A Case of Recurrent Metastatic Thymoma Showing a Marked Response to Paclitaxel Monotherapy

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We describe a case of recurrent metastatic thymoma showing an excellent response to salvage paclitaxel monotherapy. The patient had undergone a series of platinum-based chemotherapy treatments during the previous 20-month period and the patient’s disease was considered resistant to such therapy at the start of treatment with paclitaxel. This is the first report to suggest that paclitaxel has anti-thymoma activity.

Key words: thymoma – paclitaxel – chemotherapy

INTRODUCTION

Thymoma is a relatively common tumor of the anterior mediastinum and is frequently associated with immunological disorders such as myasthenia gravis, pure red cell aplasia and hypogammaglobulinemia (1–4). It usually progresses slowly and rarely produces distant metastasis and therefore surgery remains the mainstay of treatment (5). In addition, chemotherapy has been widely used in the treatment of unresectable thymoma. The most commonly used and the most active single agent is cisplatin (6). However, therapeutic efficacy has been studied with only a limited number of agents (6). In this paper, we describe a case of recurrent metastatic thymoma showing an excellent response to paclitaxel monotherapy. To our knowledge, this is the first report to suggest the effectiveness of paclitaxel in the treatment of thymoma.

CASE REPORT

A 66-year-old woman was admitted to our hospital in April 2001 because of an increase in dull pain in the upper abdominal region. She had been diagnosed as having mixed cell-type thymoma by thoracic biopsy 21 months before admission. On microscopic examination, the tumor showed solid nests composed of polygonal epithelioid cells and lymphocyte infiltration in a fibrous stroma. Parakeratosis was also seen in the solid nest (Fig. 1). At the time of initial presentation, the disease had directly invaded the sternal bone and disseminated to the pleura and liver [stage IVb according to the classification proposed by Masaoka et al. (7)]. Previous treatments for the disease had included (i) two cycles of combination chemotherapy, consisting of carboplatin and etoposide followed by 50 Gy of thoracic radiotherapy (between August 16 and November 26, 1999, (ii) two cycles of the same chemotherapy alone (between June 1 and July 18, 2000) and (iii) two cycles of a combination of cisplatin, Adriamycin and cyclophosphamide (between November 8 and December 20, 2000). Dexamethasone 8 mg was also used as an antiemetic agent during all courses of the first and third chemotherapies. The patient’s disease showed a good short-term response to the first and second chemotherapies, but resistance to the third chemotherapy.

At the time of admission, computed tomography (CT) of the chest and abdomen revealed a tumor located in the anterior mediastinum, pleura, lung and liver (Fig. 2). Asymptomatic brain metastasis was also found. Laboratory examination revealed a decrease in the hemoglobin level (6.8 g/dl), the reticulocyte percentage being within the normal range (1.5%). The serum levels of lactate dehydrogenase (LDH, 1894 IU/l), carcinoembryonic antigen (CEA, 35.7 ng/ml) and neuron-specific enolase (NSE, 243 ng/ml) were increased. The patient received paclitaxel 80 mg/m² on days 1 and 8 every 3 weeks. It was administered intravenously over 3 h, with a short premedication procedure (dexamethasone 20 mg, diphenhydramine 50 mg and ranitidine 150 mg) to avoid any allergic reaction. The adverse events related to this therapy were not more severe than grade 1, according to the National Cancer Institute Common Toxicity Criteria (8). Symptoms were improved to a
considerable degree after one cycle of chemotherapy. The patient has since received this therapy as an outpatient. CT of the abdomen after eight cycles of chemotherapy demonstrated a marked reduction in the size of the liver metastases (Fig. 3). However, the intrathoracic lesions showed no change during the treatment period. The serum levels of LDH, CEA and NSE decreased to 587 IU/ml, 11.7 ng/ml and 25.6 ng/ml, respectively. The scheme of treatment and clinical courses are shown in Fig. 4. In addition, the hemoglobin level, despite cytotoxic therapy, increased to 9.6 g/dl without any treatment for anemia. This finding suggested partial remission of the pure red cell aplasia that had complicated the thymoma in this patient.

DISCUSSION

Approximately one-third of patients with thymoma have locally advanced or metastatic disease. Metastases from thymoma usually occur within the thorax and only 1% of patients have extrathoracic lesions (1–3,5). Because of the relatively small number of patients with advanced thymoma, the efficacy of chemotherapy has not been studied extensively for a wide range of agents and the most active agent is considered to be cisplatin (6). Park et al. (9) reported that 11 (65%) of 17 patients with advanced thymoma showed a response to cisplatin with or without prednisolone. Therapy with corticosteroid has also been demonstrated to be effective for the treatment of metastatic thymoma (10). In the present case, corticosteroid was administered in combination with every chemotherapy treatment. However, this agent is not yet considered effective, since the present disease had shown resistance to the treatment prior to paclitaxel monotherapy. For multi-agent chemotherapy, combinations that include both cisplatin and adriamycin have been commonly used. These combinations have provided objective response rates of 50–92% (11,12). In addition, a combination of platinum compound and etoposide has been reported to be highly active against thymoma (13,14). However, it seems that there is no well-established standard regimen for the treatment of this disease.

Paclitaxel, a third-generation chemotherapy agent, has a dramatic effect on epithelial tumors and also advanced non-small-
cell lung cancer (NSCLC) (15–18). Groen et al. (16) reported that paclitaxel has no cross-resistance to carboplatin, cyclophosphamide, adriamycin or etoposide. Moreover, Akerley et al. suggested an advantage of weekly administration of paclitaxel over the conventional schedule for this agent (19); weekly paclitaxel therapy for advanced NSCLC (175 mg/m^2 for 6 weeks of an 8-week cycle) provided a response rate of 56% and a 1-year survival rate of 53%. The present patient received modified therapy with weekly paclitaxel (80 mg/m^2 on days 1 and 8, every 3 weeks). This regimen is an alternative arm of a randomized phase II trial that has been conducted by our group on patients with recurrent NSCLC. It is possible that this paclitaxel dose might be suboptimal for the treatment of advanced thymoma. However, in general, a reduced chemotherapy dose is required for previously treated cancer patients. In addition, a phase II study of weekly paclitaxel monotherapy indicated that the maximum tolerated dose was 80 mg/m^2 for the treatment of recurrent ovarian cancer (20).

In the present case, the serum NSE level was increased to a considerable degree. Although 11.1% of patients with thymoma are reported to have an increased level of NSE (21), it is unclear whether the chemotherapy sensitivity of this disease is correlated with the level of NSE. There have been two case reports of thymoma treated with paclitaxel-containing chemotherapy (22,23). However, to our knowledge, this is the first report to have demonstrated the efficacy of paclitaxel as a single agent against thymoma. In addition, treatment-related toxicity was well tolerated. This paclitaxel monotherapy merits further investigation as a first-line treatment for patients with invasive and/or metastatic thymoma.

References


