A Patient with Pulmonary Lymphangitic Carcinomatosis Successfully Treated with TS-1 and Cisplatin

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Abstract

A 37-year-old man was referred to our hospital with complaints of dyspnea and general fatigue. Chest radiograph and CT scan revealed thickness of bronchovascular bundles in both lungs. In spite of various examinations, the primary lesion was not identified. He received chemotherapy containing TS-1 and cisplatin. Pulmonary lymphangitic carcinomatosis disappeared and the patient achieved a good partial response. He survived for 14 months after the chemotherapy. We believe the combination of TS-1 and cisplatin is one of the attractive options for patients with cancer of unknown primary site.

Key words: TS-1, cancer of unknown primary, chemotherapy, pulmonary lymphangitic carcinomatosis

Introduction

Pulmonary lymphangitic carcinomatosis (PLC) is a serious situation and provides severe dyspnea and intractable cough. In addition, prognoses of patients with cancer of unknown primary site (CUP), who have multiple metastatic organs, have been very poor (1, 2). Although improved outcomes utilizing cisplatin-containing chemotherapy for some CUPs have been achieved, most CUPs remain relatively unresponsive to systemic chemotherapy. We present herein a case of CUP with metastases in several organs and PLC, which improved dramatically with TS-1 containing chemotherapy.

Case Report

A 37-year-old man was referred to our hospital with complaints of dyspnea and general fatigue. Chest radiograph and CT scan revealed multiple nodules of up to 5 mm in diameter and thick bronchovascular bundles in both lungs (Figs. 1, 2). In spite of various examinations including FDG-PET, the primary lesion was not detected. Brain MRI and bone scintigram showed multiple nodules, which were evaluated as distant metastases. Among serum tumor markers, both carcinoembryonic antigen (CEA) and CA125 were markedly elevated, at 26.6 ng/ml and 87.8 U/ml, respectively. The patient had several enlarged lymph nodes on his right neck, and a pathological specimen was obtained from the nodes. At microscopic analysis, the tumor was characterized by large, polygonal-shaped cells with relatively abundant cytoplasm. Neither apparent structures nor focal necrosis in the tumor was observed. Immunohistochemistry showed negative staining for CEA, CD 56, and synaptophysin. Some of the tumor cells showed faint staining for chromogranin A. It was diagnosed pathologically as poorly differentiated carcinoma, which did not indicate the primary site (Fig. 3). During these diagnostic procedures, his respiratory condition worsened and his arterial oxygen saturation (SpO2) was < 90% on room air. His performance status rapidly deteriorated to 2. We selected chemotherapy containing TS-1 (administered orally, 80 mg/m2, days 1 to 21) and cisplatin (60 mg/m2, day 8). After the fourth cycle of the chemotherapy, thickness of bronchovascular bundles lessened and most of the pulmonary nodules disappeared on chest radiograph and CT (Figs. 4, 5). Dyspnea and oxygenation rapidly improved. No severe adverse effect more than grade II hematological and non-hematological was observed, except for grade II dermatitis. After 4 cycles of this chemotherapy, the patient was discharged and continued to take TS-1 daily...
Figure 1. Chest radiograph on admission showed pulmonary nodules and reticulonodular shadow in both lungs.

Figure 2. Chest CT scan on admission revealed multiple nodules of up to 5 mm in diameter and thickened bronchovascular bundles in both lungs.

Figure 3. The specimen obtained by cervical lymph node dissection was diagnosed pathologically as poorly differentiated carcinoma, which did not indicate the primary site.

Discussion

PLC is a type of lymphatic spread of cancer cells to the pulmonary vasculature and lymphatics, occurring in 6-10% of metastatic lung cancers (3, 4). It often results in respiratory failure and cor pulmonale. The most common primary sites for PLC are the lung, stomach, breast, pancreas and uterus, in that order of frequency (3, 4). The primary symptoms of PLC are dyspnea and non-productive cough, which are caused by loss of pulmonary compliance, impairment of pulmonary diffusing capacity and alveolar capillary block (4). A previous report indicated that these symptoms usually precede the emergence of radiographic abnormalities (5). The radiographic characteristic of PLC is a diffuse reticular network which radiates from the hilum to the lung field (3, 4). The reticular network reflects a thickening of the interlobular septa secondary to dilation of lymphatics by cancer cell invasion. In addition, the characteristics of PLC on the radiograph are septal Kerley’s lines, hilar lymphadenopathy and pleural effusion. In the present patient, the findings on chest CT scan led to the diagnosis of PLC based on the progression of dyspnea and the thickness of the bronchovascular bundles in both lungs.

There has been no apparent agreement in the oncology literature regarding the definition of what constitutes metastatic CUP. However, in a general oncology service, CUP seems to constitute as much as 3 - 5% of referred solid tumors (6-8). CUP represents a heterogeneous group of metastatic tumors for which no primary site can be detected following a thorough medical history, careful clinical examination and extensive diagnostic work-up. CUP are usually categorized into four major subtypes by routine light microscopic criteria (9, 10): 1) poorly differentiated neoplasm, 2) well or moderately differentiated adenocarcinoma, 3) squamous cell carcinoma, and 4) poorly differentiated carcinoma/adenocarcinoma. Although a primary site was not identified even at autopsy in the present patient, he had elevated serum levels both of CEA and CA125. Based on these results, at the time of diagnosis, we evaluated that CUP might have originated from sites where adenocarcinoma could develop.

Patients with chemo-resistant unfavorable subsets of CUP constitute the majority. Therefore, the therapeutic strategy for CUP patients should always be individualized according to the clinical subset. Chest physicians should recognize whether the patient with metastatic CUP to the lungs belongs to any of the favorable or unfavorable groups prior to
Figure 4. Chest radiograph after the fourth cycle of the chemotherapy showed disappearance of reticulonodular shadow and pulmonary nodules.

Figure 5. After the fourth cycle of the chemotherapy, the thickness of bronchovascular bundles lessened and most of the pulmonary nodules had disappeared on chest CT scan.

recommending the appropriate therapy. Chemotherapy has been the cornerstone of treatment for patients with CUP. During the last 4 decades, almost all cytotoxic drugs have been used either as a single agent or in combination regimens. Since platinum became available in 1980s, chemosensitive favorable subsets were recognized as being able to achieve significantly better responses and survival (11, 12). Several platinum-based regimens have produced higher response rates than those reported with previous regimens (13, 14).

TS-1, a combination of fltorafur and two modulators, gimestat (CDHP) and oxonic acid, has been widely used in Japan for the treatment of advanced gastrointestinal and lung cancers; much attention has been paid to attempts to increase its antitumor effect by combining it with cisplatin (15-17). Because the present patient had elevated serum levels of CEA and CA125, which suggested that CUP might have originated from sites where adenocarcinoma could develop, we treated this patient with TS-1 and cisplatin. Our patient achieved a good partial response without any life-threatening adverse effects even though he had a poor performance status. It was very impressive that PLC and pulmonary metastatic nodules dramatically shrunk after the first course of the chemotherapy. The prognosis of patients with metastases in several organs has been very poor, and the mean survival time and one-year survival of such patients was reported to be 4 to 5 months and 4 to 8%, respectively (1, 2). However, the present patient survived for 14 months after the first course of the TS-1 containing chemotherapy. We believe TS-1 is one of the attractive options for patients with CUP.

References


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