J Infect Chemother 20 (2014) 213-216



Contents lists available at ScienceDirect

Journal of Infection and Chemotherapy

journal homepage: http://www.elsevier.com/locate/jic



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Original article

Mycobacterium tuberculosis infection in cancer patients at a tertiary care cancer center in Japan

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ARTICLE INFO

Article history: Received 12 May 2013 Received in revised form 10 October 2013 Accepted 4 November 2013

Keywords: Tuberculosis Cancer Anti-tumor agents Immunocompromised host

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The characteristics of active tuberculosis in cancer patients in Japan and the effects of this infection on cancer treatment have not yet been clarified. The records of all consecutive patients with microbiologically documented *Mycobacterium tuberculosis* infection diagnosed between September 2002 and March 2008 at Shizuoka cancer center (a 557-bed tertiary care cancer center in Japan) were reviewed. There were 24 cancer patients with active tuberculosis during the study period. Of these, 23 had solidorgan tumors, and the most common site of the underlying malignancy was the lung. Most of the patients had pulmonary tuberculosis. Among 15 patients followed up for more than 2 months prior to the diagnosis of pulmonary tuberculosis, 12 had healed scars suggestive of old tuberculosis lesions, as shown by chest imaging obtained at the time of the initial evaluation. Discontinuation of cancer therapy or more than a month's delay in surgery occurred in 10 patients with pulmonary tuberculosis. Development of active tuberculosis disease lesions as shown by chest imaging should be screened for active tuberculosis and carefully followed up. In some cases, prophylactic treatment should be considered.

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1. Introduction

Malignancy is a known risk factor for the development of active tuberculosis [1]. At the same time, immunosuppressive anti-tumor treatment is widely used among cancer patients in those countries with high rates of tuberculosis infection. Previous reports from the United States, which has a low prevalence of tuberculosis infection, showed that US-born cancer patients with an underlying solid tumor had the same tuberculosis rate as US-born patients without cancer [2–4]. Because the incidence of tuberculosis is affected by the prevalence of tuberculosis in the cancer patient population, we need to consider the locally

specific data to establish the ideal strategies for screening, early detection, and treatment of latent tuberculosis infections. However, the characteristics of active tuberculosis in cancer patients in Japan and the effects of this infection on cancer treatment have not yet been clarified. This is partly because of the absence of infectious disease departments in Japanese cancer center hospitals. Here, we describe the characteristics of cancer patients with active *Mycobacterium tuberculosis* infection at a tertiary cancer center hospital in Japan, and consider the suitable management strategies for cancer patients in a country that is intermediately endemic for tuberculosis.

2. Patients and methods

2.1. Definitions

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We reviewed the records of all consecutive patients with microbiologically documented *M. tuberculosis* infection

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¹³⁴¹⁻³²¹X/\$ - see front matter © 2013, Japanese Society of Chemotherapy and The Japanese Association for Infectious Diseases. Published by Elsevier Ltd. All rights reserved. http://dx.doi.org/10.1016/j.jiac.2013.11.005

diagnosed between September 2002 and March 2008 at the Shizuoka cancer center (a 557-bed tertiary care cancer center in Japan). The patients were identified from a microbiology database previously established for patients with *M. tuberculosis* isolated from any body site. Patient information was obtained from electronic medical records.

2.2. Definition of tuberculosis patients

Microbiologically documented *M. tuberculosis* infection was defined when clinical specimens were found to be positive by culture or polymerase chain reaction (PCR; Roche AMPLICOR MTB test[®]).

2.3. Neutropenia and lymphopenia

Neutropenia was defined as an absolute neutrophil count lower than $500/\mu$ L at the time when samples growing *M. tuberculosis* were obtained. Lymphopenia was defined as an absolute lymphocyte count of lower than $500/\mu$ L at the time when samples growing *M. tuberculosis* were obtained.

2.4. Systemic corticosteroid use

Systemic corticosteroid use was defined at a dose of more than 1 mg/(kg day) of prednisone or an equivalent dose of another corticosteroid given within the 4 weeks before diagnosis of infection.

2.5. Radiographic findings

Radiographic findings were reviewed by 2 investigators (M. Endo and T. Fujita), including a radiology specialist (M. Endo).

2.6. Deaths attributable to Mycobacterium infections

Deaths were attributed to *M. tuberculosis* if the patient died with progressive tuberculosis within 4 weeks of infection diagnosis.

