CASE REPORT

Dilemma in Diagnosing Malignant Pleural Mesothelioma with Atypical Clinical Presentation and Imaging Findings : Recurrent Chylothorax, Mediastinal Lymphadenopathies and Pulmonary Embolism

Koa Ai Jiun[1], Teh Yong Sim[2]

[1] Radiology Department, Faculty of Medicine and Health Sciences, Universiti Malaysia Sarawak (UNIMAS) 94300 Kota Semarahan, Sarawak, Malaysia
[2] Pusat Jantung Sarawak, Kuching –Semarahan Expressway 94300 Kota Semarahan, Sarawak, Malaysia

ABSTRACT

Malignant pleural mesothelioma (MPM) is a rare malignant tumor affecting the mesothelium. It commonly manifests as pleural thickening on contrast enhanced CT (CECT) thorax. We reported a case of a young lady who presented with respiratory symptoms and was initially treated as pneumonia. However, she had recurrent episodes of chylothorax with progressive internal jugular vein (IJV), brachiocephalic vein and superior vena cava (SVC) thrombosis leading to pulmonary embolism, associated with extensive mediastinal and supracalvicular lymphadenopathies. There are no evidence of pleural thickening in the initial investigations. Our case highlighted that MPM must remain in the differential diagnosis for these presentations, albeit rare.

Keywords: Malignant pleural mesothelioma (MPM), Recurrent chylothorax, Pulmonary embolism, Mediatsinal lymphadenopathies

Corresponding Author:
Koa Ai Jiun, MRAD
Email: koaaijiun@yahoo.com
Tel: +60138259062

INTRODUCTION

Malignant pleural mesothelioma (MPM) is an aggressive malignant tumor of mesothelium. It is present mostly in the elderly age group with strong relation to asbestos exposure. Imaging plays an essential role in detection and diagnosis of MPM, in which Computed Tomography (CT) is the primary imaging modality used for the diagnosis and staging of the disease. Key CT findings that suggest MPM include unilateral pleural effusion and nodular pleural thickening which will lead to tumoral encasement of the lung. Although rarely reported, there are reported cases of MPM which presented with chylothorax, pulmonary embolism as well as mediastinal lymphadenopathies.

CASE REPORT

A 39 years old lady, passive smoker, and worked as a cahsier in a mini-market; presented with cough, shortness of breath, fever and night sweat for 1 week duration. She was treated as right lobar pneumonia with parapneumonic effusion. CECT Thorax showed right pleural effusion with no evidence of pleural thickening or enhancement (Fig. 1). The pleural fluid was drained and macroscopically it was milky and turbid in appearance, with pleural fluid Triglycerides of 4.175 mmol/L (normal < 1.1 mmol/L), ratio of pleural fluid to

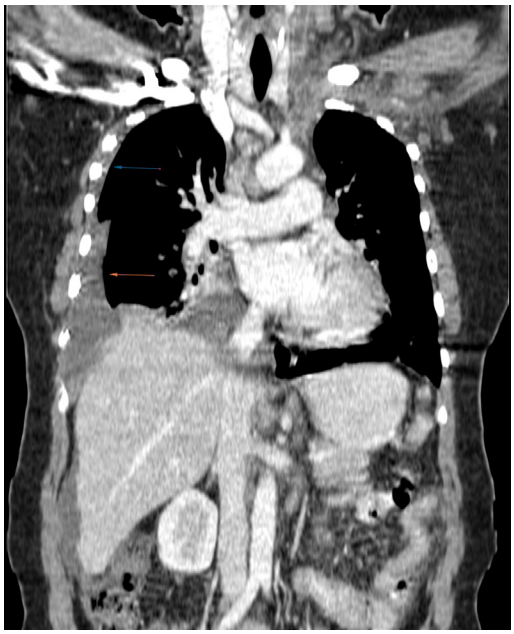

Figure 1: CECT Thorax coronal view: Minimal right pleural effusion (orange arrow) with no evidence of pleural thickening (blue arrow)

