Doctor, may I request MRI for my "lung mass"

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Case 1

A 56-year-old gentleman was referred to Wong Tai Sing Hospital for evaluation of lung shadow on chest X ray in June 2017. The patient was a property maintenance staff with past medical history of hypertension, hyperlipidemia, impaired fasting glucose and varicose vein followed up at general outpatient clinic (GOPC). He was a non-smoker. He complained of cough with whitish sputum during and consulted GOPC in April 2017. He also had 1 episode of small amount of blood stained sputum, otherwise there were no other respiratory symptoms or constitutional symptoms. On physical examination he did not have any cervical lymphadenopathy or finger clubbing. The examination of chest or other system was unremarkable. CXR at GOPC (Figure 1) showed a 2cm right upper zone subpleural lesion with well-defined medial border but indistinct lateral border, which slowly increased in size compared with previous CXR. Therefore, the patient was referred for further investigation.

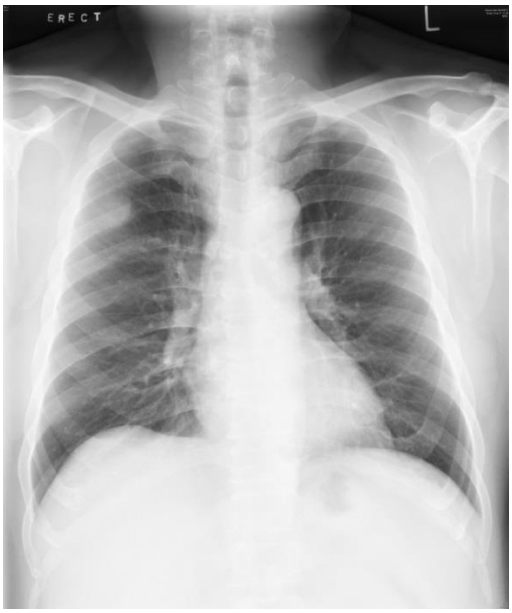

Figure 1. Right upper zone subpleural lesion with well-defined medial border but indistinct lateral border

Computer tomography (CT) with contrast was arranged (Figure 2), which showed a pleural-based lesion over the right posterior-lateral hemithorax at the level of posterior-segment of the right upper lobe. It measured 3cm x 1cm in size, and was well-defined with minimal contrast enhancement. It did not showed any invasion into lung parenchyma or erosion of the ribs. There were no mediastinal lymphadenopathies or pleural effusion.

