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Case report

Paclitaxel-induced remission in docetaxel-refractory anthracycline-pretreated metastatic breast cancer

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Paclitaxel and docetaxel are excellent agents with a high antitumor effect for the treatment of previously anthracycline-exposed metastatic breast cancer. There has been no standard treatment for patients who undergo therapy of a taxan-resistant metastatic breast cancer. Paclitaxel has partial non-cross-resistance *in vitro* with docetaxel in inhibiting microtubule disaggregation. We present the case of a patient with docetaxel-refractory anthracycline-pretreated metastatic breast cancer who achieved remission with paclitaxel. [© 2000 Lippincott Williams & Wilkins.]

Key words: Anthracycline, docetaxel, metastatic breast cancer, paclitaxel.

Introduction

For patients who have a high risk of rapid dissemination (short disease-free interval, hormone receptor-negative tumor), combination chemotherapy is the initial treatment of choice. Many studies have demonstrated that anthracycline-containing regimens are a first-line chemotherapy for patients with metastatic breast cancer, with reported response rates of 43–82%.[1–7]

The advent of taxanes as salvage therapy has improved response and further prolonged overall survival in patients who received treatment of previously anthracycline-exposed metastatic breast cancer. Docetaxel has resulted in response rates of 30–43% in this group of patients.[8–10] The majority of patients eventually relapse and need third-line chemotherapy.

Preclinical studies demonstrated only partial cross-resistance between paclitaxel and docetaxel.[11,12] A clinical study indicated the absence of complete resistance to docetaxel in patients with paclitaxel-resistant breast cancer.[13]

Conversely, we present the case of a patient with docetaxel refractory metastatic breast cancer who achieved remission with paclitaxel.

Case report

A 39-year-old woman underwent modified radical mastectomy in June 1997. The tumor was invasive ductal carcinoma and estrogen receptor-negative, progesteron receptor-negative with lymph node metastasis (T2, N1, Stage II B of the UICC/AJCC). The patient received five courses of combination chemotherapy with cyclophosphamide, mesothorexate and 5-fluorouracil until October 1997. There was no evidence of disease on physical examination, chest X-ray, bone scintigram or computed tomography (CT) scan of her liver. Her right supraclavicular metastatic lymph node, 3×2 cm in diameter, was found by needle aspiration biopsy and ultrasonography in May 1998. The patient received six courses of combination chemotherapy with cyclophosphamide, epirubicin and 5-fluorouracil in partial response. The chemotherapy was changed to treatment with docetaxel at a standard dose as prescribed in Japan of 60 mg/m^2, infused over 1 h every 3 weeks with granulocyte colony stimulating factor (G-CSF) in the hope of improved response. After two courses of docetaxel from November to December 1998 her supraclavicular metastatic lymph

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node disappeared in complete response; however, it regrew during the fifth course in April 1999. It was treated with radiation therapy for complete response. The patient subsequently presented multiple metastatic lung tumors in November 1999. In December 1999 she was started on therapy with a weekly 1-h paclitaxel infusion at 60 mg/m^2 for 3 weeks, followed by 1 week break.

To date, the patient has received three courses of paclitaxel without G-CSF support. She tolerates the treatment well without major side effects. Her multiple metastatic lung tumors continue to be diminished in partial response after one course of paclitaxel (Figure 1).

