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Diffuse Large B-cell Lymphoma Arising from Chronic Tuberculous Empyema

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Pyothorax-associated lymphoma is a relatively rare type of lymphoma that occurs in patients who have long histories of tuberculous pleuritis or induced pneumothorax. It is a type of non-Hodgkin's lymphoma of mainly the B-cell phenotype and is strongly associated with Epstein－Barr virus infection. A majority of these cases have been reported in Japan, although some cases have occurred in Western countries. Here, we describe a case of pyothorax-associated lymphoma in a patient with a 30-year history of chronic tuberculous empyema. The patient underwent decortication under the impression of chronic empyema with fistula. The histopathologic diagnosis was a diffuse large B-cell lymphoma associated chronic inflammation.

Key words: 1. Lung
2. Empyema
3. Pyothorax-associated lymphoma

CASE REPORT

A 60-year-old man was referred to our outpatient clinic because of persistent air leakage lasting 17 days from his chest tube, which had been inserted for empyema at another hospital. His chief complaint was large amounts of purulent sputum. He had a past history of diabetes mellitus and tuberculous pleuritis treated with antituberculous medicine 30 years ago. He had not been treated previously for empyema by drainage procedures such as closed thoracostomy, percutaneous catheter aspiration, or drainage. A chest computed tomography (CT) scan showed loculated pleural fluid collection with air density and pleural wall thickening with enhancement and calcification. Further, a 2.2-cm mass-like lesion adjacent to the margin of an empyema cavity was identified retrospectively (Fig. 1). On physical examination, there was general weakness without fever or weight loss. Laboratory tests revealed a slightly elevated C-reactive protein level of 1.0 mg/dL, while other parameters were within the normal range. Seven days after admission, we planned decortication because of prolonged air leakage and the patient's desire for surgery. The patient underwent decortication via posterolateral thoracotomy under one-lung ventilation. The fibrinous contents of the empyema cavity were removed, and the lung was decorticated without difficulty. Parenchymal air leaks following decortication were repaired with absorbable sutures. No suspicious tumor was found. Therefore, the operation was completed after the confirmation of the full expansion of the lung.

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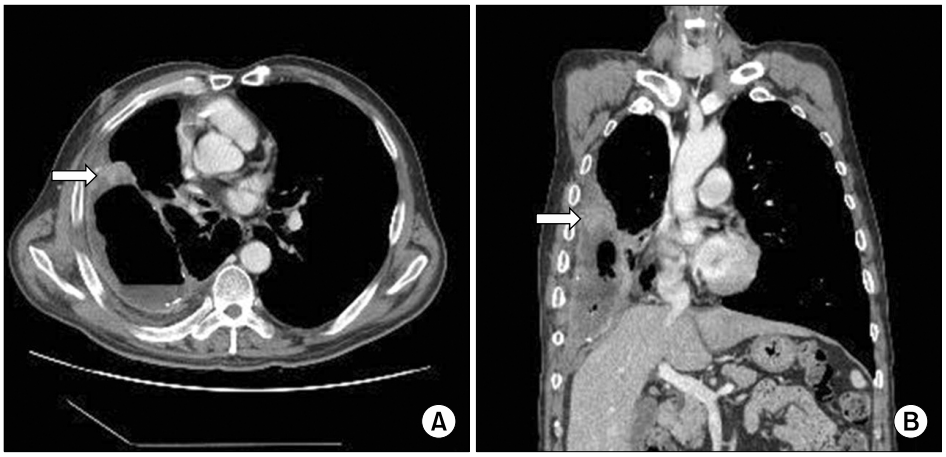

Fig. 1. Chest computed tomography scan shows empyema cavity with pleural enhancement and calcification with a 2.2-cm mass-like lesion (arrow). (A) Axial view. (B) Coronal view.

