Primary Mediastinal Liposarcoma, with 6 Years of Follow-up to Autopsy, Revealed Histopathological Features of Primary and Metastatic Lesions

Satoshi Konno¹, Satoshi Oizumi¹, Naofumi Shinagawa¹, Eiki Kikuchi¹, Jun Konishi¹, Kenichiro Ito¹, Nobuyuki Hizawa², Akihiro Takiyama³, Shinya Tanaka³ and Masaharu Nishimura¹

Abstract

Primary mediastinal liposarcoma was observed in a 73-year-old man. Because of tight adhesions to adjacent tissues, neither complete resection nor surgical debulking of the tumor was possible. A T-tube was inserted into the patient’s trachea for severe dyspnea, and he was treated with radiotherapy and an oral peroxisome proliferator-activated receptor-γ agonist. The patient died 6 years after the initial diagnosis. Autopsy revealed liposarcoma composed of 3 subtypes in the primary tumor: well-differentiated, dedifferentiated, and round cell components. Round cell and dedifferentiated liposarcomas were predominantly observed in the metastatic nodules.

Key words: mediastinal liposarcoma, primary, metastasis, autopsy, radiotherapy

(Inter Med 49: 771-775, 2010)
(DOI: 10.2169/internalmedicine.49.2974)

Introduction

Liposarcoma is the most common type of soft tissue sarcoma, occurring in the lower extremities and retroperitoneum (1). Primary mediastinal liposarcoma is rare and thought to represent less than 1% of all mediastinal tumors (2). Because of its lower frequency, the clinical features of primary mediastinal liposarcoma remain unclear, and hence, standard therapeutic strategies for this tumor have not yet been established. Here, we report an autopsy case of unresectable primary mediastinal liposarcoma that we followed for 6 years from the initial diagnosis, and we present the histopathological findings of the primary and metastatic lesions observed at autopsy. In the present case, 3 different histological findings (well-differentiated, dedifferentiated, and round cell type components) were observed in the primary tumor, and the dedifferentiated and round cell components were predominantly observed in the metastatic lesions. This is the first case of unresectable primary mediastinal liposarcoma that was followed to autopsy, which revealed the histopathological features of the primary and various metastatic lesions.

Case Report

A 73-year-old man presented with a 6-month history of gradually progressive, nonproductive cough and inspiratory dyspnea in November 2000. On admission, he had stridor in both expiratory and inspiratory phases of respiration. On computed tomography (CT), a large tumor was located in the midline posterior mediastinum, extending into the neck through the thoracic inlet and into the anterior portion of the left atrium. Large, homogenous, fat-dense regions were identified at the thoracic inlet level and at the level of the subcarina (Fig. 1a, 1b). The lesion in the thoracic inlet level...
compressed the trachea. Solid regions were detected between these 2 fat-dense regions (Fig. 1c) and at the level of the left atrium (Fig. 1d). Magnetic resonance imaging (MRI) showed a high signal intensity on both T1- and T2-weighted images at the thoracic inlet level and at the level of the subcarina (Figure not shown). Regions corresponding to Fig. 1c and Fig. 1d included a mixture of high and low signal intensities on both T1- and T2-weighted images (Figure not shown). Brain and abdominal CT scans showed no metastatic lesions.

Based on the CT and MRI findings, primary mediastinal liposarcoma was strongly suspected. The patient underwent surgery for possible complete resection or surgical debulking to relieve dyspnea. Gross examination showed that the tumor was encapsulated, extending from the neck to the anterior portion of the heart. Neither complete resection nor debulking of the tumor was possible because it adhered tightly to adjacent structures, especially to the membranous portion of the trachea and esophagus. Histopathological examination of the biopsy specimens obtained from the homogenous fat-dense regions (corresponding to the levels shown on the CT scan in Fig. 1a, 1b) revealed a well-differentiated type of liposarcoma characterized by mature adipoid tissues with various sized fatty droplets, including bizarre, nucleated lipoblasts (Fig. 1e). On the other hand, a biopsy specimen of the solid regions (corresponding to the level shown in Fig. 1c, 1d) revealed a dedifferentiated liposarcoma composed of sarcomatous tissue with dense collagenous tissue (Fig. 1f).

In April 2001, 3 months after the surgical procedure, the patient was urgently admitted to our hospital because of severe dyspnea. CT images revealed narrowing of the trachea caused by further enlarged tumor. Tracheostomy was performed with the insertion of a silicon T-tube (13.0-mm internal diameter), and his dyspnea improved. Subsequently, the patient received radiotherapy to the tumor, from the neck
to a point 3 cm below the carina, for a total dose of 30 Gy in 12 fractions over a 3-week period. Furthermore, prescription of a peroxisome proliferator-activated receptor-γ (PPAR-γ) agonist, pioglitazone, in expectation of differentiation of the liposarcoma, was started (at a single daily dose of 800 mg, orally) in February 2002. Pleural effusions on the right and left sides were observed in October 2002 and September 2003, respectively. The effusion on the right side did not increase further after repeated drainage procedures, and pleurodesis with OK-432 10KE was effective on the left side. Although the part of the tumor receiving radiotherapy was well controlled (Fig. 2a), the remaining tumor behind the heart, without radiotherapy, increased gradually (Fig. 2b). In April 2007, about 6 years after the initial diagnosis, the patient died of heart failure and pneumonia.