Table 1

Patient characteristics	No. of patients (%)
	No. of patients (%)
Underlying cancer	
Lung	6 (25)
Esophagus	3 (13)
Colon	3 (13)
Stomach	2 (8)
Prostate	2 (8)
Pharynx	2 (8)
Pancreas	2 (8)
Breast	2 (8)
Thyroid	1 (4)
Non-Hodgkin lymphoma	1 (4)
Site of infection	
Lung	21 (88)
Lymph node	2 (8)
Intestine	1 (4)
Clinical presentation	
Fever	11 (46)
Sputum	11 (46)
Cough	8 (33)
Asymptomatic	7 (29)
Asymptomatic and abnormal chest radiograph	6 (25)
Weight loss	4(17)
Dyspnea	3 (13)
Lymph node adenopathy	2 (8)

3. Results

3.1. Patients and disease characteristics (Table 1)

There were 24 cancer patients with active tuberculosis during the period studied. Eighteen patients (75%) were men and 6 (25%) were women. The median age was 72 years (range, 56–89 years). Twenty-three patients had solid-organ tumors. The one patient with hematological malignancy had non-Hodgkin lymphoma. The most common site for the underlying malignancy was the lung (6 patients). Four patients (17%) had received systemic corticosteroids. Four patients had lymphopenia, and 1 had concomitant neutropenia. Twenty-one patients (88%) had pulmonary tuberculosis, 2 (8%) had tuberculous lymphadenitis, and 1 (4%) had intestinal tuberculosis. Among symptomatic patients, the most common symptoms were fever (11 patients) and sputum (11 patients). The tuberculosis that developed in 7 patients during or within 30 days of chemotherapy was found to be pulmonary tuberculosis. No patients had ever received anti-tuberculosis drugs. Seven patients were asymptomatic, and 6 of these only had abnormal findings on plain chest radiography or pulmonary computed tomography (CT). One patient was found on CT to have lymph node adenopathy, which was considered metastatic pancreas cancer. The antimicrobial susceptibility status of 21 M. tuberculosis isolates was available. All strains tested were found to be susceptible to isoniazid, rifampin, pyrazinamide, and ethambutol. Among 21 pulmonary tuberculosis patients, 16 were diagnosed by sputum, 3 by bronchoalveolar lavage (BAL), 1 by both sputum and BAL, and 1 by lung biopsy. Twelve patients (54%) had smear-positive sputum. Of the 7 patients who developed active tuberculosis during or within 30 days of chemotherapy, 4 (57%) were smear-positive.

Fifteen patients received follow-up for more than 2 months prior to the diagnosis of tuberculosis (range, 2–35 months). Of these patients, 12 (12/15: 80%) had healed scars suggestive of old tuberculosis lesions as shown by plain chest radiography or CT obtained at initial evaluation at presentation to our hospital.

All 7 patients who developed active tuberculosis during or within 30 days of chemotherapy had pulmonary tuberculosis. Of these patients, 5 had healed scars suggestive of old tuberculosis lesions, 1 had chronic bronchitis, and 1 patient had old nonspecific pleurisy on chest radiography or chest CT taken before the initiation of chemotherapy. Six patients were diagnosed with simultaneous active tuberculosis and malignancy. Three patients had been followed by another institute for cancer and were referred to our hospital for further investigation, where they were diagnosed with tuberculosis. Of the 12 patients who had healed scars suggestive of old tuberculosis lesions, 7 (58%) had no history of tuberculosis.

Death was attributed to *M. tuberculosis* diseases in 1 patient who developed the disease during chemotherapy for pancreatic cancer, and then developed acute respiratory distress syndrome. Delay of cancer therapy (discontinuation of chemotherapy, or more than a month's delay in surgery) was necessary in 10 patients with pulmonary tuberculosis.

4. Discussion

To the best of our knowledge, this is the first report in English to detail the characteristics of patients with tuberculosis and cancer in a Japanese tertiary cancer center hospital. The present study demonstrated that patients with tuberculosis at our Japanese tertiary care cancer center who had lung cancer as their most common underlying disease were older than similar patients in the United States [2,3]. Seven (29%) patients were asymptomatic and had no identifiable risk factors other than malignancy such as corticosteroid administration. During initial evaluation at our institute, we

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