

Chylothorax Associated with Lymphangioliomyomatosis: A Patient with an Operative Pitfall

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Abstract: A 25-year-old woman presented to our hospital with a 1-week history of cough and shortness of breath. A chest radiograph showed a left-sided pleural effusion that contained chyle. The findings of other examinations suggested no distinct disease. We made the diagnosis of idiopathic chylothorax and operated only on the left side because magnetic resonance thoracic ductography depicted the thoracic duct on the left side. The intraoperative finding was chylous effusion flowing through a pleural fistula over a cystic lesion. We resected the lesion and ligated the thoracic duct in a left thoracotomy. The histopathologic diagnosis was Lymph Angioleio Myomatosis (LAM), which recurred after the operation. Sirolimus was given along with redo ligation of thoracic duct, resulting in cessation of chylothorax. A preoperative evaluation on possible LAM might have prevented the recurrence in combination with sirolimus.

Keywords: Lymphangioliomyomatosis; Magnetic Resonance Thoracic Ductography; Thoracic Duct; Sirolimus.

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Abbreviations: CD34: Cluster of Differentiation; CT34: Computed Tomography; HMB45: Human Melanoma Black; LAM45: Lymph Angioleio Myomatosis; MRTD: Magnetic Resonance Thoracic Ductography; MTOR: Mammalian Target of Rapamycin; SMA: Smooth Muscle Actin; TD: Thoracic Duct

Introduction

Light [1] classified the factors responsible for chylothorax into four categories: tumor, trauma, idiopathic, and miscellaneous. The leading cause of chylothorax is tumor while trauma is second. In the absence of these etiologic factors, chylothorax is labeled idiopathic. Roy and colleagues [2] reported that the diagnosis of lymphoma was established after a patient presented with chylothorax. We present the case of a patient with left-sided

chylothorax who underwent left thoracotomy to no avail, as an example of a pitfall in the management of chylothorax.

Herewith the patient gave an informed consent for the publication.

Patient, Methods and Results

A 25-year-old woman presented to our hospital with a 1-week history of cough and shortness of breath. Mediastinal emphysema had been diagnosed 2 years earlier, and 6 years prior, the patient had been in a traffic accident. Radiography and Computed Tomography (CT) of the chest showed the left-sided pleural effusion had a chylous texture. Lipoprotein analysis of the pleural effusion showed the proportion of chylomicrons was 32%. No malignant cells or bacteria were found in the pleural effusion. Laboratory tests showed no abnormalities. Tumor markers were not detected [1, 8]. Fluorodeoxyglucose positron emission tomography showed no lesions suspicious for malignancy. Chest CT showed equivocal cystic lesions distributed in both lungs (Figure 1). The diameter of these lesions was so small that we ignored these lesions and diagnosed the chylothorax as idiopathic. Heavily T2-weighted Magnetic Resonance Thoracic Ductography (MRTD) delineated a string-like lesion on the left side (Figure 2) that was thought to be the Thoracic Duct (TD).

Management with a low-fat diet was unsuccessful in controlling the chylothorax, thus we operated on the left side. The intra operative finding was chylous effusion flowing through the pleural fistula over the cystic lesion (Figure 3). The cystic lesion corresponded to a soft-tissue tumor visualized on the chest CT scan obtained for

evaluation of mediastinal emphysema 2 years previously. Ligation of the TD and resection of the cystic lesion were performed through the left thoracotomy.

Histopathologic examination showed that the specimen was characterized by smooth muscle-like spindle cells immune reactive to Human Melanoma Black 45 (HMB45; Invitrogen Corp., Carlsbad, CA), Smooth Muscle Actin (SMA; Nichirei Biosciences, Inc., Tokyo, Japan) and by the tumor lumen immune reactive to anti-lymphangioendothelial cell monoclonal antibody D2-40 (Nichirei Biosciences, Inc.) (Figures 4a-4e). The tumor was not immune reactive to Cluster of Differentiation 34 (CD34) and factor VIII monoclonal antibodies (Nichirei Biosciences, Inc.). The patient's condition was diagnosed as Lymph Angioleiomyomatosis (LAM), and the patient was referred to a university hospital to undergo further treatment for chylothorax. Beginning Postoperative Day 43, sirolimus (2mg per day; Rapamune, Pfizer AG, Zurich, Switzerland) was administered but chylothorax persisted. On Postoperative Day 58, the patient underwent a thoracic operation to ligate the TD with success. As of this writing 2 years postoperatively, sirolimus has been in use without recurrence of chylothorax.

