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Case Report

First-Line Treatment with Carboplatin plus *nab*-Paclitaxel and Maintenance Monotherapy with *nab*-Paclitaxel for a Thymic Carcinoma: A Case Report

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Keywords
Carboplatin · *nab*-Paclitaxel · Maintenance · First-line treatment · Thymic carcinoma

Abstract
Thymic carcinomas are rare malignant tumors, located in the anterior mediastinum. For the treatment of these carcinomas, several chemotherapy regimens have been suggested, including carboplatin plus paclitaxel. However, because of the rarity of these tumors, the standard chemotherapy regimen has not yet been established. Here, we report a case of thymic carcinoma that responded to first-line carboplatin plus nanoparticle albumin-bound paclitaxel (*nab*-paclitaxel) therapy with continuation maintenance *nab*-paclitaxel monotherapy. A 78-year-old male presented to a hospital with the chief complaint of dyspnea. Cardiomegaly was detected on chest X-ray scans, and marked pericardial effusion was observed by echocardiography. Chest computed tomography scans revealed the presence of a mediastinal mass, pericardial thickening, and pericardial effusion. The serum levels of the tumor marker CYFRA 21-1 (cytokeratin-19 fragment) were elevated. Eventually, he was diagnosed

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with squamous cell carcinoma of the thymus, which was staged as cT4N3M0 or stage IV (according to the tumor-node-metastasis classification). Chemotherapy with carboplatin on day 1 and *nab*-paclitaxel on days 1, 8, and 15, every 4 weeks was initiated. After the administration of 4 cycles of this regimen, the tumor diameter appeared reduced, and the serum CYFRA 21-1 levels were normalized. After a 1-month interval, the serum CYFRA 21-1 levels increased again; therefore, maintenance *nab*-paclitaxel monotherapy was initiated. At the end of the treatment, the patient experienced a progression-free survival of 10.3 months. Carboplatin plus *nab*-paclitaxel may be an appropriate alternative first-line treatment for thymic carcinomas. Additionally, maintenance *nab*-paclitaxel monotherapy may prolong the progression-free survivals of patients with thymic carcinomas.

Introduction

Thymic carcinomas are rare malignant tumors located in the anterior mediastinum. These tumors arise from the thymic epithelium and have been reported to account for 12–36% of all thymic epithelial tumors [1–3]. Complete surgical resection is the preferred method of treatment for thymic carcinomas with no distant metastases. In cases with unresectable tumors or distant metastases, systemic chemotherapy is administered. Several chemotherapy regimens have been suggested, such as the ADOC (cisplatin, doxorubicin, vincristine, and cyclophosphamide) [4], CODE (cisplatin, vincristine, doxorubicin, and etoposide) [5], and carboplatin plus paclitaxel [6] regimens. However, because of the rarity of these tumors, the standard regimen of chemotherapy has not yet been established.

Here, we report a case of thymic carcinoma that responded to treatment with a carboplatin plus nanoparticle albumin-bound paclitaxel (*nab*-paclitaxel) regimen; moreover, continuation maintenance monotherapy with *nab*-paclitaxel may have enabled a prolonged progression-free survival in this patient.

Case Presentation

A 78-year-old male presented to a hospital with the chief complaints of dyspnea and ache in his left shoulder. Cardiomegaly was detected on chest X-ray scans, and the presence of pericardial effusion and moderate aortic regurgitation was observed by echocardiography. He was treated with diuretic agents, and his symptoms improved. Three months later, he presented to the hospital again with worsening dyspnea. Worsening cardiomegaly was detected on chest X-ray scans (Fig. 1a), and marked pericardial effusion was observed on echocardiography. Pericardiocentesis was performed, and 1,500 mL of hemorrhagic pericardial effusion fluid was drained. Chest examination by computed tomography revealed the presence of a mediastinal mass, pericardial thickening, and pericardial effusion (Fig. 1b, c), and the patient was transferred to our hospital for treatment. He showed marked emaciation (he was 164.6 cm tall and weighed 43.6 kg) and a low blood pressure (81/47 mm Hg). He was assessed to have an Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 2. His laboratory findings from a complete blood cell count analysis were almost normal; his hepatic and renal functions were normal; his albumin levels were lower than normal (2.7 mg/dL), and his C-reactive protein levels were high (10.00 mg/dL). The levels of the soluble serum tumor marker CYFRA 21-1 (cytokeratin-19 fragment) were increased (36.0 ng/mL). After further examination, he was diagnosed with squamous cell carcinoma of

the thymus. According to the tumor-node-metastasis staging system, the carcinoma stage was cT4N3M0 or stage IV.