serum lactate dehydrogenase of 1.583, ratio of pleural fluid to serum protein of 0.79 and ratio of pleural fluid to serum cholesterol level of less than 1. Overall the pleural fluid analysis were consistent with chylothorax. The pleural fluid was also sent for Culture & Sensitivity, Acid-Fast Bacillus (AFB), gram staining and GeneXpert, all with negative results. Pleural fluid cytology showed a highly cellular fluid with dense population of benign and reactive mesothelial cells, however no atypical cells seen. Subsequently, over the period of two months the patient presented with recurrent episodes of bilateral chylothorax and the repeated fluid analysis from bilateral pleural fluid again showed similar findings of chylothorax with abundant reactive mesothelial cells and no atypical cells. This is followed by blind right pleural biopsy which showed partially degenerated tissue with no definitive malignant cells. On her 3rd admission for bilateral chylothorax, chest tube were inserted and right intrapleural streptokinase was instilled. Despite the intrapelural streptokinase, this patient had recurrent episodes of chylothorax following that. Patient was put on high protein and fat free diet.

The repeated CT Thorax after the pleursl drainage did not show any evidence of pleural thickening or lung mass. However, there was now thrombus within the right descending pulmonary artery (Fig. 2) as well as in the left Internal jugular vein (IJV), left brachiocephalic vein and SVC with multiple new mediastinal (Fig. 3) and supraclavicular lymphadenopathies.

Pleural fluid was also sent for flow cytometry as the repeated CT findings showed extensive mediastinal and supraclavicular lymphadenopathies with lymphoma as a differential; however there were no evidence of immature or clonal lymphocytes in the pleural fluid. Pleuroscopic guided right parietal pleural biopsy was performed and the histopathological examination (HPE) findings showed atypical mesothelial cells proliferation

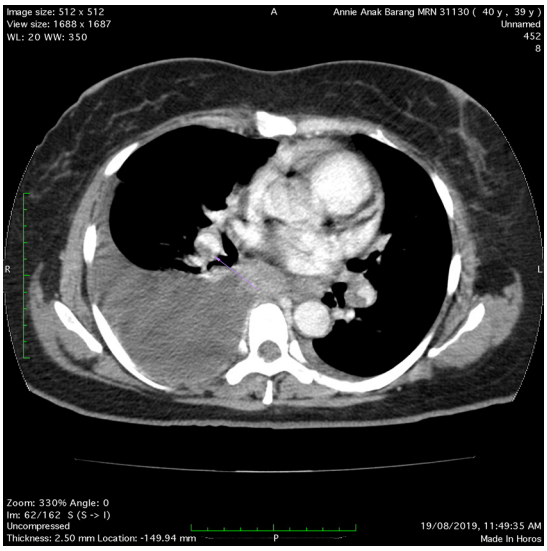

Figure 2: CECT Thorax axial view. Filling defect within right descending pulmonary artery (arrow)

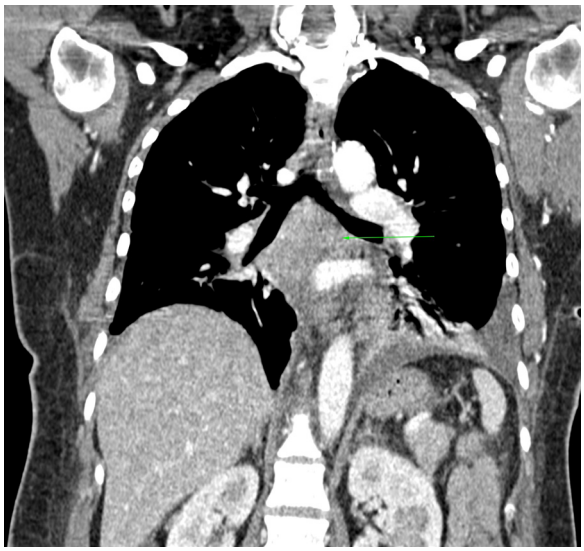

Figure 3: CECT Thorax coronal view. Extenstive subcarinal lymphadenopathies (arrow)

which could be reactive process or even representing an underlying mesothelioma, however the tissue sample was too superficial without underlying adipose or muscle tissue to assess stromal invasion. In addition to this, the CT findings did not support the diagnosis of mesothelioma as the typical imaging findings of mesothelioma were absent in this case. Thus the only conclusion given from this tissue sample was atypical mesothelial proliferation.