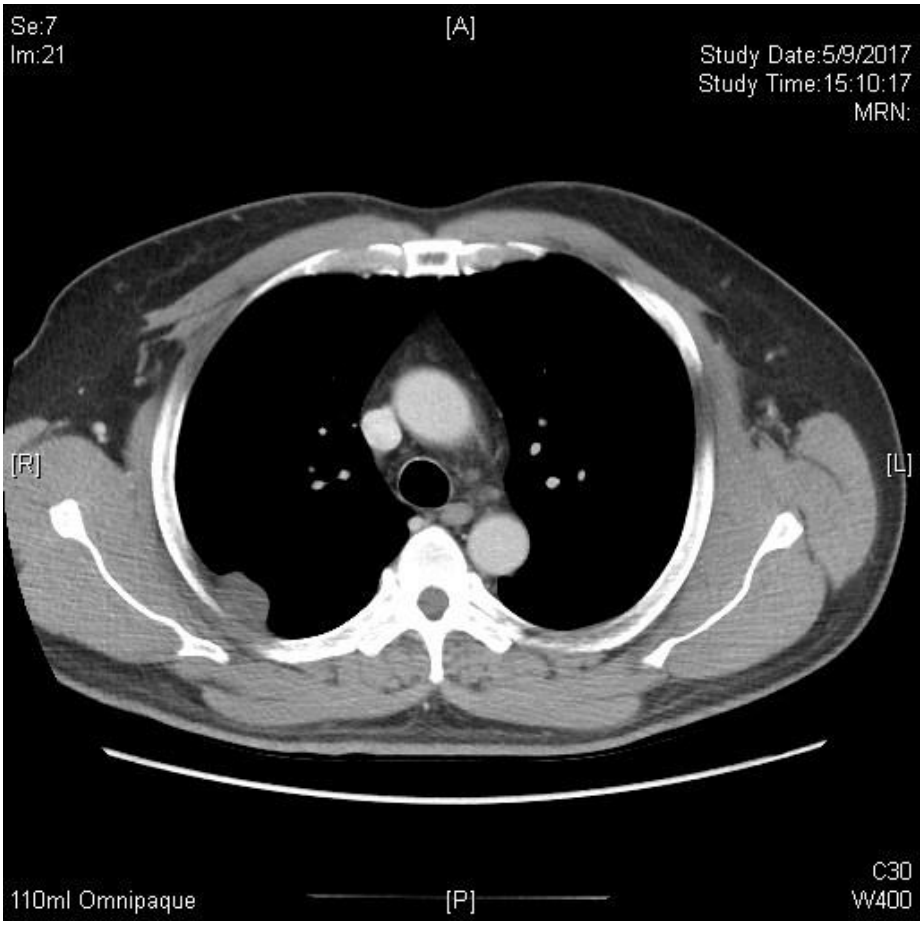

Figure 2. Pleural-based lesion over the right posterior-lateral hemithorax at the level of posterior-segment of the right upper lobe

The management approach to patients with suspected pleural lesion will be outlined. Patients may remain asymptomatic especially with small pleural lesion. Symptoms such as chest or shortness of breath should be checked. Recurrent hypoglycemia may be present in patients with solitary fibrous tumor of the pleura due to secretion of insulin-like growth factor.[1] Environmental exposure and occupation is important for diseases such as asbestosis. For past medical history, particular attention should be paid to prior malignancy as pleural metastasis is the most common pleural tumor. Upon physical examination, finger clubbing and

cervical lymphadenopathy should be checked. Pleural effusion may be detected, but chest exam may be normal.

For imaging approach to suspected pleural lesion, the first step is to differentiate between pulmonary and extra-pulmonary lesion (Table 1).[2]

Pulmonary	**Extra-pulmonary**
Acute angle with chest wall	Obtuse angle with chest wall
Non-tapered ill-defined border	Tapered well-defined border Incomplete border sign
Centered in the lung	Centered along chest wall
Engulf pulmonary vasculature on axial imaging	Displaces vasculature on axial imaging

Table 1. Differentiation between pulmonary and extra-pulmonary lesion (Modified from reference 2)

Incomplete border sign was demonstrated in our case. This can be attributed to the fact that medial margin of the pleural lesion was tangential to the x-ray beam and had good inherent contrast with the adjacent lung. On the other hand, the outer margin was en face or partially en face with the x-ray beam and merged with the pleura thus this part of the border was obscured.[3]

After localizing the lesion to extrapulmonary area, the next step is to differentiate whether the lesion is a pleural or an extrapleural one (Table 2).

Pleural	**Extrapleural**
Outward displacement of extrapleural fat	Inward displacement of extrapleural fat
Rib erosion relatively uncommon	Rib erosion relatively more common

Table 2. Differentiation between pleural and extra-pleural lesion (Modified from reference 2)

CT is the most commonly utilized imaging modality for evaluation of pleural lesion. It can confirm the location and determine extent of the pleural lesion. It is superior than MRI for

detecting calcification and bony destruction and useful for guidance for FNA or biopsy.[4] On CT, features suggestive of pleural malignancy include circumferential pleural thickening, nodular pleural thickening, mediastinal pleural involvement and parietal pleural thickening more than 1cm.[5]

Magnetic resonant imaging (MRI), while less commonly employed, is another handy tool for evaluation of pleural disease. It has superior soft tissue contrast- and spatial-resolution compared with CT. It is good at demonstrating infiltration of the chest wall, diaphragm or other adjacent tissues by malignant disease which is important in determining resectability.[6] Morphological features of pleural malignancy are similar to that of CT (mediastinal pleural involvement, circumferential pleural thickening, nodularity, contour irregularity, and infiltration of the chest wall or diaphragm). A retrospective study published in CHEST in 2000 found that if one or more morphological features were present, it would give a sensitivity 96% and specificity of 80% for pleural malignancies.[7] One important point raised by this study was that tuberculous empyema, when extensive, may involve the mediastinal pleura. Apart from morphological features, signal intensity on MRI also aids the diagnosis. High signal intensity in relation to intercostal muscles on T2-weighted and/or contrast-enhanced T1-weighted images was found to be suggestive for a malignant pleural disease. Combining morphologic features with the signal intensity features, MRI had sensitivity up to 100% and a specificity of 93% in the detection of pleural malignancies.[7]