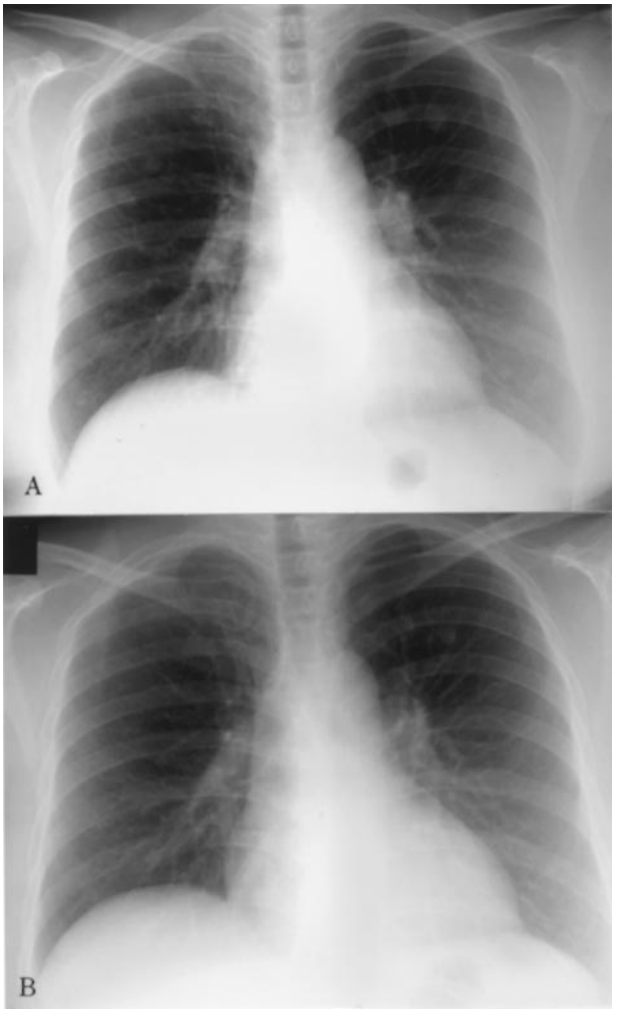

Figure 1. (A) Chest X-ray before therapy with a weekly 1-h paclitaxel regimen. Bilateral multiple metastatic lung tumors are found. (B) Chest X-ray after one course of paclitaxel. They are diminished in partial response.

Discussion

Many studies have demonstrated that anthracycline-containing regimens are a first-line chemotherapy for patients with metastatic breast cancer, with reported response rates of 43–82%.[1–7] Combination chemotherapy containing anthracycline has led to higher response rates and longer survival for patients with recurrent breast cancer compared to combination chemotherapy without anthracycline.[3,6,14,15]

The advent of taxanes as salvage therapy has further prolonged overall survival.[16] Docetaxel has resulted in response rates of 30–43% in previously anthracycline-exposed metastatic breast cancer.[8–10] Unfortunately, docetaxel resistance occurs in several months.

Docetaxel resistance seems to be defined as the patient having experienced progressive disease while receiving docetaxel with at least two cycles at a dose of 60 mg/m^2 (in Japan). Concerning dosage, 75–100 mg/m^2 of docetaxel has been injected over 1 h every 3 weeks in Europe and the US.[27–30] In Japan, administration of 60 mg/m^2 of docetaxel every 3 weeks is considered standard.[17]

In two *in vitro* studies, some breast cancer cell lines showed only partial cross-resistance between paclitaxel and docetaxel.[11,12] A phase II clinical study showed that docetaxel was active in patients with paclitaxel-resistance breast cancer.[13] Conversely paclitaxel may be active in patients with docetaxel-resistant breast cancer.

Recently, weekly 1-h paclitaxel has been demonstrated to be well tolerated, with a feasible administration schedule.[18–20] The overall response to weekly paclitaxel compared favorably with the responses observed regimens of 3-, 24- and 96-h paclitaxel every 3 weeks in patients with metastatic disease. Paclitaxel doses of 135–250 mg/m^2 have been administered over 3–96 h.[21–25]

The dose of 175 mg/m^2 has been the standard of paclitaxel every 3 weeks regimens. The standard dose of weekly 1-h paclitaxel has not yet been defined, although only one dose-limiting toxicity has occurred at 100 mg/m^2.[26] We administered a weekly paclitaxel dose of 60 mg/m^2, about one-third the dose of the standard 175 mg/m^2 for paclitaxel every 3 weeks.

We presented the case of a patient with docetaxel-refractory anthracycline-pretreated metastatic breast cancer who achieved remission with paclitaxel without major side effects.

Conclusion

Paclitaxel should be considered for patients with docetaxel-refractory breast cancer. Trials of this third-line chemotherapy are necessary.

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