Case report

A rare clinical presentation of Waldenström Macroglobulinemia mimicking lung cancer

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ABSTRACT

Waldenström macroglobulinemia rarely presents as pulmonary symptoms, and even rarer as chylothorax. We present a patient who presented with bilateral pleural effusion and a 30 mm solid lesion in the lung. Biochemical analysis of the pleural fluid revealed chylothorax. The 18-fluorodeoxyoxygenase positron emission tomography, bronchoscopy, endobronchial ultrasound, and cytological examination of the pleural fluid, showed no apparent cause of the chylothorax. The diagnostic breakthrough was made with flow cytometry of the pleural fluid, which revealed a small group of clonal B-cells. Biopsy from the parietal pleura and bone marrow led to the diagnosis Waldenström macroglobulinemia. This demonstrates that flow cytometry should be considered when routine diagnostics do not lead to a reach a specific diagnosis.

1. Introduction

In patients with lung tumors, the clinical task is to confirm or invalidate the suspicion of lung cancer and to determine the TNM-classification if lung cancer is demonstrated [1]. A corner-stone in the diagnostic work-up of the patient is bronchoscopy and endobronchial ultrasound (EBUS) [2]. In the case of pleural fluid, thoracentesis with cytological examination of the fluid is recommended [3]. We present a patient where the diagnostic breakthrough was achieved by an analysis which is not considered routine in the guidelines for lung cancer diagnosis.

2. Case presentation

A 70-year-old male, previously healthy and with a smoking history of 15 pack-years, presented to his primary care physician with increasing shortness of breath and weight loss through six weeks. Chest X-ray and later computed tomography (CT) of thorax and abdomen showed a 30 mm solid lesion in the middle lobe and bilateral pleural effusion (Fig. 1). The tumor board suspected T1cN0M0 lung cancer and concurrent benign systemic disease causing...
pleural effusion.

An 18-fluorodeoxyglucose positron emission tomography with low dose CT (18-FDG PET-CT) showed no increased metabolic activity in neither lung tumor, mediastinal lymph nodes, nor pleura (Fig. 2).

Bronchoscopy with mucosa biopsy and bronchial lavage of the right middle lobe showed no signs of malignancy or infectious disease, and endobronchial ultrasound revealed morphologically normal mediastinal lymph nodes.

Diagnostic and therapeutic thoracenteses were performed repeatedly from both sides with various appearances as serous, chylous, blood-stained, or salmon-coloured. Biochemical analyses showed an exudate with lactate dehydrogenase (LDH) of 140 U/L (serum-LDH 220 U/L) and protein of 50 g/L (serum-protein 61 g/L) and elevated leucocyte count of approximately 6000 *10^6/L, mainly mononuclear leukocytes. Pleural triglycerides were increased (124─557 mg/dL), with normal cholesterol (<50─104 mg/dL). Pleural pH and glucose were normal. Pleural fluid cytology was repeatedly without malignant cells.

After repeated thoracenteses and no apparent cause of recurrent chylothorax, the pleural fluid analyzed by flow cytometry, and the patient was referred for video-assisted thoracoscopic (VATS) biopsy of the right parietal pleura. Flow cytometry showed 94% T-cells with a CD4:CD8 ratio of 6.9:1, and 1% CD5 CD10 clonal B-cells thus raising the suspicion of lymphoma. Histological examination of the right parietal pleura revealed lymphoplasmacytic lymphoma, including the MYD88 L265P mutation, and the patient was referred to haematologists. A bone marrow biopsy showed 60% lymphoid infiltration, and final diagnosis was Waldenström macroglobulinemia.

3. Discussion

Waldenström macroglobulinaemia (WM) is a low-grade B-cell lymphoproliferative disorder characterized by bone marrow infiltration by lymphoplasmacytic cells associated with a monoclonal immunoglobulin M protein in the serum [4]. The typical clinical features of WM are anemia, thrombocytopenia, hepatosplenomegaly, lymphadenopathy, and rarely hyperviscosity. Pulmonary and pleural involvement due to WM is rather rare, only occurring in 3─5% of cases [5].

Chylothorax is an uncommon cause of pleural effusion, and is most commonly caused by the disruption of the thoracic duct or its tributaries. It is characterized by the presence of chylomicrons in the pleural effusion or a pleural triglyceride of ≥110mg/dL [3]. Malignancy is the second most common cause and should be suspected in absence of surgical trauma. Malignant lymphomas cause 60─80% of malignant chylothorax [3,6].

Malignant chylothorax is often macroscopically milky with biochemically a lymphocyte-predominant exudate but may be serous, neutrophile-predominant, transudative, and with highly variable levels of protein and LDH [6,7]. Indolent rather than aggressive lymphomas are more often associated with chylothorax. It is speculated that patients with indolent lymphomas are unaware of their disease until their thoracic ducts are damaged [6].

Only few reports of chylothorax as initial manifestation of WM has been described previously [8─10] and none of them bilateral (Table 1). A few other reports describe onset of chylothorax months to years after WM diagnosis [11─17]. In only three reports, pleural fluid flow cytometry diagnosed WM as chylothorax cause [12,14,17]. Flow cytometry is pivotal in diagnosis of hematologic malignancies [18], BTS guidelines on workup of unilateral pleural effusion support flow cytometry of pleural fluid if lymphoma is suspected [3]. The clinical challenge in our case was the absence of lymphoma suspicion, bilateral pleural fluid with macroscopically and biochemically variable appearance.

Our case demonstrates that flow cytometry of pleural fluid could be considered in a patient initially suspected of lung cancer and presenting with bilateral pleural effusion if bronchoscopy, EBUS and repeated pleural fluid cytology and biochemistry do not lead to a specific diagnosis.

Statement of ethics

Written informed consent was obtained from the patient.

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**Fig. 1.** Diagnostic computed tomography at presentation showing a 30 mm tumor in the middle lobe and bilateral pleural effusion.
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Declaration of competing interest

None.

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