Excisional biopsy of the left supraclavicular lymph nodes were performed by the Otorhinolaryngology team, however the HPE again was inconclusive in which the specimen was negative for granulomatous inflammation or malignancy.

Following this, linear endobronchial ultrasound (EBUS) guided biopsy of the subcarinal lymph nodes was performed and was initially reported as negative for granulomatous inflmammation and malignancy. The primary team decided to proceed with CT guided right internal mammary lymph node biopsy. The immunohistochemical (IHC) stains showed positivity for WT-1, prodoplanin, calretinin, AE1/AE3 and Ber-EP4 (focal), and negative reactivity for LCA, S100, TTF-1 and ER. The previous sample of subcarinal lymph nodes from EBUS was reviewed and additional IHC were performed, and the atypical cells are positive for prodoplanin, calretinin, WT-1 and CK 5/6. Final HPE diagnosis of metastatic malignant mesothelioma (subtype epitheloid) was made after taking in consideration of IHC results from both the internal mammary and subcarinal lymph nodes.

A repeated CECT Thorax 5 months after the initial presentation showed loculated right pleural effusion with rim enhancement encasing the right lung (Fig. 4), worsening mediastinal lymphadenopathies and worsening central vein thrombosis. Patient was referred

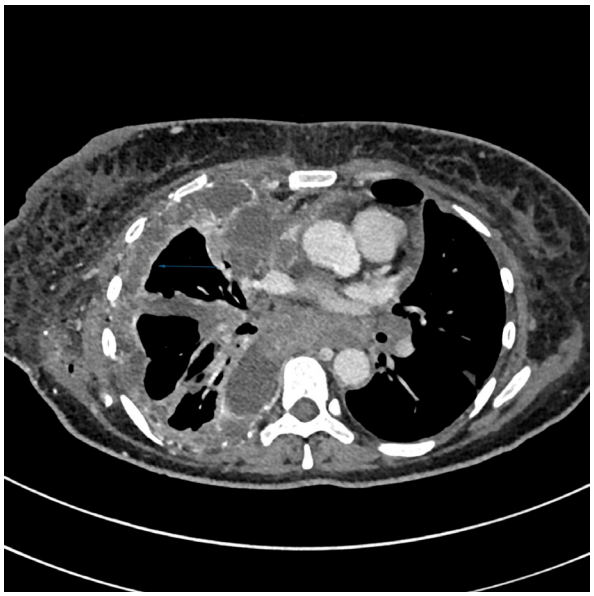

Figure 4: CECT Thorax Axial view. Multi-loculated right pleural effusion with pleural enhancement (arrow) encasing the right lung

to Radiotherapy Unit (RTU) for continuation of care, and patient was started on chemotherapy with Cisplastin-Pemetrexed regime. After 2 cycles of chemotherpy in our hospital, patient requested to be transferred back to her hometown division hospital and continued receiving chemotherapy from there.

DISCUSSION

Epidemiologic studies have shown that MPM is present mostly in the elderly aged group with male predominance and history of asbestos esposure. Statistics indicate that less than two percent of those diagnosed with MPM are less than 40 years old. We present a rare case of MPM in a young female who is 39 years old in with no history of asbestos exposure.

MPM has a strong relationship with asbestos exposure. However, literature reviews showed that there are small numbers of patients with confirmed MPM with no demonstrable exposure to asbestos. In this case, the patient was a cashier in a mini-market and was not known to be exposed to asbestos. The husband of this patient was a heavy smoker and they had been married for the past 15 years. However to date, there are no direct relationship between smoking and MPM.

This case report shows the challenges in establishing the diagnosis of MPM. At times, radiologic differential diagnosis may be required for the judgement of compensation when the pathologic diagnosis was uncertain, as seen in this case. MPM was not considered as the possible diagnosis initially as the typical findings of nodular pleural thickening which was commonly present in MPM was not present in this case. Yoon Kyung Kim et al reported that 96.1% of MPM manifestation is pleural thickening (1). Tamer Dogamn et al also reported that the most common CT finding of MPM is pleural thickening and it is present in 90-92% of patients (2). Contrary to these studies, our patient did not present with pleural thickening initially (Fig. 1). Loculated pleural effusion with rim enhancement encasing the right lung was only present in the CT images 5 months after the initial presentation.

