Advanced Thymic Cancer Treated with Carboplatin and Paclitaxel in a Patient Undergoing Hemodialysis

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Abstract

A 53-year-old man with an asymptomatic anterior mediastinal tumor undergoing hemodialysis was referred to our institution. He was diagnosed with thymic basaloïd carcinoma based on the findings of a chest tomography-guided biopsy and successfully treated with carboplatin (300 mg/m²/day) and paclitaxel (200 mg/m²/day) on day 1 for six three-week cycles. To our knowledge, this is the first report regarding the efficiency of a carboplatin dose-definition method based on the body surface area with paclitaxel in a hemodialysis patient. This report may therefore be useful for treating hemodialysis patients who are candidates for carboplatin and paclitaxel therapy.

Key words: thymic cancer, hemodialysis, carboplatin, paclitaxel

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Introduction

Over 300,000 patients are currently under hemodialysis in Japan, and substantial improvements in renal replacement therapy have resulted in prolonged survival among these patients. Patients undergoing hemodialysis tend to exhibit a higher incidence of various cancers (1). Therefore, the proportion of hemodialysis patients dying of cancer has gradually increased. The rate of cancer death among all Japanese dialysis patients between 2004 and 2011 ranged from 9.0% to 9.8%, compared to 7.1% to 8.5% between 1991 and 2003 (2). However, due to inconclusive chemotherapeutic results, some patients diagnosed with advanced cancer are reluctant to undergo chemotherapy and some oncologists are unwilling to prescribe such experimental procedures.

Thymic cancer is a rare type of thymic neoplasm, with an incidence of only 0.15 per 100,000 cases based on the Surveillance, Epidemiology and End Results database (3). These tumors are classified as either squamous cell carcinoma or a rarer type of carcinoma, such as basaloïd carcinoma, an extremely rare histological type of thymic cancer that has not been thoroughly investigated (4). We herein describe the case of a patient with advanced thymic basaloïd carcinoma who underwent hemodialysis while receiving systemic chemotherapy.

Case Report

A 53-year-old man was referred to our institution with an asymptomatic anterior mediastinal tumor. The patient was anuric and had received hemodialysis for five years for end-stage renal disease related to type 2 diabetes mellitus. Hemodialysis was performed for four hours using a polysulfone membrane (APS™ Asahi Kasei, Tokyo, Japan) three times a week. Chest computed tomography showed an anterior mediastinal tumor measuring 7 cm in diameter with slight calcification (Fig. 1A). An examination of a computed tomography-guided needle biopsy specimen revealed a solid mass consisting of small- to medium-sized round tumor cells with a high nuclear-to-cytoplasmic ratio separated by a thin fibrous septum (Fig. 2). On an immunohistochemical

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Figure 1. Enhanced chest computed tomography scan showing an anterior mediastinal tumor measuring 7 cm in diameter, with slight calcification (A), direct invasion of the tumor into the sternum (B) and pleural dissemination (C).

Figure 2. Representative Hematoxylin and Eosin staining biopsy specimen at original magnification [×100 (A)] and high-power magnification [×600 (B)].

analysis, the tumor cells were found to express keratin, cytokeratin 5, CD117, CD5 and bcl-2; however, staining for TTF-1, CD56, synaptophysin, LCA, CD3 and CD20 was negative. The patient was accordingly diagnosed with thymic basaloid carcinoma. At the time of diagnosis, the mediastinal tumor was considered to be inoperable due to the presence of direct invasion into the sternum with pleural dissemination (Fig. 1B, C) and classification indicating advanced stage disease (stage 4a according to the Masaoka staging system). On a physical examination, the patient’s
The patient was treated with carboplatin (300 mg/m$^2$/day) and paclitaxel (200 mg/m$^2$/day) on day 1 every three weeks. The hemodialysis session was started the same day one hour after the completion of the administration of carboplatin and paclitaxel and continued for four hours. On day 16 of the first cycle of chemotherapy, grade 4 neutropenia (minimum 400/μL) was noted. However, the patient quickly recovered by day 18 (750/μL) without granulocyte-colony stimulating factor support. No other severe adverse events were observed during the chemotherapy treatment. After six cycles of carboplatin and paclitaxel, computed tomography showed moderate regression of the anterior mediastinal mass (Fig. 3). Ten months after the completion of treatment, the patient remains alive, without any signs of progression.