Carboplatin was administered on day 1 at a dose of a targeted area under the concentration-time curve of 5, and *nab*-paclitaxel at a dose of 70 mg/m^2 on days 1, 8, and 15 for every 4 weeks. Four cycles of this regimen were administered. During 3 of 4 cycles, grade 3 or 4 neutropenia occurred, and 3 doses of *nab*-paclitaxel on day 15 or 8 could not be administered. The patient did not experience any other severe adverse events. After the administration of 2 cycles of this regimen, chest computed tomography scans revealed a reduction of the tumor diameter (Fig. 2a); administration of 2 additional cycles led to further reductions (Fig. 2b). The ECOG PS of the patient improved to 0 (zero). The serum CYFRA 21-1 levels decreased to 2.3 ng/mL. After the interval of 1 month, these levels increased again to 4.3 ng/mL. Resultantly, maintenance *nab*-paclitaxel monotherapy at a dosage of 70 mg/m^2 on days 1 and 8, for every 3 weeks was initiated. A total of 8 cycles of maintenance *nab*-paclitaxel monotherapy were administered in 4.8 months, after which the tumor showed regrowth. The patient experienced a total of 10.3 months of progression-free survival from the start of chemotherapy. After the regrowth of the tumor, the patient has received second-line treatment. Till date, the patient has been alive for a total of 22.0 months from the start of first-line chemotherapy.

Discussion

In the present case report, we noted 2 important clinical observations: (1) the carboplatin plus *nab*-paclitaxel regimen may be effective as a first-line treatment for thymic carcinomas, and (2) maintenance *nab*-paclitaxel monotherapy might prolong the progression-free survival in patients with thymic carcinomas. These observations are further discussed in-depth.

Firstly, our study suggests that carboplatin plus *nab*-paclitaxel may be effective as first-line treatment for thymic carcinomas. To the best of our knowledge, this is the first report describing the efficacy of such treatment. Till date, carboplatin plus *nab*-paclitaxel therapy has proved to be efficacious in 3 cases of thymic carcinomas that have been reported in English journals; however, all of these cases had undergone previous treatments [7–9]. Some retrospective [10] and prospective [6] studies have reported that carboplatin plus paclitaxel has been effective for the treatment of thymic carcinomas. However, *nab*-paclitaxel is a nanoparticle albumin-bound formulation of paclitaxel. This new generation paclitaxel has been more effective in the treatment of non-small cell lung cancers (NSCLCs); moreover, it is less toxic, in terms of the incidence of peripheral neuropathy, neutropenia, arthralgia, and myalgia [11]. For NSCLCs, the doses of carboplatin and *nab*-paclitaxel are as follows: carboplatin at a dose of an area under the concentration-time curve of 6 on day 1 and *nab*-paclitaxel at a dose of 100 mg/m^2 on days 1, 8, and 15 for every 3 weeks [11]. In the present case, the doses of carboplatin and *nab*-paclitaxel had to be reduced because the patient was elderly and had poor PS. Nevertheless, the treatment was effective. Thus, we conclude that carboplatin plus *nab*-paclitaxel therapy may be a good alternative first-line treatment for thymic carcinomas.

Secondly, our study also suggests that maintenance *nab*-paclitaxel monotherapy might prolong the progression-free survivals of patients with thymic carcinomas. In NSCLCs, the administration of maintenance paclitaxel monotherapy after carboplatin plus paclitaxel treatment prolonged the progression-free and overall survivals in treated patients [12]. Resultantly, the use of maintenance paclitaxel monotherapy was adopted at a phase III trial

comparing carboplatin plus weekly paclitaxel with carboplatin plus standard paclitaxel for the treatment of NSCLCs [13]. In the present case of thymic carcinoma, *nab*-paclitaxel monotherapy maintained a stable condition for the disease for 5.5 months. Thus, we conclude that maintenance *nab*-paclitaxel monotherapy after carboplatin plus *nab*-paclitaxel treatment might prolong the progression-free survivals of patients with thymic carcinomas.

For the treatment of thymic carcinomas, the continuation of carboplatin plus *nab*-paclitaxel could be better than the administration of maintenance *nab*-paclitaxel monotherapy. At the phase III study of NSCLCs, the cycles of carboplatin plus *nab*-paclitaxel could be continued till the time of disease progression [11]. However, it has been demonstrated that the patients with advanced NSCLCs did not show improved overall survivals during the administration of 6 cycles of first-line platinum-based chemotherapy, compared with the administration of 3 or 4 cycles of such regimens [14]. Moreover, the accumulation of carboplatin may cause hypersensitivity reactions in the patients [15]. For cases in which the continued administration of carboplatin is difficult because of the occurrence of adverse events, continuation maintenance *nab*-paclitaxel monotherapy might prove to be an appropriate alternative treatment.