Positive emission tomography (PET)/ PET-CT was also evaluated for its efficacy for pleural diseases. Meta-analysis in 2014 showed PET/PET-CT had a sensitivity 95% and specificity 82% for pleural malignancy.[8] False positive results may be present in infection or inflammatory lesions e.g. after talc pleurodesis. False negative results can be present in small malignant lesions or low-grade malignancies with low proliferative activity e.g. epithelioid subtypes of mesothelioma. The role of dual time-point 18F-FDG-PETor PET/CT in differentiating between malignant and benign pleural lesions is still controversial.[9]

For solitary pleural lesion, the differential diagnoses should include metastatic and primary pleural tumors, as well as benign pathologies that mimic pleural tumors. Pleural metastasis is the most frequently encountered pleural tumor. Primary pleural tumors are uncommon and are divided into mesothelial tumors (e.g. malignant mesothelioma), lymphoproliferative disorders (e.g. primary effusion lymphoma) and mesenchymal tumors (e.g. solitary fibrous tumor) according to the WHO classification.[10] Benign pathologies that can mimic pleural tumors include loculated

fluid or pleural pseudotumor, pleural plaque, thoracic splenosis and thoracic endometriosis

Our patient had CT guided pleural biopsy which showed a cores of tumor tissue. It was composed of short spindle cells in a collagenous stroma. Mitotic figures were not seen, which suggested benign pathology. Immunostaining result showed some of the spindle cells are S100 positive and some are CD 34 positive, which was suggestive of Schwannian differentiation and endoneurial fibroblast differentiation.[11] The overall features are spindle cell neoplasm, suggestive of pleural Neurofibroma.

The final diagnosis of our patient was pleural neurofibroma. Neurofibroma is a benign peripheral nerve sheath tumor, which comprised of a mixture of Schwann cells, fibroblasts, perineurial cells, and mast cells.[12] The majority is solitary and not associated with neurofibromatosis type 1 (NF 1). Neurofibroma are divided into localised, diffuse and plexiform types. While localized cutaneous neurofibroma is the most common form, neurofibroma can potentially involve any nerve from the root level to the smallest branch.

Localised pleural neurofibroma is a very rare disease entity of the pleura. We have performed a literature search and only found 1 case report and 1 case series describing the disease. Langman et al. reported a 78-year-old female who complained of shoulder pain without any respiratory symptoms.[11] Chest X ray showed a 2.5 cm pleural based nodule. She received VATS excision with no recurrence on 6 years of follow up. Mayo Clinic published a case series in 2015 which described 15 cases of pleuroparenchymal peripheral nerve sheath tumors, including 3 cases of neurofibroma.[13] Patients presented with shortness of breath, cough or incidental finding. No details regarding treatment were provided, but all patients had good outcome with no mortality reported with an average of 43 months of follow up.

On the other hand, pleural neurofibroma in NF 1 was more well reported in the literature. It is associated with risk of spontaneous hemorrhage and hemothorax, due to the angiogenic and invasive properties of the abnormal Schwann cells in plexiform neurofibromas.[14] Intercostal arteries and subclavian arteries are commonly involved.[15] Aggressive surgical treatment is required in hemodynamically unstable patients due to high mortality (up to 30% mortality).

Pleural neurofibroma in NF 1 patients is also associated with risk of malignant transformation into malignant peripheral nerve sheath tumor (MPNST), especially with plexiform neurofibroma. There is an estimated 5% lifetime risk of malignant transformation, which can

present as chest pain or rapid growth of a nodule within an existing plexiform neurofibroma.[16] Potential pitfalls exist when obtaining tissue diagnosis for MPNST. There is potential sampling error because benign areas could be contiguous with the malignant ones.[17] Pleural MPNST could be misdiagnosed as mesothelioma or non-small cell lung cancer as well.[18]

In view of the potential complications of hemorrhage and malignant transformation, features of NF 1 were explored. The patient had 5 well defined brownish spots over bilateral lower limbs, largest one measuring 6mm, otherwise there were no café-au-lait spots seen. He did not have any cutaneous neurofibroma, axillary or inguinal freckling. His neurological exam including the cranial nerves and vision were normal. There was no bone deformity. He did not have any family history of NF. He did not fulfill the National Institutional of Health diagnostic criteria for neurofibromatosis type 1.[19] In view of the increasing size of the pleural neurofibroma, he was referred to the cardiothoracic surgeon for excision. However, the patient defaulted follow-up. He was planned for serial imaging monitoring of the pleural neurofibroma.

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