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Case Report Open Access

# The Effectiveness and Tolerance of TS-1 a Monotherapy for Relapsed Thymic Cancer Patient Who could not Tolerate Platinum Compounds

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## Abstract

**Background:** The optimal chemotherapeutic regimens for thymic cancers still remain controversial, although systemic chemotherapy is an important therapeutic modality for unresectable thymic cancer. In general, platinum-based regimens such as CODE and ADOC are widely used. However, several serious side effects of the platinum therapy may significantly restrict its efficacy for clinical application. We herein describe a case with a good response to TS-1 treatment for relapsed thymic cancer in a patient who could not tolerate platinum compounds.

**Case report:** A 73-year-old woman was diagnosed with thymic cancer, Masaoka stage IVa, in May 2009. She underwent the concurrent chemoradiation therapy. In September 2011, lung metastasis of the thymic cancer was noted in the right upper lobe. It was difficult to continue platinum-based chemotherapy due to various life-threatening side effects of the treatment. In June 2013, the chest CT scan revealed the growth of the right upper lobe metastatic tumor and left upper lobe atelectasis due to a metastatic polyploidy lesion in the left upper bronchus. The patient underwent partial resection of the lesion and repeat resections in June and September 2014. At the same time, the right upper lobe metastatic tumor had continued to grow. The patient received chemotherapy with TS-1 monotherapy. There were no severe toxicities and the right upper lobe metastatic tumor showed a marked reduction in size. At present, TS-1 therapy has been continued and the patient remains well with an excellent performance status.

**Conclusion:** TS-1 may be a good alternative treatment for patients who cannot tolerate platinum compounds.

**Keywords:** TS-1; Effectiveness; Tolerance; Thymic cancer

## Introduction

Thymic cancer is a rare and invasive mediastinal neoplasm. Systemic chemotherapy is an important therapeutic modality for unresectable thymic cancer. However, the treatment options are extremely limited due to the lack of evidence on effective treatments, even in the first-line setting. In addition, several serious side effects of the chemotherapy may significantly restrict its efficacy. We herein describe a case that showed a good response to TS-1 treatment for relapsed thymic cancer in a patient who could not tolerate platinum compounds.

## Case report

A 74-year-old female was initially evaluated for a mediastinal mass detected on chest computed tomography (CT) in May 2009. Contrast-enhanced CT showed an anterior mediastinal mass with a poorly defined margin. The interface between the lesion and surrounding organs was not clear. We elected to perform surgery, as there were no other signs of distant metastasis. The intraoperative findings showed that the mass had invaded the bilateral lungs, sternal bone and pericardium (Masaoka stage IVa). Due to the presence of extensive invasion, a biopsy of the tumor was performed, and the pathological results of the biopsy specimen were consistent with a diagnosis of primary thymic epidermoid keratinizing squamous cell carcinoma (World Health Organization (WHO) type C). Following the biopsy, the patient underwent chemoradiotherapy with a total delivered external beam dose of 60 Gy and CODE chemotherapy, (consisting of cisplatin, vincristine, doxorubicin and etoposide), with a good objective clinicoradiographic response.

Regular follow-up with planned CT imaging was performed after the chemotherapy. In September 2011, lung metastasis of the thymic cancer was noted in the right upper lobe on the follow-up CT imaging, and the patient underwent ADOC chemotherapy (consisting of a combination of adriamycin, cisplatin, vincristine and cyclophosphamide). However, it was difficult to continue the chemotherapy regimen because the patient's performance status worsened due to the onset of various life-threatening side effects of the treatment, which included frequent neutropenic fever and a severe electrolyte imbalance. In June 2013, the patient developed dyspnea. A chest CT scan revealed the growth of the right upper lobe metastatic tumor and left upper lobe atelectasis. A metastatic polypoid lesion was noted in the left upper bronchus on bronchoscopy. The lesion was treated by bronchoscopic resection using snare electrocautery, although the lesion was partially resected because the peripheral part of the segmental bronchus (B3) was found to be the origin of the polypoid tumor and bronchoscopy could not be used to reach this site. The patient refused chemotherapy because she was concerned about a prolonged recovery. Therefore, regular follow-up with planned CT imaging was performed. In March 2014, she developed dyspnea caused by the regrowth of the polypoid metastatic thymic cancer in the left

upper bronchus. The patient underwent a repeat partial resection of the lesion via bronchoscopy. Furthermore, in June and September 2014, we performed a partial bronchoscopic resection for the polypoid lesion. At the same time, the right upper lobe metastatic tumor had continued to grow (Figure1).