Contrary to our expectations, however, the histopathological diagnosis after the operation was malignant lymphoma. Histopathological examination revealed a diffuse destructive proliferation of large cells with areas of necrosis. The cell population was mainly composed of large lymphoid cells. Immunohistochemically, the tumor cells were positive for leukocyte common antigen, CD79a, Ki-67 (range, 70–80%), and CD3, and negative for CD20. Further, *in situ* hybridization for EBER was positive (Fig. 2). After the identification of a monoclonal proliferation of B-cells by an immunoglobulin heavy- chain gene rearrangement, the final diagnosis of diffuse large B-cell lymphoma with an aberrant expression of a T-cell marker was made.

The postoperative period was uneventful, and the chest tube was removed on postoperative day 12. We considered the possibility of incomplete resection, and the patient was referred to the hematology department for adjuvant chemotherapy.

DISCUSSION

Pyothorax-associated lymphoma (PAL) is a rare malignant lymphoma developing in the pleural cavity after long-standing pyothorax. According to the current World Health Organization histological classification published in 2005, PAL is defined as 'a neoplasm of large B-cells, typically with immunoblastic morphology, usually presenting as a pleural mass.' It occurs in patients with a history of long-standing pyothorax resulting from pulmonary tuberculosis or tuberculous pleuritis and is strongly associated with the Epstein–Barr virus (EBV) [1]. A majority of these cases have been reported in Japan, although some cases have occurred in Western countries. It is assumed that the higher prevalence in Japan is caused by a higher incidence of EBV infection and lung collapse therapy for tuberculosis in Asia, particularly in Japan [2,3]. The etiology of PAL is not clearly understood. However, previous reports have suggested that artificial pneumothorax, EBV latent infection, cytokines such as interleukin-6 and -10, and oxidative stress produced during chronic inflammation might be important factors for PAL development [4].

Nakatsuka et al. [5] reported a summary of clinical and pathological findings in 106 patients with PAL in Japan. The median age of the patients was 64 years (range, 46 to 82 years) with a male/female ratio of 12.3:1. The interval between the onset of pleuritis and the initial symptoms of lymphoma was 37 years (range, 20 to 64 years). All of the cases were of non-Hodgkin's lymphoma, among which the diffuse large B-cell type was the most common (88%). Further, 70% of the patients were EBV positive.

The definitive diagnosis of PAL can be made by histopathological and immunohistochemical examinations of biopsy or surgically resected specimens [6]. A typical histological examination demonstrates a diffuse destructive proliferation of large cells with a predominant population of immunoblasts. Lymphoma cells are mostly positive for CD20 and CD79a in the immunohistochemical examination. According to the pathological findings by Aozasa et al. [4], a majority of the cases were CD20+ and/or MBI+, CD45RO-, and CD3-, and were of the B-cell lineage. However, there could be an aber-

