Letter to the Editor

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Apparent beneficial effects by nab-paclitaxel in the treatment of refractory metastatic ovarian carcinoma

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Background

Ovarian epithelial cancer is the fourth most frequent cause of cancer death in women and the most lethal gynecologic cancer in the United States [1–4]. Although responsive to platinum-based cytotoxic chemotherapy [5], the overall long-term survival has improved minimally over the past few decades [1], and most women with ovarian cancer still have a recurrence of the disease and die within 5 years [2,6] because of eventual drug resistance [7,8]. Although recurrent ovarian carcinoma may remain sensitive to platinum compounds, particularly if relapse occurs after 6 months, the value of such second-line therapy and its impact on survival is modest [3,4,8–10]. Numerous cytotoxic agents with limited antitumor activity in the second-line or third-line setting have been identified and tested [11]. These agents often poorly tolerated and lengthy remissions are infrequent [3,4,8–10].

Case presentations

From April 2004 to August 2008, we treated four consecutive patients with platinum-resistant ovarian and peritoneal carcinoma with nab-paclitaxel with a protocol different from the one Teneriello *et al.* [12] instituted in their patients, yet we obtained similar results with no significant reported side effects. We have used a protocol, similar to that use by Rizvi *et al.* [13] in the treatment of stage IV non-small-cell lung cancer. We used nab-paclitaxel 100 mg/m^2 intravenously (i.v.) over 30 min on days 1, 8, and 15 every 28 days. The patients were followed up for 38, 29, 36, and 29 (average 33) months.

The current analysis was performed in August 2008. All the four patients receiving nab-paclitaxel showed significant and persistent reduction in their CA-125 levels. When tumor response was evaluated by Response Evaluation Criteria In Solid Tumors, using imaging studies, one patient showed CR (no radiological evidence of tumors), lasting 26 months, one patient showed PR with more than 30% reduction in tumor size, lasting 27 months and two patients showed SD (tumor sizes remained the same as measured radiologically), lasting 7 months. No serious side effects were observed.

Case one is a 58-year-old female with stage IV high-grade invasive primary peritoneal serous carcinoma, who was initially treated with six cycles of docetaxel plus carboplatin after optimal surgical debulking. After a platinum-free interval of 6 months, recurrent disease was identified. The patient was placed on combination chemotherapy with nab-paclitaxel 100 mg/m^2, administered i.v. over 30 min on days 1, 8, and 15 every 28 days, carboplatin (area under curve=6, Q4 weeks) and bevacizumab (15 mg/kg, Q3 weeks) followed by maintenance with bevacizumab and nab-paclitaxel for 12 months. The CA-125 level decreased from 130 to 5 U/ml, and complete disappearance of tumor was confirmed by radiological studies. The patient has been in complete remission for 26 months after completion of the treatment with nab-paclitaxel.

Case two is a 73-year-old female with a stage IV poorly differentiated primary peritoneal carcinoma, who was initially treated with six cycles of docetaxel plus carboplatin. The disease recurred after 16 months, and she was treated with a repeat combination of platinum and paclitaxel. She initially responded with decreased serum levels of CA-125. The response was short lasting and it recurred again. The patient then received a variety of regimens including combination chemotherapy with topotecan plus liposomal doxorubicin, gemcitabine and bevacizumab with response lasting 6 months. As the serum levels of CA-125 and tumor size were increasing, she was placed on nab-paclitaxel 100 mg/m^2, administered i.v. over 30 min on days 1, 8, and 15 every 28 days. The patient continued on this regimen for 7 months. The CA-125 level gradually decreased from 138 to 24 U/ml, and radiological monitoring of the tumor showed that the patient's tumor size had remained stable (SD), which lasted 7 months, when she died because of a massive pulmonary embolism.

Case three is a 53-year-old female with stage IIIC ovarian clear cell adenocarcinoma, who initially underwent cytoreductive surgery of the tumor. The patient remained to have large residual mass, which was treated by six cycles of chemotherapy with carboplatin plus docetaxel after. The tumor did respond to this treatment with

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declining of CA-125 levels for 6 months but was then found to be progressively elevated and a significant disease detected by PET-computed tomography scan. A variety of chemotherapy agents such as liposomal doxorubicin, topotecan in combination with bevacizumab, and gemcitabine were administered, which resulted in short lasting decrease of CA-125 level and the tumor size remained stationary. The disease eventually recurred with increase of the tumor size on imaging studies and increase of CA-125 levels. Therefore, administration of nab-paclitaxel 100 mg/m^2, i.v. over 30 min on days 1, 8, and 15 every 28 days in combination with bevacizumab was initiated, which resulted in more than 30% reduction of the tumor size (PR) after completion of six cycles of treatment. The CA-125 level also reduced to 30 from a baseline of 274 U/ml, the response lasted for 27 months, when the tumor was found to be resistant again. The patient therefore was treated with other chemicals.

Case four is a 64-year-old female with a stage IV ovarian serous carcinoma, who was initially treated with a total of six cycles of carboplatin plus paclitaxel, followed by extensive cytoreductive surgery. After the surgery, the patient was found to have significant residual disease with liver involvement. Initially, she was treated with the same chemicals, but CA-125 levels were found to be progressively elevated. Therefore, she was treated with various cytotoxic agents such as topotecan, bevacizumab, and gemcitabine with some clinical response lasting for a few months. Then she was found to be resistant again with rising CA-125 levels and increase of tumor mass. This prompted us to initiate nab-paclitaxel 100 mg/m^2, administered i.v. over 30 min on days 1, 8, and 15 every 28 days plus bevacizumab, which was continued for 7 months resulting in a 20% reduction of the target lesion size, and decrease of liver and omental metastatic lesions size (stable disease). The CA-125 level constantly decreased from a baseline of 50 and has remained below 10 U/ml. The patient remained symptoms free for 7 months, and then she died suddenly, probably because of a massive myocardial infarction.

Discussion

Finding an effective therapeutic agent for the treatment of platinum refractory ovarian cancer has been the subject of numerous clinical trials for the past several decades. In this correspondence, we are reporting effectiveness of nab-paclitaxel in the treatment of four patients with platinum-resistant metastatic ovarian epithelial carcinoma and primary peritoneal carcinoma. Our report is different from the report by Teneriello *et al.* [12] in two ways, who found significant effects in platinum-sensitive patients. First, we used nab-paclitaxel in platinum-resistant disease, second we used nab-paclitaxel with a schedule of 100 mg/m^2, administered i.v. over 30 min on days 1, 8, and 15 every 28 days rather than 260 mg/m^2 of nab-paclitaxel i.v. over 30 min on day 1 of each 21-day cycles, which we found patients can tolerate chemotherapy better without many side effects except for some tingling sensation in the extremities. We also treated two more cases of platinum refractory ovarian carcinoma with nab-paclitaxel, which seem to have the same above-mentioned benefits and results, but the follow-up period is too short to warrant any definite conclusion or to include in this case report.

Conclusion

We report four consecutive cases of the beneficial effects of using nab-paclitaxel in the treatment of patients who are refractory to standard chemotherapy including platinum refractory of ovarian or primary peritoneal carcinoma. The side effects of such treatment are minimal and generally tolerated, and administration of the drug is easy and feasible.

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