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A case of diffuse large B-cell lymphoma originating from chest wall complicated by benign asbestos pleural effusion

Nobuyuki Kondo[1], Yukihisa Inoue[1], Hiroaki Takeyama[1], Akiko Kobayashi[1], Osamu Matsubara[2] & Yasuto Jinn[1]

[1]Department of Pulmonary Medicine, Hiratsuka Kyosai Hospital, Hiratsuka, Japan.
[2]Department of Pathology, Hiratsuka Kyosai Hospital, Hiratsuka, Japan.

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Correspondence
Nobuyuki Kondo, Department of Pulmonary Medicine, Hiratsuka Kyosai Hospital, Oiwake 9-11, Hiratsuka City, Kanagawa 254-8502, Japan. E-mail: kondo-n@kkr.hiratsuka.kanagawa.jp

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Abstract

A 78-year-old man with exposure to asbestos was admitted to our hospital for back pain. A chest computed tomography showed right pleural effusion and a significant increase in the size of masses in the right chest wall over an interval of six months. He did not undergo further examinations and expired one month later. Autopsy revealed the presence of diffuse large B-cell lymphoma (DLBCL) and complicated by benign asbestos pleural effusion. We considered that this tumour had originated from the soft tissue in the chest wall based on the radiological and autopsy findings. The present report highlights that primary DLBCL of chest wall might be associated with chronic inflammation due to asbestos-related pleural diseases.

Introduction

Chest wall lymphoma (CWL) is a rare form of chest wall tumours. The definitive diagnosis of CWL is often challenging because adequate specimen is necessary for the definite diagnosis. At the advanced stage, radiological findings of CWL is also mimicking those of other chest wall tumours, such as pyothorax-associated lymphoma (PAL) and malignant mesothelioma. Therefore, it is essential to distinguish CWL from malignant mesothelioma, especially in a patient with asbestos exposure. Here, we report a case of primary diffuse large B-cell lymphoma (DLBCL) presenting as chest wall tumour complicated by benign asbestos pleural effusion, which was confirmed by autopsy.

Case Report

The patient is a 78-year-old Japanese man, with 25 pack-year smoking history, worked as an arc welder for 26 years. He had no history of tuberculosis. Because a transcutaneous pleural biopsy showed fibrous plaques without malignant findings, he was diagnosed with benign asbestos pleural effusion six years prior to admission. Then, he presented with right back pain for two months prior to admission. There was no associated fever, night sweat, or respiratory symptoms. Physical examination showed palpable, immobile masses in the right posterior chest wall. Complete blood examination indicated normocytic anaemia (haemoglobin 8.5 g/dL). The levels of serum lactate dehydrogenase and soluble interleukin (IL)-2 receptor were elevated (453 IU/L and 9740 U/mL, respectively). The levels of tumour markers for lung cancer (carcinoembryonic antigen, cytokeratin 19 fragment, and Pro-gastrin-releasing peptide) were within the normal range. Over an interval of six months, computed tomography (CT) revealed a significant increase in the size of masses between the innermost intercostal muscle and inner intercostal muscle which had invaded into extrapleural fat and parietal pleura (Fig. 1). Lymphadenopathy, splenomegaly, and hepatomegaly were not identified. Although pleural fluid analysis and transcutaneous pleural biopsy were performed, a definitive diagnosis was not established. He did not undergo further examination and received palliative care because of his medical complications such as recurrent strokes and diabetes. He expired one month after admission, and a full autopsy was performed. Macroscopic findings at autopsy showed pleural plaques, and the tumour was located