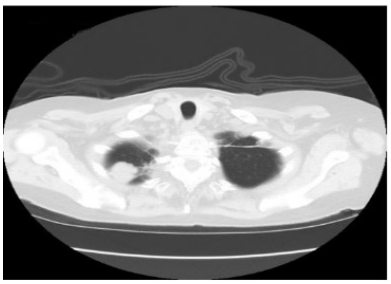

**Figure 1:** A chest CT scan showed the presence of a right upper lobe metastatic tumor.

The patient received chemotherapy with TS-1 monotherapy because she consented to this chemotherapy. The schedule was followed by oral administration twice daily after breakfast or dinner, at 80 mg/m2/day for 2 weeks, followed by 2 weeks of rest. There were no severe hematological or nonhematological toxicities and no dose reduction was necessary. The right upper lobe metastatic tumor showed marked reduction in size on follow-up CT (Figure 2). At present, S-1 therapy has been continued, and the patient remains well with an excellent performance status and no evidence of either widespread or other metastases.

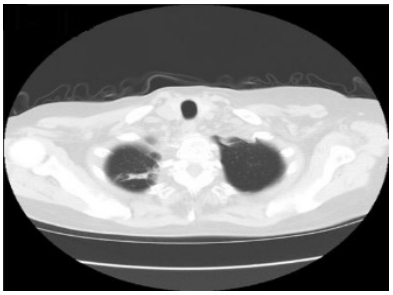

**Figure 2:** A chest CT showed remarkable tumor shrinkage.

## Discussion

Platinum-based regimens, such as CODE (cisplatin, vincristine, doxorubicin, and etoposide) and ADOC (cisplatin, doxorubicin, vincristine, and cyclophosphamide), are widely used as first-line chemotherapy, although the optimal chemotherapeutic regimens in advanced thymic cancers still remain controversial [1,2]. However, the chemotherapy regimens for relapsed thymic cancer are extremely limited due to a lack of evidence regarding effective treatments. Platinum-based chemotherapy has repeatedly been shown to be of benefit in certain patients [3]. However, several serious side effects of platinum may significantly restrict its efficacy for clinical application, such as nephrotoxicity, ototoxicity, neurotoxicity, hematological toxicity and gastrointestinal toxicity. These adverse effects can impair the functional status of the patients, decrease the tolerance ability for further therapies and result in many severe complications [4,5].

According to previous clinical reports, TS-1 may be useful as an alternative chemotherapy agent for thymic cancer. TS-1 is an orally active combination of tegafur (a prodrug of 5-fluorouracil [5-FU]), gimeracil (an inhibitor of dihydropyrimidine dehydrogenase, which degrades fluorouracil), and oteracil (an inhibitor of the phosphorylation of fluorouracil in the gastrointestinal tract which result in a reduction of the gastrointestinal toxic effects of fluorouracil) in a molar ratio of 1:0.4:1. TS-1 therapy is used in the treatment of various cancers, such as gastric cancer or non-small cell lung cancer. TS-1 is generally well tolerated compared with the side effects of platinum-based regimens, although the side effects associated with TS-1 therapy include bone marrow depression, nausea, diarrhea, skin rash and weight loss.

In general, single-drug chemotherapy may be used for the patients who may not tolerate combination chemotherapy well, such as those in poor overall health or elderly patients. In the present case, mono-chemotherapy with TS-1 was effective and the side effects associated with S-1 were minor. Several previous reports have described the efficacy of TS -1 as a "next-line" regimen for relapsed thymic cancer [6-8]. Conversely, TS-1 may be also a good option for patients who cannot tolerate platinum compounds although further clinical studies are needed to confirm the present findings.

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