fig. 4). She had a hypersensitive reaction to carboplatin after 7 cycles of treatment, so we changed to combination chemotherapy with docetaxel (70 mg/m²) and cisplatin (60 mg/m²) (DP therapy), and have performed 7 courses of DP therapy with good effect (Fig. 4 and 5).

We will evaluate a treatment response by measurement of tumor size on CT or MRI and continue a chemotherapy until the tumor will disappear complately. We will follow up once a month after chemotherapy.

Discussion

The treatment of advanced or recurrent cervical cancer has been improved by the introduction of new active chemotherapy agents, of which cisplatin is considered the most active,

with response rates of 20% to 30%,⁴ and it is now routinely employed as part of the initial therapy.⁵ Other drugs, such as ifosfamide,⁶ topotecan,⁷ gemcitabine,⁸ and vinorelbine⁹ also have documented activity, however, the continued poor prognosis of this patient population stresses the need to identify more effective agents and combination regimens.

Recently, clinical trials of paclitaxel performed on cervical cancer patients have placed this compound in the forefront of the most active drugs against this disease. 10-12 It was demonstrated that combination regimens, paclitaxel plus cisplatin or topotecan plus cisplatin, are superior to cisplatin alone with respect to improvements in the response rate, PFS, and quality of life. 13,14 In patients with advanced squamous cell cervical cancer, a single dose of docetaxel had a 34% clinical response rate. 15 Nagao et al. reported an 80% response rate of neoadjuvant combination chemotherapy of docetaxel and carboplatin in advanced cervical cancer. 3

In our case, the patient had stage 4b uterine cervical cancer and was in poor condition with multiple lung metastases, and we chose first-line combination chemotherapy with paclitaxel and carboplatin because of fewer complications. We had to change carboplatin due to a hypersensitive reaction and selected combination chemotherapy of docetaxel and cisplatin, expecting a further response due to no change for lung metastasis after 6 cycles of TC therapy. The good prognosis of this case suggested that combination chemotherapy of taxanes and platinum is effective against advanced squamous cell cervical cancer.

References

- 1. Jemal A, Siegel R, Ward E, Murray T, Xu J, Smigal C, Thun MJ (2006) Cancer Statistics, 2006. CA Cancer J Clin 56: 106–130
- 2. D'Agostino G, Dicterfano M, Greggi S, Salerno M, Ferrandina G, Poerio A, Mancuso S, Scambia G (2002) Neoadjuvant treatment of locally advanced carcinoma of the uterine cervix with epirubicin, paclitaxel and cisplatin. Cancer Chemother Pharmacol 49: 256–260
- 3. Nagao S, Fujiwara K, Oda T, Ishikawa H, Koike H, Tanaka H, Kohno I (2005) Combination chemotherapy of docetaxel and carboplatin in advanced or recurrent cervix cancer. A pilot study. Gynecolgic Oncology 96: 805-809
- 4. Bonomi P, Blessing JA, Stehman FB, DiSaia PJ,

- Walton L, Major FJ (1985) Randomized trial of three cisplatin dose schedules in squamous-cell carcinoma of the cervix: a Gynecologic Oncology Group study. J Clin Oncol 26: 477-482
- 5. Thigpen JT, Shingelton H, Homesley H, Lagasse L, Blessing J (1981) Cis-platinum in treatment of advanced or recurrent squamous cell carcinoma of the cervix: a phase II study of the Gynecologic Oncology Group. Cancer 48: 899-903
- 6. Sutton GP, Blessing JA, Adcock L, Webster KD, DeEulis T (1989) Phase II study of ifosfamide and mesna in patients with previously treated carcinoma of the cervix: a Gynecologic Oncology Group study. Invest New Drugs 7: 341-343
- 7. Muderspach LI, Blesssing JA, Levenback C, Moore JL Jr (2001) A phase II study of topotecan in patients with squamous cell carcinoma of the cervix: a gynecologic oncology group study. Gynecol Oncol 81: 213-215
- 8. Schilder RJ, Blessing JA, Morgan M, Mangan CE, Rader JS (2000) Evaluation of gemcitabine in patients with squamous cell carcinoma of the cervix: a phase II study of the gynecologic oncology group. Gynecol Oncol 76: 204-207
- 9. Muggia FM, Blessing JA, Method M, Miller DS, Johnson GA, Lee RB, Menzin A; Gynecologic Oncology Group study (2004) Evaluation of vinorelbine in persistent or recurrent squamous cell carcinoma of the cervix: a Gynecologic Oncology Group study. Gynecol Oncol 92: 639-643
- Kudelka AP, Winn R, Edwards CL, Downey G, Greenberg H, Dakhil SR, Freedman RS, LoCoco S, Umbreit J, Delmore JE, Arbuck S, Lover E, Gacrama P, Fueger R, Kavanagh JJ (1997) An update of a phase II study of paclitaxel in advanced or recurrent squamous cell cancer of the cervix. Anticancer Drugs 8: 657-661
- Curtin JP, Blessing JA, Webster KD, Rose PG, Mayer AR, Fowler WC Jr, Malfetano JH, and Alvarez RD (2001) Paclitaxel, an active agent in nonsquamous carcinomas of the uterine cervix: a Gynecologic Oncology Group study. J Clin Oncol 19: 1275-1278
- 12. Cerrotta A, Gardan G, Cavina R, Raspagliesi F, Stefanon B, Garassino I, Musumeci R, Tana S, De Palo G (2002) Concurrent radiotherapy and weekly paclitaxel for locally advanced or recurrent squamous cell carcinoma of the uterine cervix. A pilot study with intensification of dose. Eur J Gynaecol Oncol 23: 115-119
- 13. Moore DH, Blessing JA, McQuellon RP, ThalerHT, Cella D, Benda J, Miller DS, Olt G, King S, Boggess JF, Rocereto TF (2004) Phese III study of cisplatin with or without paclitaxel in stage IVB, recurrent or persistent squamous cell carcinoma of the cervix: a Gynecologic Oncology Group Study. J Clin Oncol 22: 3113–3119
- 14. Long HJ, Bundy BN, Grendys EC Jr, Benda JA, McMeekin DS, Sorosky J, Miller DS, Eaton LA, Fiorica JV; Gynecologic Oncology Group Study

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(2005) Randomized phase III trial of cisplatin with or without topotecan in carcinoma of the uterine cervix: a Gynecologic Oncology Group Study. J Clin Oncol 23: 4626-4633

15. Garcia AA, Blessing JA, Vaccarello L, Roman LD;

Gynecologic Oncology Group Study (2007) Phase II clinical trial of docetaxel in refractory squamous cell carcinoma of the cervix: a Gynecologic Oncology Group Study. Am J Clin Oncol 30: 428-431