**Discussion**

We herein presented the first case report of advanced thymic basaloid carcinoma treated with a combination of carboplatin and paclitaxel in a patient undergoing hemodialysis. This treatment combination was selected for its doublet therapy, reported patient feasibility for those undergoing hemodialysis and recommended use as a regimen according to the National Comprehensive Cancer Network guidelines for thymic carcinoma. The response rate to this combination therapy in patients with thymic carcinoma has been reported to be 21.7% (5). In addition, combined carboplatin and paclitaxel is a well-investigated chemotherapy regimen for patients undergoing hemodialysis. For example, pharmacokinetic studies show similar curves for paclitaxel the plasma concentrations in patients undergoing hemodialysis as well as those with a normal renal function for a given dosage (6). However, the definition of the proper carboplatin dose remains controversial. Carboplatin is primarily metabolized in the kidneys and easily dialyzed during hemodialysis due to its low protein binding capacity and intermediate molecular weight (7). Therefore, the plasma concentration of carboplatin is affected by the dose and timing of treatment in addition to the duration of hemodialysis. Several studies have reported the use of carboplatin-based therapy during hemodialysis (Table) (8-11). However, as of yet, there is no established consensus regarding the optimal timing and duration of hemodialysis with respect to the chemotherapy regimen in hemodialysis patients. One pharmacokinetics study of carboplatin suggested the optimal time to perform hemodialysis following carboplatin administration is up to three hours (7). The dose of carboplatin is calculated based on the Calvert formula [i.e. dose (mg) = area under the concentration-time curve (AUC) × (glomerular filtration rate +25)], with the glomerular filtration rate considered to be zero in most of case reports of anuric hemodialysis patients (12). However, this method may be inadequate, as the Calvert formula was originally validated only in patients with a glomerular filtration rate of 33-136 mL/min (13). In addition, this method does not take into consideration the patient’s physique; therefore, the dose of carboplatin calculated using this method may be too low. In contrast, the doses of other chemotherapeutic agents are calculated based on the patient’s body surface area. Inoue et al. described the efficiency of a carboplatin dose-definition method based on the body surface area in pharmacokinetic studies of hemodialysis patients (14). In the present case, the dose of carboplatin calculated according to the body surface area-based method (495 mg) was actually four-fold higher than the dose calculated using the Calvert formula (125 mg). Therefore, it is likely that the body surface area-based carboplatin dose definition is reasonable for application in patients with renal insufficiency, and we used this method to determine the carboplatin dose in combination with paclitaxel.

In the present case, we calculated the dose of carboplatin based on the patient’s body surface area in combination with the standard paclitaxel dose; this regimen showed both favorable safety and efficacy. However, the administration of chemotherapy in patients undergoing hemodialysis may increase the risk of hematological toxicities, and particular care should therefore be applied in such cases. Combined carboplatin and paclitaxel therapy is a widely used chemotherapeutic regimen for various cancers, including thymic carcinoma. Many oncologists consider this combined therapy to be an effective treatment for non-small cell lung cancer, ovarian cancer, melanoma and/or carcinoma of unknown primary origin. We suggest that this combined therapy, which uses a body surface area-based carboplatin dose definition, is an adequate regimen for use in patients undergoing
hemodialysis with the above advanced cancers. Although further prospective studies, including pharmacokinetic analyses, are warranted, this case report provides useful information for routine clinical practice in treating patients undergoing hemodialysis with rare cancers who are considered to be candidates for treatment with carboplatin and paclitaxel.

The authors state that they have no Conflict of Interest (COI).

References


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