Figure 1. Computed tomography showing soft-tissue tumor (arrows).

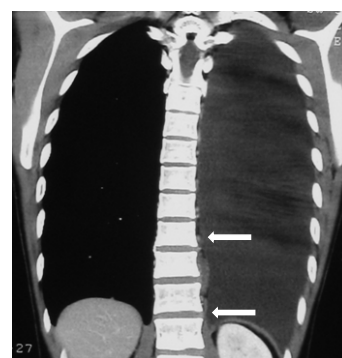


Figure 2. Magnetic resonance thoracic ductogram, showing absence of the thoracic duct but presence of a soft-tissue tumor (arrows).



Figure 3. Intraoperative photograph showing leakage of chyle through a pleural fistula over a cystic lesion.

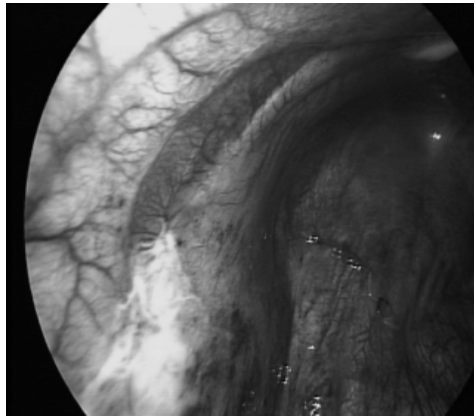


Figure 4. Photomicrograph of the resected specimen showing cysts and immature smooth-muscle proliferation. 4(a, b), hematoxylin and eosin at low-power field (4a; scale bar, 100 micrometers) and at high-power field (4b; scale bar, 10 micrometers). 4c, 4d, and 4e, immune histochemistry (scale bar, 10 micrometers) showing tumor cells positive for smooth muscle actin (4c)

and human melanoma black 45 (4d) as well as the tumor lumen positive for anti-lymphangioendothelial cell monoclonal antibody D2-40 (4e).

