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Analysis of the impact of lung cancer treatment on nontuberculous mycobacterial lung diseases

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ABSTRACT

Background: Although nontuberculous mycobacteria (NTM) lung diseases can occur in association with lung cancer, no study has evaluated the effect of lung cancer treatment on NTM lung diseases. Therefore, the present study aimed to retrospectively examine the effect of lung cancer treatment on NTM lung diseases.

Methods: Patients diagnosed with NTM lung diseases in combination with cytologically or histologically proven lung cancer between January 1, 2010 and October 31, 2014 were enroled. The clinical history of eligible patients was retrospectively reviewed.

Results: Seven hundred twenty-eight patients were diagnosed with NTM lung diseases. Among these patients, 29 (3.9%) also had lung cancer. Of the 29 patients with NTM and lung cancer, 62% had *Mycobacterium avium* complex as the pathogenic organism. The most common lung cancer histology was adenocarcinoma (62.1%). Anti-cancer cytotoxic chemotherapy was administered to seven patients, and the two patients who did not receive NTM treatment showed worsening of their NTM lung disease.

Conclusion: Whether NTM lung disease should be treated during anti-cancer chemotherapy has not been not clarified by this study. Induction of anti-NTM therapy should be made after careful consideration, because the duration of anti-NTM treatment is long and anti-mycobacterial drugs have extensive effects on anti-cancer drugs. However, we think that anti-NTM therapy should be introduced after consideration of the worsening of symptoms and radiological findings associated with NTM lung disease.

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1. Introduction

Over the past few decades, the incidence of nontuberculous mycobacterial (NTM) lung diseases has been increasing [1,2]. Currently, lung cancer is the most frequently diagnosed cancer and the most common cause of cancer-related death worldwide [3]. In a recent Japanese study, 2.4% of patients with NTM lung diseases also had lung cancer [4]. Studies carried out in other countries revealed that 6.5% of patients with *Mycobacterium avium* complex (MAC) disease also had lung cancer [5]. The incidence of NTM lung disease occurring in association with lung cancer will presumably increase because of an increase in the incidence of both diseases.

The main limitations of effective therapy for NTM lung diseases are the lack of antimicrobial agents with a low toxicity to the host and good *in vivo* activity against the organism [6], and a high relapse rate even in immunocompetent patients. Cytotoxic chemotherapy for lung cancer results in an immunocompromised state [7]; therefore, it may have a harmful immunosuppressant effect on patients with NTM lung diseases. No study has evaluated the effect of cancer treatment on the clinical course of NTM lung diseases. Thus, the present study aimed to examine the effect of lung cancer treatment on the pathophysiology of NTM lung diseases.

2. Patients and methods

2.1. Study approval

The present study was approved by the Institutional Review Board of the National Hospital Organization Kinki-Chuo Chest Medical Center on June 30, 2015 (approval number: 494).

2.2. Study population

In total, 728 patients with microbiologically confirmed NTM lung disease admitted to the Kinki-Chuo Chest Medical Center, Osaka, Japan, between January 1, 2010 and October 31, 2014 were screened. The diagnostic criteria of the American Thoracic Society/Infectious Diseases Society of America (ATS/IDSA) from 2007 [6] were considered for diagnosing NTM lung disease. Twenty-nine consecutive patients with NTM lung disease occurring simultaneously with cytologically or histologically proven lung cancer at Kinki-Chuo Chest Medical Center were enroled.

2.3. Classification of subjects

We classified the enroled patients into the following three groups: NTM preceding, lung cancer preceding, and concurrent. If the interval between the diagnosis of NTM lung disease and that of lung cancer was less than 1 month, we classified patients into the concurrent group. Patients in whom the diagnosis of lung cancer preceded that of NTM lung disease by more than 1 month were classified into the lung cancer preceding group. Patients in whom the diagnosis of NTM lung disease preceded that of lung cancer by more than 1 month were classified into the NTM preceding group.

2.4. Clinical course

The clinical history of the enroled patients was retrospectively reviewed in consideration with the following variables: sex; age; body mass index (BMI); laboratory data; radiological findings; bacteriological examination including sputum or other appropriate respiratory samples; lung cancer histological data, stage at diagnosis, and treatment including the anti-cancer drug regimen, surgical resection, and radiation therapy.

2.5. Definition of NTM lung disease deterioration

We defined NTM lung disease deterioration as the worsening of symptoms and/or radiological findings presumably due to NTM lung disease progression or an increased mycobacterial population in sputum cultures after lung cancer treatment. Worsening of symptoms was defined as follows: increased cough, sputum, bloody sputum, fever, or dyspnea that was deemed to be caused by NTM lung disease.

Based on a previous study [8], we classified the radiographic forms of NTM lung disease as follows: nodular/bronchiectatic (NB) disease, fibrocavitary (FC) disease, NB+FC disease, and unclassified disease. NB disease was defined by the presence of multiple nodules and bronchiectasis found in a computed tomography (CT) scan; FC disease, by apical fibrocavitary lesions. If a patient had coexisting NB and FC diseases, this disease type was defined as NB+FC. If the radiographic abnormalities did not display any specific pattern because of an underlying pulmonary disease, or if a case had several nodules with consolidation, we defined this occurrence as an unclassifiable disease. Cases in which these findings became exacerbated or were newly observed were defined as deteriorated.

3. Results

Among 728 patients diagnosed with NTM lung diseases between January 1, 2010 and October 31, 2014, 29 (3.9%) also had lung cancer.

The patients' characteristics are summarized in Table 1. The patients were predominantly men with a median age of 77 years. Fourteen (48.2%) patients had never smoked cigarettes. Eleven patients were classified into the NTM preceding group; 14, into the lung cancer preceding group; and 4, into the concurrent group. The pathogens in 31.0% of cases were *Mycobacterium avium* and *M. intracellulare,* and in 13.8% of cases, *M. kansasii* and *M. gordonae*. The most common lung cancer histology was adenocarcinoma (62.1%). In the NTM preceding group, 11 cases of lung cancer occurred during the study period with an incidence rate of 6.7/1000 person-years. CT findings confirmed NB disease in 15 patients (51.7%), FC disease in 7 (24.1%), NB+FC disease in 4 (13.8%), and an unclassified disease in 3 (10.3%). Table 2 summarizes the lung cancer treatment strategies. Surgical resection was the most common treatment strategy in all three groups; 8 patients underwent surgical resection before NTM lung disease was diagnosed. Four patients received the best supportive care.

Seven patients received chemotherapy (Table 3). In these patients, the pathogens were *M. intracellulare* in 3 and *M. avium, M. gordonae, M. chelonae*, and *M. kansasii* in each of the

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