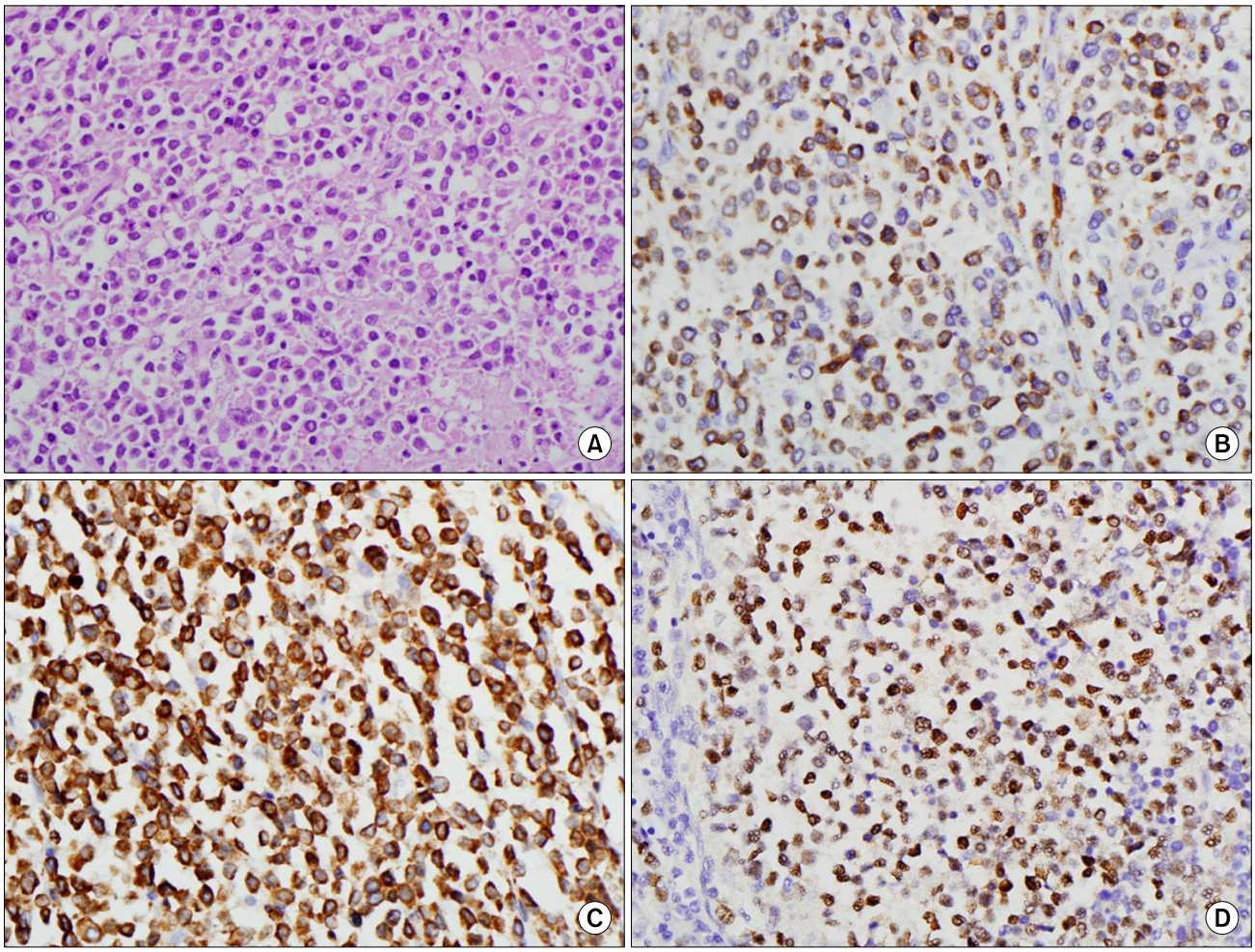

Fig. 2. Histopathologic and immunohistochemical findings (×400). (A) Diffuse proliferation of large lymphoid cells with karyorrhectic debris (H&E). The tumor cells are immunopositive for (B) CD79a, (C) CD3. (D) And *in situ* hybridization for EBER is positive.

rant phenotype with the expression of some T-cell markers, as in our case.

Ueda et al. [7] analyzed the radiological features of PAL to help in the diagnosis of this rare malignant lesion. They reported that a typical radiological finding of PAL was a pleural soft-tissue mass adjacent to the margin of a coexistent empyema cavity and the shape of the mass demonstrated on the CT scan was mostly lenticular or crescentic. We were able to find a mass-like lesion on the CT scan retrospectively by reviewing the report of Ueda et al. Although the optimal treatment is not well-established, most patients with PAL have received chemotherapy and/or radiotherapy, as reported in the literature. The prognosis of PAL reported in 2002 is poor, with a five-year survival rate of 21.6%, although a better survival rate is observed in patients who are responsive to chemotherapy [5]. However, a recent survey reported an improved overall five-year survival rate of 35% and suggested several prognostic factors for the overall survival [8].

In summary, we have reported a case of PAL of a B-cell origin resulting from tuberculous pleuritis. Although PAL is a relatively rare disease, it should be considered a potential diagnosis in patients with a history of chronic pyothorax.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article has been reported.

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