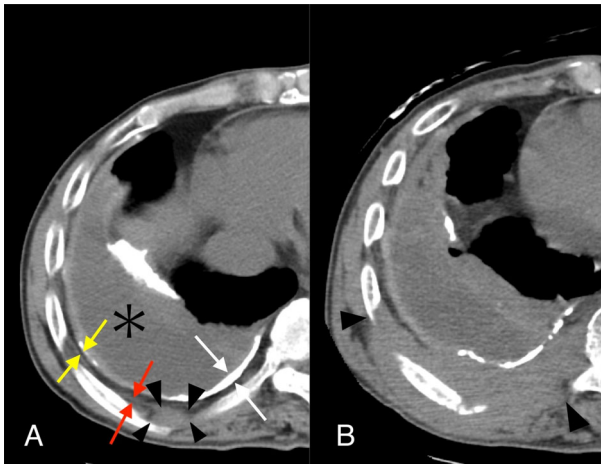

Figure 1. A chest computed tomography (CT) scan findings demonstrated that the tumour had originated from the soft tissue of chest wall. (A) At six months prior to admission, chest wall tumour (black arrow heads) was located in the chest wall between the innermost intercostal muscle (red arrows) and inner intercostal muscle. There was moderate amount of pleural effusion (asterisk). Imaging of parietal pleura (white arrows) showed calcification. Low-density lesion outside parietal pleura indicated extrapleural fat (yellow arrows). (B) At one month prior to admission, CT revealed a significant increase in the size of tumour (black arrow heads), which had invaded into the ribs.

outside the parietal pleura. Histopathological staining of the tumour tissue showed the proliferation of medium-sized lymphocytes. These cells were immunohistochemically positive for CD20, CD5, and bcl-2, and negative for cyclin D1 (CCND1), CD10, and CD138. Ki67 was highly expressed in the tumour tissue (80%) (Fig. 2). In situ hybridization study demonstrated that the lymphoma was negative for Epstein–Barr (EB) virus infection. Therefore, the findings were mostly consistent with DLBCL. Asbestos bodies were also found in the lungs. He was finally diagnosed with primary DLBCL of the chest wall, complicated with benign asbestos pleural effusion.

Discussion

Primary malignant lymphoma involving chest wall is relatively rare among extranodal lymphoma. It is classified into three subtypes, namely primary effusion lymphoma, PAL, and CWL. PAL is mostly associated with tuberculous pleurisy or chronic pyothorax. It has been postulated that PAL usually originates from parietal pleura following long-standing chronic inflammation [1]. In contrast, CWL often originates from soft tissues in the chest wall. It is difficult to distinguish CWL from PAL by radiological findings at