It is uncertain whether carboplatin plus *nab*-paclitaxel therapy is effective for all histopathological subtypes of thymic carcinomas. These histopathological subtypes are as follows: squamous cell carcinomas; neuroendocrine carcinomas, including small-cell and large-cell neuroendocrine carcinomas, and carcinoid tumors; mucoepidermoid carcinomas; and others [1]. The histopathological subtypes of the 3 cases previously reported were as follows: squamous cell carcinoma [7], large-cell neuroendocrine carcinoma [8], and lymphoepithelioma-like carcinoma [9]; all of them were reported to be effectively treated with carboplatin plus *nab*-paclitaxel. It has also been reported that carboplatin plus *nab*-paclitaxel was more effective for the treatment of squamous cell carcinoma than that of non-squamous cell carcinomas in NSCLCs [11]. A prospective study is needed to evaluate the efficacy of carboplatin plus *nab*-paclitaxel treatment for thymic carcinomas of all known histological subtypes.

Conclusions

We report a case of thymic carcinoma treated with first-line carboplatin plus *nab*-paclitaxel with maintenance *nab*-paclitaxel monotherapy. We conclude that carboplatin plus *nab*-paclitaxel may be a good alternative first-line treatment for thymic carcinomas. Additionally, maintenance *nab*-paclitaxel monotherapy might prolong the progression-free survivals of patients with thymic carcinomas.

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Statement of Ethics

The authors have no ethical conflicts to disclose.
Written consent was obtained from the patient for the publication of this case report.

Disclosure Statement

The authors declare that they have no conflicts of interest to disclose.

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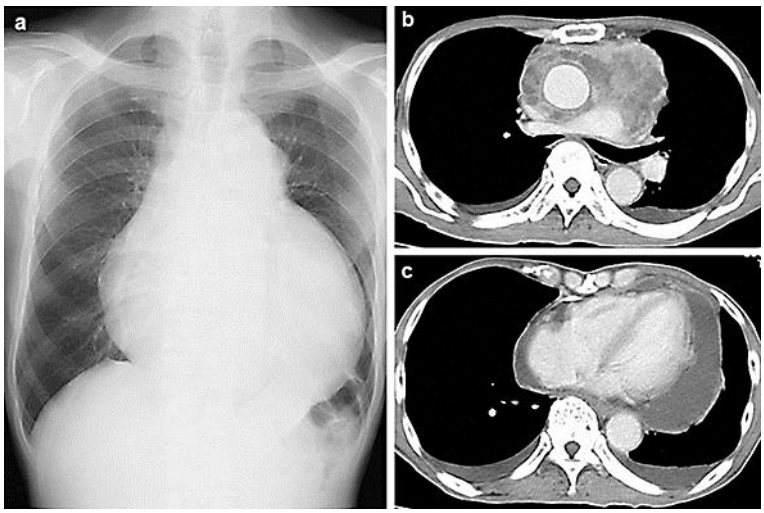

Fig. 1. Initial chest X-ray and chest computed tomography scans. **a** Significant cardiomegaly is present. **b** An anterior mediastinal mass can be observed on chest computed tomography scans after pericardiocentesis. **c** Pericardial effusion and pericardial thickening suggest the presence of carcinomatous pericarditis.

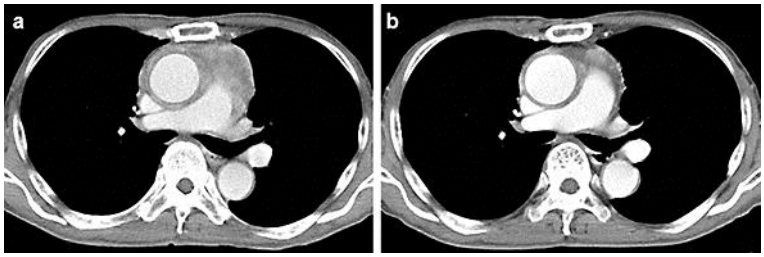

Fig. 2. The findings of chest computed tomography scans after the administration of 2 and 4 cycles of carboplatin plus *nab*-paclitaxel therapy. **a** Chest computed tomography scan obtained after the administration of 2 cycles of the regimen. The tumor appears reduced in diameter. **b** Chest computed tomography scan taken after the administration of 4 cycles of the regimen. The tumor appears markedly reduced in diameter.