Successful S-1 Monotherapy for Chemorefractory Thymic Carcinoma

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Abstract. The optimal chemotherapeutic regimen for inoperable thymic carcinoma remains uncertain and little information is available regarding the usefulness of salvage chemotherapy. S-1, a newly developed oral fluorouracil antitumor drug, has been reported to be effective in the treatment of gastrointestinal tumors and non-small cell lung cancer. This case study reports a case of chemorefractory thymic cancer with a good response to S-1 monotherapy. S-1 was used as sixth-line chemotherapy and the response was the first remarkable tumor regression in the patient’s clinical course. S-1 appears to have significant activity against thymic carcinoma.

Thymic carcinoma differs from thymoma not only morphologically but also biologically (1, 2). Thymic carcinoma is a thymic epithelial neoplasm with cytological malignant features and a clinical course that tends to be much more aggressive than that of thymoma (1-4). Thymic carcinoma also tends to metastasize widely, which leads to a highly lethal clinical course (1-4), especially in inoperable cases. Thus, systemic chemotherapy may play an important role in treatment of thymic carcinoma. Cisplatin-based chemotherapy has repeatedly been shown to be of benefit in certain patients (5, 6). However, the treatment options for chemorefractory or relapsed thymic cancer are extremely limited because of a lack of evidence regarding effective treatments. This case study describes a case of chemorefractory thymic cancer that showed a good response to S-1 monotherapy.

Case Report

A 48-year-old woman was admitted to the host hospital because of acute onset of dyspnea in August 2004. Chest computed tomography (CT) revealed a large anterior mediastinal mass and massive pericardial effusion. Immediate pericardiocentesis improved her cardiopulmonary distress and percutaneous CT-guided biopsy of the anterior mediastinal mass was also performed. The histological findings revealed squamous cell carcinoma of the thymus. According to the classification of Masaoka et al. (8), the patient had unresectable, locally advanced disease (IVa). The patient was initially treated with four cycles of cisplatin, doxorubicin, vincristine, and cyclophosphamide followed by two cycles of cisplatin and CPT-11 combination chemotherapy. Although the pericardial effusion disappeared, the size of the anterior mass remained unchanged. Treatment with carboplatin (CBDCA) and paclitaxel was started as third-line chemotherapy in March 2006. The size of the anterior mass was reduced slightly, but the patient did not achieve partial response by the RECIST criteria after six courses of chemotherapy. Subsequently, the patient was treated with various non-platinum regimens, including gemcitabine plus docetaxel or amrubicin, but these treatments failed to reduce the tumor size. Thus, the best tumor response to the prior five chemotherapeutic regimens during the entire clinical course was stable disease. The tumor size increased after these chemotherapies. Additional palliative treatment for the patient was considered. S-1 was administered orally at a dose of 80 mg/m² initially every two weeks in May 2009. The schedule was followed by three weeks of S-1 administration and a two-week drug-free interval. Although pigmentation (grade 2) and diarrhea (grade 1) occurred during S-1 administration, no other apparent hematologic or non-hematologic toxicities were observed for one year. With regard to the tumor responses, the mediastinal mass showed marked reduction in size (Figure 1A, B). At present, S-1 therapy has been continued, and the patient remains well with partial response status.

Discussion

This case report describes a positive experience with successful salvage chemotherapy with S-1 for unresectable thymic carcinoma in a patient resistant to prior platinum-containing chemotherapy. S-1 used as sixth-line chemotherapy
was the only agent that showed encouraging results throughout the clinical course in this case. Ono et al. reported a similar case of chemorefractory thymic cancer with a good response to S-1 as fourth-line treatment (9). The patient also failed to respond to prior chemotherapeutic regimens, including CBDDA plus paclitaxel, amrubicin, and gemcitabine. Furthermore, the effectiveness of S-1 as first-line therapy against thymic cancer was also reported in monotherapy (10) and in combined chemoradiotherapy (11).

Based on these clinical reports, it should be emphasized that S-1 may be useful as an alternative chemotherapy agent for thymic carcinoma. S-1 is a novel oral fluoropyrimidine derivative consisting of tegafur and two modulators, 5-chloro2,4-dihydroxypyridine (CDHP) and potassium oxonate (Oxo), in a molar ratio of 1:0.4:1. Tegafur is a prodrug of 5-fluorouracil (5-FU) and CDHP may act to prolong high 5-FU activity in blood by acting as a reversible competitive inhibitor of dihydropyrimidine dehydrogenase (DPD), an enzyme involved in 5-FU degradation. Oxo was able to reduce 5-FU-induced gastrointestinal toxicity through competitive inhibition of orotate phosphoribosyltransferase. S-1 has been reported to be active against various solid tumors, including gastric cancer (12) and non-small cell lung cancer (13). It has been demonstrated that the anticancer activity of S-1 is closely related to the intratumoral expression of DPD and thymidylate synthase (14). Thus, immunohistological analysis of these enzymes in thymic cancer may be helpful for elucidating the pharmacological mechanisms of action of S-1. To the Authors’ knowledge, there have been no previous reports regarding the expression profiles of these enzymes in thymic cancer. Further clinical experience and studies are required to determine the therapeutic benefit of S-1 in unresectable thymic cancer.

In summary, several case reports, as well as the observations in the present case, indicate that S-1 is a novel agent with good activity against advanced thymic carcinoma. This novel agent merits further clinical investigation for treatment of patients with thymic carcinoma.
References


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