Autopsy examination revealed a large tumor localized in the posterior part of the mediastinum extending to the neck and to the anterior portion of the heart. Behind the heart, the main tumor mass, 17×11 cm in size (Fig. 3a), was observed, corresponding to the abnormal density area detected on CT 2 months before the patient’s death (Fig. 2b). The tumor had a well-demarcated, lobular appearance composed of both yellowish fatty lesions and a whitish, solid, firm mass. Microscopic examination of the yellowish part (Fig. 3a, portion A) demonstrated a well-differentiated component of liposarcoma (Fig. 3b), whereas the whitish part (Fig. 3a, portion B) possessed the features of dedifferentiated liposarcoma (Fig. 3c). Furthermore, foci of the round cell type of liposarcoma, characterized by uniform round to oval-shaped cells, were present in both areas (Fig. 3d, only the pathological findings from portion B are shown). Multiple metastases were observed in the liver, bilateral lungs, bilateral Gerota’s fascia, the left adrenal gland, mesentery, left fifth rib, and the left side of the neck. Microscopically, the metastatic lesions in the liver, lower lobe of the right lung, Gerota’s fascia, adrenal gland, and mesentery were mainly composed of a round cell component of liposarcoma (Fig. 3e), while those of the upper lobe of the right lung were mainly composed of a dedifferentiated component (Fig. 3f).

**Discussion**

Liposarcoma is the most common soft tissue sarcoma, occurring frequently in the lower extremities and retroperitoneum (1). The clinicopathological and prognostic features of liposarcoma arising in the extremities and retroperitoneum have been well reported (1, 3-5). However, documentation in the literature on mediastinal liposarcoma is limited because of its rarity. After the recent statements of the World Health Organization (WHO) classification of soft tissue sarcomas (6), only 2 studies have described primary mediastinal liposarcomas (7, 8). Accordingly, a case report of primary mediastinal liposarcoma is still valuable and, to the best of our knowledge, this is the first report of an unresectable mediastinal liposarcoma detailing the clinical course from initial diagnosis to autopsy and describing the histopathological features of the primary and metastatic lesions.

The histological findings of metastatic liposarcoma arising from a primary in the retroperitoneum have been well-described (9-12). Well-differentiated liposarcoma tends to be low grade and has been reported to have fewer metastases, whereas myxoid/round cell, pleomorphic, and dedifferentiated types of liposarcoma have more aggressive behavior and higher rates of metastases. However, in the case of primary mediastinal liposarcoma, few studies have described the metastatic findings. In particular, after the recent statements of the WHO classification of soft tissue sarcomas (6), only one study, by Hahn and Fletcher, in which 2 of 24 cases showed distant metastases exhibiting dedifferentiated and pleomorphic-like components in each, has addressed this issue (7). In the present case, 3 different histological findings, including well-differentiated, dedifferentiated, and round cell type components, were observed in the primary tumor. In contrast, the dedifferentiated and round cell types were predominantly observed in the metastatic regions, thus suggesting that these 2 histological components have more strong potential for metastasis, as indicated by previous reports on the different origins of this tumor (1, 13, 14).

Surgical excision has been curative for most primary mediastinal liposarcomas, especially well-differentiated ones, despite their large size (15-17). There have also been several
reports of very large primary mediastinal liposarcomas that adhered to adjacent tissues (18-20); even in such cases, partial excision usually relieved symptoms related to the compressive effects of the tumor. However, in the present case, tight adhesion to adjacent structures, possibly due to the fibrous environment associated with its variety of histopathological subtypes of liposarcoma, especially in the dedifferentiated subtype, allowed neither complete resection nor even debulking of the tumor. The unresectability of the tumor caused an unfavorable clinical course in this case.

Because of the low incidence of primary mediastinal liposarcomas, treatment strategies are extrapolated from those for similar tumors in other places, particularly for unresectable cases such as the one described in this report. A recent review of a large number of patients with liposarcoma in the extremities suggests the efficacy of postoperative radiotherapy to decrease the local recurrence rate (1). Furthermore, several case reports of mediastinal liposarcoma also suggested the efficacy of postoperative radiotherapy (1, 15, 18). In the present case, it seemed that the part of the tumor that received radiotherapy was well controlled, whereas the rest of the tumor that did not receive radiotherapy progressed, suggesting that radiotherapy might have contributed to local control of the tumor.

It has been reported that the nuclear receptor PPAR-γ plays a central role in adipocyte differentiation (21, 22). Of note, Demetri et al reported 3 cases of liposarcoma in which PPAR-γ agonist administration induced histological and biochemical differentiation in vivo (23). It is difficult to discuss the efficacy of this agent based on the clinical course of this case, but further clinical studies would provide evidence for the efficacy of these agonists in the treatment of this tumor.

In summary, this report describes a case of unresectable primary mediastinal liposarcoma that we followed for 6
years from initial diagnosis to autopsy. Further accumulation of case reports and descriptions of patients with this tumor would help develop standard treatments for this tumor, particularly for unresectable cases, as described in this report.

Acknowledgement
The authors would like to express their sincere gratitude to Dr. Koichi Yamazaki, the former associate professor of the First Department of Medicine, Hokkaido University School of Medicine, who died recently.

References