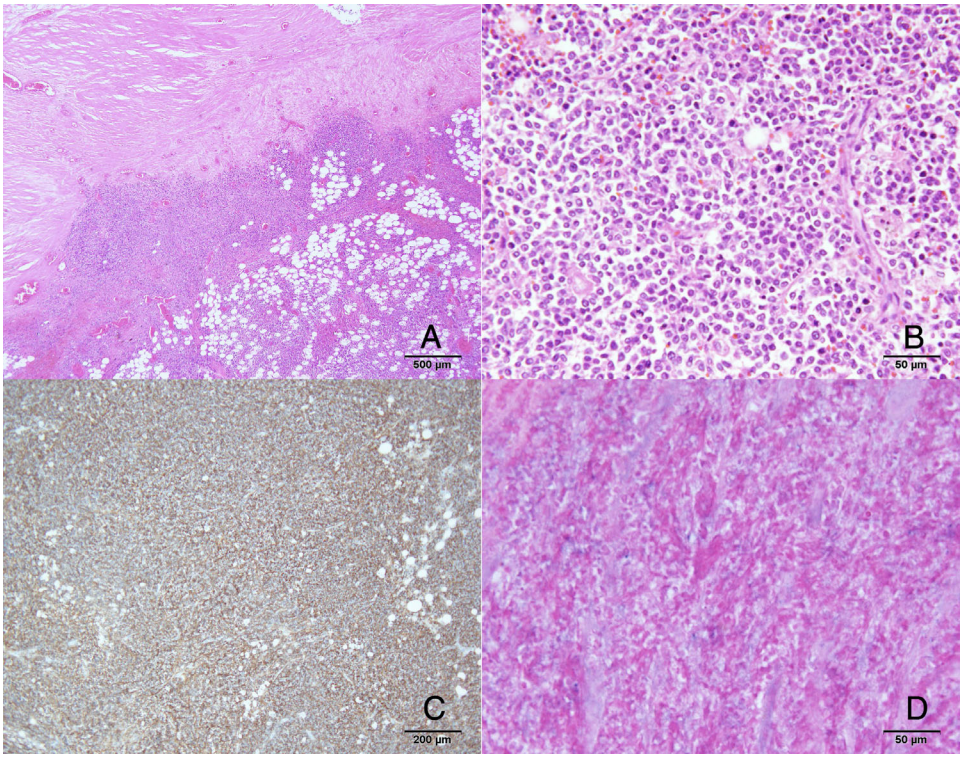

Figure 2. Histopathology of chest wall at autopsy. Fibrous thickening of the parietal pleura was surrounded by atypical dense lymphoid infiltrates (A, haematoxylin and eosin (H&E) stain, original magnification 36×). The lymphoid infiltrates were composed of medium-sized monocytoid cells (B, H&E stain, original magnification 360×). These lymphoid cells were positive for CD20 (C, CD20 immunostain, clone L26; Ventana, USA; original magnification 90×), and negative for Epstein-Barr virus Early small RNAs in situ hybridization (EBER-ISH) (D, EBER peptide nucleic acid (PNA); Dako, Denmark; original magnification 360×).

the advance stage due to the similarity of clinical manifestations. In our case, CT findings showed that CWL had originated from the soft tissue between the innermost intercostal muscle and inner intercostal muscle at the early stage of the disease.

DLBCL is the most common histological type of PAL and CWL. Although the pathogenesis of PAL has not been fully elucidated, it is strongly associated with EB virus infection. Aozasa et al. indicated that EB virus load was correlated with the tumour size during chemoradiotherapy, suggesting an important role of EB virus infection in tumourigenesis [1]. Aozasa et al. demonstrated that latent EB virus infection could be associated with the different patterns of gene expression involved in apoptosis, signal transduction, and interferon response between patients with PAL and DLBCL without EB virus infection [1]. In contrast to PAL, CWL does not show evidence of latent EB virus infection. Therefore, the pathogenesis of CWL may differ from that of PAL.

Asbestos is the general term used to describe naturally occurring fibres composed of hydrated magnesium silicates. This material is used for a variety of construction and insulating purposes. Exposure to asbestos results in the development of various thoracic diseases, including lung cancer, benign asbestos pleural effusion, and malignant mesothelioma. A Danish cohort study revealed that long-term exposure to asbestos might also be associated with overall haematological malignancies, including malignant lymphoma [2]. Only two cases of CWL associated with exposure to asbestos were previously reported; one was DLBCL [3] and the other was low-grade marginal zone lymphoma [4]. Exposure to asbestos might have provided an important focus of tumourigenesis. Asbestos fibres generate reactive oxygen and nitrogen species, which lead to DNA damage. Oxidants are responsible for the initiation of numerous signal transduction pathways that are linked to cell proliferation and apoptosis. Inhalation of asbestos also produces various inflammatory cytokines, which lead to a state of chronic non-resolving inflammation in the chest wall. It has been reported that IL-6 is involved in the activation of several pathways, such as signal transducer and activator of transcription 3 (STAT3), Ras/mitogen-activated protein kinase (MAPK)/extracellular signal-regulated kinase (ERK), and phosphatidylinositol 3-kinase (PI3K)/protein kinase B (AKT), resulting in stimulation of cancer cell survival [5]. Thus, these mechanisms may eventually lead to the development of malignant lymphoma following exposure to asbestos.

In this report, we presented a case of DLBCL originating from the chest wall complicated by benign asbestos pleural effusion. It is important to consider the possibility of CWL in chest wall tumour with a background of exposure to asbestos.

Disclosure Statement

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

Author Contribution Statement

Nobuyuki Kondo wrote the manuscript. Yukihisa Inoue was involved in data interpretation. Akiko Kobayashi and Hiroaki Takeyama were involved in data analysis. Osamu Matsubara and Yasuto Jinn provided expertise and feedback. All authors critically revised the report, commented on drafts of the manuscript, and approved the final report.

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