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Toxicity and efficacy of chemotherapy for non-small cell lung cancer with cavitary lesions

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ABSTRACT

Background: Concurrent chemoradiation in stage III non-small cell lung cancer (NSCLC) patients with cavitary lesions is reported to cause serious lung complications and is a predictor of poor survival. However, the efficacy and toxicity associated with chemotherapy for advanced NSCLC patients with cavitary lesions is not clear. We investigated the toxicities, particularly hemoptysis and cavity infection, and efficacy associated with chemotherapy for NSCLC patients with cavitary lesions.

Methods: We retrospectively reviewed consecutive patients who received first-line chemotherapy, including platinum-based chemotherapy, single-agent chemotherapy, or epidermal growth factor receptor-tyrosine kinase inhibitors, at our institution between January 2008 and December 2010.

Results: We found tumor cavitation prior to treatment in 23 of 415 NSCLC patients (5.5%). The response rate of all the patients was 30%, and the median survival time (MST) was 8.9 months. The MST of the 15 patients treated with platinum-based chemotherapy was 11 months. Grade 1 bronchopulmonary hemorrhage occurred in 2 patients. Grade 3 cavitary infection occurred in 2 patients, resulting in the discontinuation of chemotherapy.

Conclusions: This study indicates that the toxicity of chemotherapy for NSCLC patients with cavitary lesions is tolerable; however, the development of cavitary infection should be carefully considered. In addition, this study suggests that the efficacy of chemotherapy for NSCLC patients with cavitary lesions is similar to the response rates reported in the literature; however, the survival of these patients may be worse than that for general NSCLC patients.

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1. Introduction

Approximately 5–15% of all lung cancer patients present with radiological cavitation, potentially due to tumor necrosis from ischemia and/or bronchial obstruction [1–3]. In addition, 7–24% of primary lung cancer patients experience hemoptysis, with a few fatal cases reported [3–5]. Previous reports suggest that cavitated tumors treated with chemotherapy and/or radiotherapy result in difficult to treat, serious hemoptysis and infectious complications [6,7]. Tumor cavitation awareness has increased since the linkage of this finding with the toxicity and efficacy of antiangiogenic agents in non-small cell lung cancer (NSCLC) [8,9].

Two previous reports noted that concurrent chemoradiation in stage III NSCLC patients with tumor cavitation resulted in serious lung complications and was a predictor of poor survival [10,11]. However, it remains unclear whether chemotherapy for advanced lung cancer with cavitary lung lesions is associated with serious and difficult-to-treat infectious complications. As the response to chemotherapy has not been previously reported for patients with NSCLC, we conducted a retrospective study to investigate the toxicities, particularly hemoptysis and cavitary lesion infection, and efficacy of chemotherapy in NSCLC patients with tumor cavitation.

2. Patients and methods

2.1. Patient selection

Computed tomographic (CT) results from 1267 NSCLC patients who visited the Shizuoka Cancer Center between January 2008 and December 2010 were reviewed. A total of 501 patients had unresectable tumors or could not undergo radical chemoradiotherapy. We identified 415 patients with a pathological diagnosis of NSCLC who also received first-line platinum-based or single-agent chemotherapy or epidermal growth factor receptor (EGFR)-tyrosine kinase inhibitors (TKIs).

2.2. Definition of a cavitary lesion

All the patient CT scans taken prior to chemotherapy were reviewed for tumor cavitation by a diagnostic radiologist (M.E.) and 2 pulmonologists (T.T. and T.S.). The presence of cavitation was considered when (1) the longest diameter of the cavity was >10 mm in the mediastinal window of the CT image, (2) the thickness of the cavitation wall was >1 mm in the lung window of the CT image (Fig. 1), and (3) the cavity wall was irregular and the lesion did not develop into a wall cyst or bulla.

2.3. Evaluation

Chemotherapeutic response was assessed according to the Response Evaluation Criteria In Solid Tumors version 1.1 [12]. Chest and abdominal CT, brain magnetic resonance imaging, and positron emission tomography-CT/bone scintigraphy were performed during initial staging. To ascertain disease progression or relapse of overall disease, the patients were evaluated by physical examination, chest radiography, and CT of the chest and abdomen approximately every 6–8 weeks during and after the treatment period. Clinical disease staging was assessed according to the Union for International Cancer Control staging criteria (sixth edition) [13].

Overall survival (OS) was measured from the start of first-line chemotherapy to the date of death or last follow-up. Censored cases were defined as those surviving at the last follow-up date without confirmation of death.

Hemoptysis and cavitary infection were evaluated in accordance with the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0. The CTCAE defines hemoptysis and cavitary infection as “bronchopulmonary hemorrhage” and “lung infection,” respectively; therefore, these terms were used in this article.

We also assessed chemotherapy compliance by evaluating administered cycles of chemotherapy, interruption of chemotherapy, dose reduction, discontinuation, and dose delay.

2.4. Statistical analysis

All categorical variables were assessed, and univariate analyses were performed using the χ^2 or Fisher’s exact test,

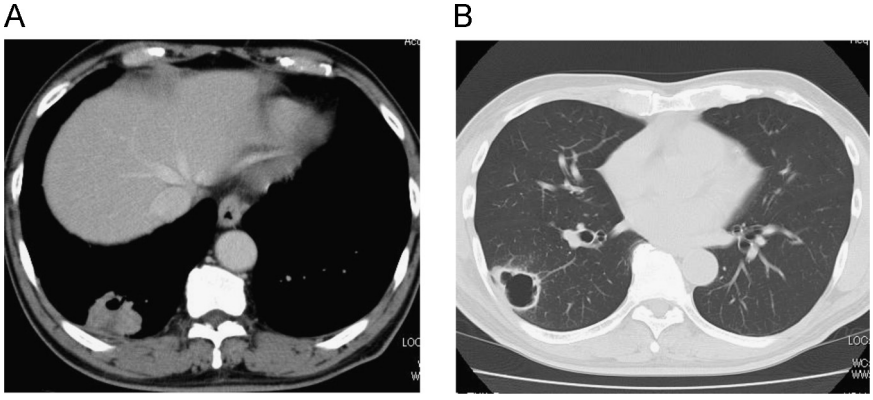

Fig. 1 – (A) Computed tomographic (CT) image showing a primary tumor in the right lower lobe with a cavitation diameter greater than 10 mm. (B) CT image showing a primary tumor in the right lower lobe with an irregular cavitation wall with a thickness >1 mm.