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CLINICAL TRIAL REPORT

Intrathoracic injection of paclitaxel for a patient with stage IV serous ovarian cancer: a case report

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Abstract
Background There have so far only been few reports on the intrathoracic injection (IT) of paclitaxel for ovarian cancer.
Case The patient was treated with IT paclitaxel to control a large volume of pleural effusion as neoadjuvant chemotherapy. A total of 220 mg (110 mg in each thoracic cavity) of paclitaxel was administrated and the pleural effusion dramatically decreased. The intrathoracic concentration of paclitaxel was 1,524.0, 107.5, 8.1, 11.0 and 3.8 μm/l at 0, 24, 48, 72 and 96 h, respectively. The plasma concentration was 0.05, 0.11, 0.07, 0.04 and 0.02 μm/l, respectively.
Conclusion An extremely high concentration was maintained over 96 h and there was slight transition into general circulation following IT administration. IT paclitaxel might be effective in some patients with ovarian serous adenocarcinoma who have a refractory tumor in the thoracic cavity.

Keywords Ovarian cancer · Paclitaxel · Intrathoracic injection · Pharmacokinetics

Introduction

Paclitaxel is generally administered intravenously. However, there have so far only been few reports on the intrathoracic injection (IT) of this agent which have noted the pharmacokinetic advantages of this method [1–3].

This report presents a case of stage IV serous ovarian cancer. In this case, the patient was treated with IT paclitaxel to control the malignant pleural effusion as neoadjuvant chemotherapy (NAC).

Case report

A 65-year-old Japanese female presented with an abdominal mass, abdominal distension and dyspnea. Computed tomography (CT) and magnetic resonance imaging showed a right adnexal tumor and multiple metastatic tumors in the abdominal cavity. A large volume of ascites and pleural effusion was present and the cytology revealed an adenocarcinoma. The level of serum CA125 was 1,553 U/ml. An exploratory laparotomy was performed and several metastatic tumors were resected from the mesenterium. The pathological examination revealed a serous adenocarcinoma, which was thought to have originated from the ovary. After the operation, a weekly administration of paclitaxel and carboplatin (TC) (paclitaxel: 60–80 mg/m^2, day 1, 8, 15 and carboplatin: area under the curve (AUC) = 2, day 1, 8, 15; 28-day interval) was administered as NAC for two cycles. The serum CA125 level decreased to 654 U/ml and almost all the tumors disappeared, except for the one on the right adnexa, while there was still bilateral pleural effusion and the amount of daily drainage from the thoracic catheter was 300–1,000 ml. A large amount of pleural effusion might affect the circulatory and respiratory system, thus control of the effusion was essential for interval cytoreductive surgery (ICS). Therefore, IT paclitaxel was administered. She had been given 110 mg (80 mg/m^2) of paclitaxel and

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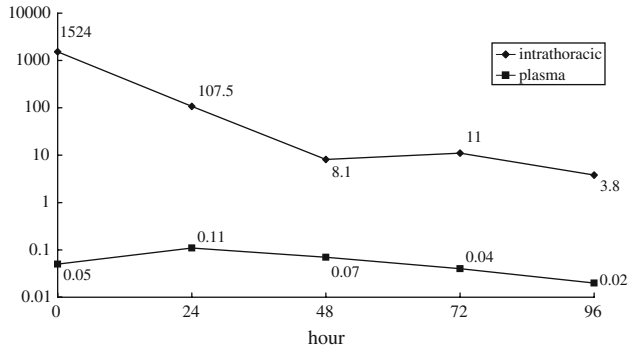

Fig. 1 The intrathoracic and plasma concentration of paclitaxel

190 mg of carboplatin on day 1 of the third course of weekly TC. Perng et al. [1] reported that 175–225 mg/m^2 of paclitaxel is feasible for intrathoracic administration, therefore, she was administered a total dose of 160 mg/m^2 paclitaxel (80 mg/m^2 × 2) on day 8 and 15. A total of 220 mg (110 mg in each thoracic cavity) of paclitaxel was administrated on day 8 in normal saline through the thoracic catheter. Bilateral catheters were clamped for 96 h and then opened again. The pleural effusion dramatically decreased and there was no drainage after 11 days. Although a small amount of effusion of the right thoracic cavity still existed, cytological examinations of the left and right effusion were negative on the sixth and thirteenth day after the treatment, respectively. Serum CA125 decreased to 103 U/ml fifteenth day after the IT and the partial response was obtained by CT according to the RECIST criteria (i.e. a 42% reduction of metastatic tumors in the abdominal cavity and the disappearance of the pleural effusion).

The intrathoracic concentration of paclitaxel was 1,524.0, 107.5, 8.1, 11.0 and 3.8 μm/l at 0, 24, 48, 72 and 96 h, respectively. The plasma concentration was 0.05, 0.11, 0.07, 0.04 and 0.02 μm/l at 0, 24, 48, 72 and 96, respectively. The AUC from 0 to 96 h of the intrathoracic and the plasma samples was 21,445 and 6.0 μm h/l (Fig. 1). The toxicities included grade 1 nausea and chest pain and grade 3 leukopenia, neutropenia and anemia.

The patient then underwent one more cycle of weekly TC (general administration), ICS and adjuvant chemotherapy. She is alive with disease (peritoneal dissemination) at 12 months after the initial treatment, and the pleural effusion has not so far increased.

Discussion

Serous adenocarcinoma of the ovary is often sensitive to TC therapy and this treatment reduces malignant pleural effusion. However, in some wide spread cases, the tumors seem to be partially resistant to these agents. There are two possibilities, the tumor may be insensitive, or the tumor is not properly exposed to the anticancer drug. The latter probably applies in the current case.

The elimination half-life of paclitaxel is about 6.5 h and the maximum plasma concentration is about 5.9 μm/l, when it is administered by 3-h intravenous infusion (IV, 175 mg/m^2) [4]. An extremely high concentration was maintained over 96 h and there was slight transition into general circulation following IT administration in the current case. Perng et al. [1] reported the intrathoracic AUC from 0.5 to 96 h ranged from 4,167 to 43,754 μm h/l (paclitaxel 82.5–225 mg/m^2) and our data was similar to them. When the general plasma AUC (18.5μm h/l by 3-h IV of 175 mg/m^2 paclitaxel [4]) is compared with that for IT in this case, the intrathoracic exposure is calculated that to be 1,160 times greater.

In conclusion, IT paclitaxel might therefore be effective in some patients with ovarian serous adenocarcinoma who have a refractory tumor in the thoracic cavity. A prospective study is therefore needed to determine the clinical efficacy of IT paclitaxel for ovarian cancer.

Conflict of interest statement None.

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