This patient initially presented with recurrent bilateral chylothorax. Although chylothorax is a very rare presentation of MPM, there are several cases reported where chylothorax is one of the manifestation of MPM. According to Lauryn A. Benninger at al, as of year 2018, there are 6 reported cases of MPM in which chylothorax is the initial manifestation of MPM (3). The chylous pleural effusion seen in MPM most likely developed following the obstruction of the thoracic duct from infiltration of the malignant mesothelial cells into the surrounding lymph nodes (3).

Another rare manifestion of MPM which is present in our patient is venous thrombosis. The second CT of this patient revealed presence of pulmonary embolism with thrombosis at the right descending pulmonary artery (Fig. 2). There is also evidence of left IJV, proximal left subclavian vein, left brachiocephalic vein and SVC thrombosis. Hypercoagulability state is present in all malignant disease and this will in consequence leads to venous thrombosis.

Darley et al in his article explained the possible relation between venous thrombosis and recurrent chylothorax. They postulated that the presence of venous thrombosis in the jugular and subclavian junction may cause the rupture of the thoracic duct and this in turn resulted in chylothorax (4). This may explain the relation between the jugular and subclavian thrombosis with recurrent chylothorax as presented in our patient. The venous thrombosis could be the main contibuting factor which leads to persistent chylothorax as seen in this patient.

Literatures had shown that in some cases of chylothorax and malignant multiloculated pleural effusions, intrapleural streptokinase does help to improve a patient's condition. However the use of intrapleural streptokinase is not established and further studies are required to determine its role for chylothorax. As reported in this case, this patient had recurrent episodes of chylothorax even after the administration of intrapleural streptokinase.

Lymphatic spread causing lymphadenopathies in MPM is a rare condition even in an advanced case of MPM. Nind et al reported that lymphatic spread was only present in 13.5% of the cases in a study with 200 patients who are confirmed cases of MPM (5). Mediastinal lymphadenopathies (Fig. 3) were present in our patient during the initial presentation; and over the time, they had significantly increased in size and

numbers. Two months after the initial presentation, there were also evidence of left supraclavicular and internal mammary lymphadenopathies. As extensive mediastinal lymphadenopathies were not common in MPM, thus the initial work up for this patient was swerved towards the direction of lymphoma and tuberculosis.

CONCLUSION

We reported a case of MPM with rare initial manifestation of recurrent chylothorax, pulmonary embolism which resulted from internal jugular, brachiocephalic and SVC venous thrombosis as well as mediastinal lymphadenopathies in the absence of initial nodular pleural thickening. Although this growth pattern is rare and unusual, our case highlight that MPM must remain in differential diagnosis of these manifestation, albeit rare.

ACKNOWLEDGEMENT

This article is supported by Universiti Malaysia Sarawak (UNIMAS), Respiratory Unit Sarawak General Hospital and Pathology Unit Sarawak General Hospital.

REFERENCES

1. Yoon Kyung Kim, Jeung Sook Kim, Kyung Won Lee, Chin A Yi, Jin Mo Koo, Soon-Hee Jung. Multidetector CT Findings and Differential Diagnoses of Malignant Pleural Mesothelioma and Metastatic Pleural Diseases in Korea. Korean Journal of Radiology 2016;17 (4):545-554
2. Tamer Dogamn O, Salk I, Tas F, Epozturk K, Gumus C, Akkurt I, et al. Thoracic Computed Tomography Findings in Malignant Mesothelioma. Iran Journal of Radiology. 2012;9 (4):209-11
3. Lauryn A. Benninger, Julia A. Ross, Marino E. Leon, Raju Reddy. An Unusual case of chylothorax. Respiratory Medicine Case Reports 25 (2018) 318-322
4. David R. Darley, Emily Granger, Allan R. Glanville. Chest Pain and recurrent chylothorax: an unusual presentation of malignant pleural mesothelioma. Respirology Case Reports 5(5) 2017
5. N.R. Nind, R.L. Attanoos and A.R. Gibbs. Unusual intraparenchymal growth patterns of malignant pleural mesothelioma. Histopathology, Vol 42, No. 2, pp. 150-155, 2003