Figure 4-a

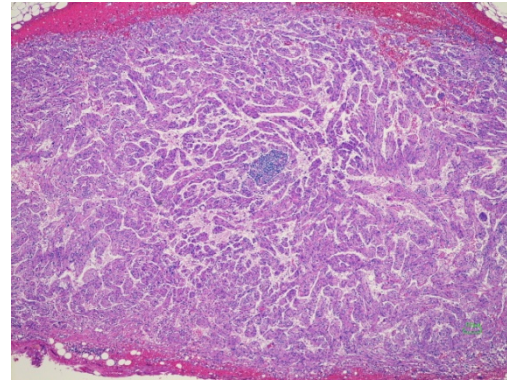


Figure 4-b

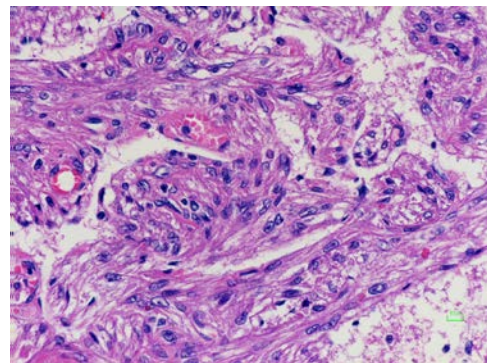


Figure 4-c

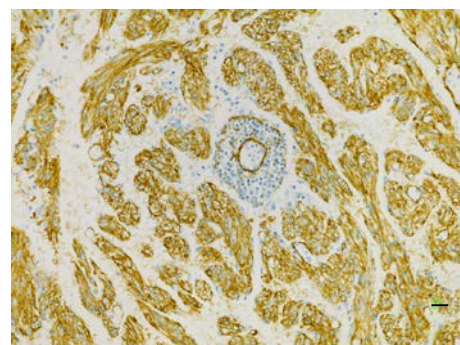


Figure 4-d

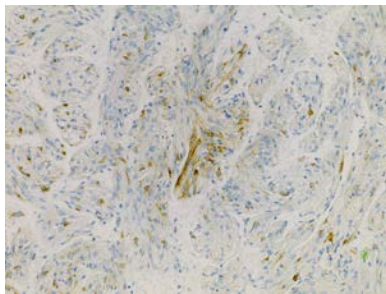
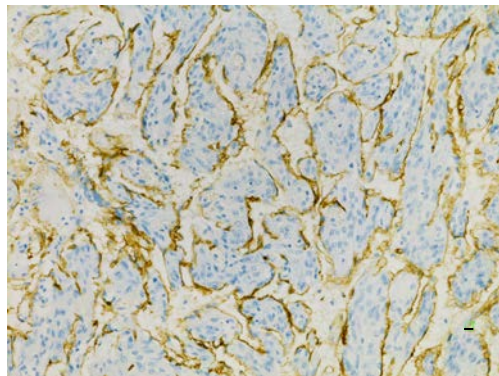


Figure 4-e



Discussion

The TD ascends extrapleurally in the posterior mediastinum along the right side of the anterior surface of the vertebral column. At the level of the fourth through sixth thoracic vertebrae, the duct crosses to the left side of the vertebral column and continues cephalad to enter the superior mediastinum between the aortic arch and the subclavian artery and the left side of the esophagus. Adachi [3] classified the anatomic configuration of the TD into nine types based on location and outflow. The TD has a number of variations [3, 4]. Okuda et al. [4] reported that the TD is conventionally visualized with lymphangiography.

MRTD, however, facilitates noninvasive evaluation of the TD and can be used to identify the configuration of the duct. On the basis of the MRTD imaging findings in this case, we believed our patient had a variation of the TD, and we operated on the left side. This treatment represented a pitfall in the management of chylothorax.

The cause of chylothorax should be investigated because patients occasionally need treatment not only of chylothorax but also of the underlying disease. Our patient had no diseases specific to chylothorax. Management strategies for chylothorax include maintaining nutrition and reducing the flow of chyle, relieving dyspnea by removing chyle, and direct closure to stop chylous flow. Our patient therefore underwent TD ligation and resection of the cystic lesion.

Pulmonary LAM is an uncommon disease in women and is characterized by smooth-muscle cell infiltration and cystic destruction of the lung [5]. LAM also can involve the mediastinal and retroperitoneal lymph nodes as well as axial lymphatic vessels [6]. Immuno reactivity with HMB45 is not a prerequisite for LAM but when present with consistent histologic changes is highly specific for this condition [7]. Matsui et al [8] suggested that the dilatation of lymphatic vessels observed is a consequence of obstruction of the flow of lymph or chyle. Chylothorax has been described in 0–14% of patients with LAM at presentation and in 22–39% during the course of the disease [9]. LAM without pulmonary change is not a leading cause of chylothorax because both LAM and chylothorax are rare diseases. Matsui et al. [8] reported that the diagnosis of extra pulmonary LAM with the clinical manifestations of pulmonary LAM never or rarely precedes that of pulmonary LAM, as occurred in our patient.

Excision of the TD and mediastinal lymph node masses does not have promise for controlling chylous effusion in patients with LAM [9]. Resection of the cystic lesion led to recurrence of chylous effusion in our patient. Had the lesion not been resected, we would not have diagnosed LAM. The optimal management of chylothorax in LAM challenges chest physicians. The pitfall in this case was that extra pulmonary LAM preceded the diagnosis of pulmonary LAM, which led to the recurrence. A preoperative evaluation on possible LAM might have prevented the recurrence in combination with sirolimus, an inhibitor of Mammalian Target of Rapamycin (mTOR) with efficacy for LAM [10].

Further studies with a larger number of patients are needed to investigate the diagnosis and treatment of LAM as well as chylothorax complicating LAM.

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