A hint for abnormal thoracic shadow: look behind the heart

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Shareable abstract (@ERSpublications)
Can you diagnose this woman with a history of uterine fibroids in the previous year and a recent finding of intrathoracic mass on chest radiography? https://bit.ly/44mQ9Jj

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A 59-year-old woman presented with progressive dyspnoea and intermittent wheezing for the past year. She has a background history of seropositive rheumatoid arthritis, diabetes mellitus, hypertension and adrenal insufficiency secondary to exogenous steroid usage. She underwent a total abdominal hysterectomy in 2013 for uterine leiomyoma.

She has never smoked, has no history of atopy, and has no family history of bronchial asthma. She was initially treated for bronchial asthma at a private clinic, but her symptoms did not improve with inhaled corticosteroids and long-acting β-agonists. Her previous spirometry showed an obstructive pattern with forced expiratory volume in 1 s (FEV_1) 1.03 L (60.9%), forced vital capacity (FVC) 1.55 L (75.9%) and an FEV_1/FVC ratio of 66.38%. However, the bronchodilator response was negative with a post-bronchodilator FEV_1 of 1.05 L (62.1%). On clinical examination there is no joint swelling or deformity. She is not tachypnoeic with a respiratory rate of 20 breaths per min, oxygen saturation of 95% under room air, blood pressure of 124/70 mmHg and heart rate of 84 beats per min. There are focal rhonchi over the right upper chest wall. Spirometry results show normal spirometry with a negative bronchodilator response. A chest radiograph was performed (figure 1).

Task 1

Describe the chest radiograph shown in figure 1.

Go to Answers >>

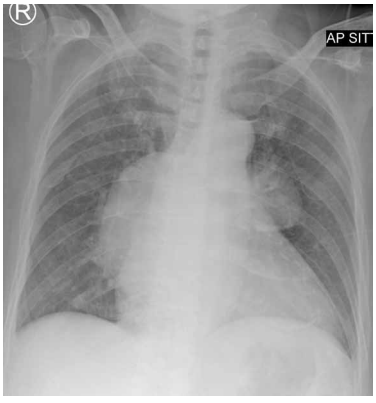

FIGURE 1 Chest radiograph.

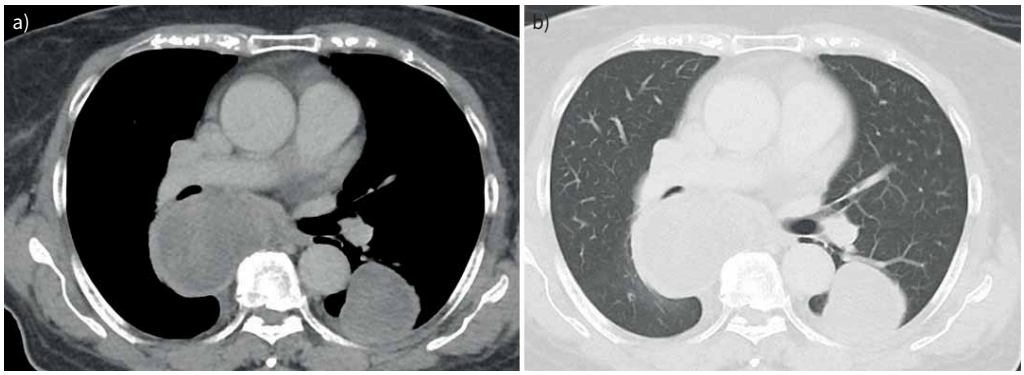

FIGURE 2 Contrast enhanced computed tomography thorax.

A contrast enhanced computed tomography (CT) of the thorax was performed to delineate the anatomic location of the mass and local effect on adjacent structures.

Task 2

What does the CT of the thorax show (figure 2)?

Go to Answers >>

Task 3

What are the abnormalities seen in positron emission tomography (PET)-CT shown in figure 3?

Go to Answers >>

The location of the lesions posteriorly in the thoracic cavity gave rise to a diagnostic dilemma. As the borders between the right-sided intrathoracic lesion and the pleura, chest wall as well as posterior mediastinum were not clearly delineated, a multitude of differential diagnoses were entertained when the patient was first seen. An ultrasound-guided biopsy was subsequently performed on the left-sided intrathoracic mass. The histopathological examination revealed epithelioid neoplasm with smooth muscle differentiation with immunohistochemical stain positive for CD34, desmin, smooth muscle actin and oestrogen receptor (figure 4). Progesterone receptor, HMB45, h-caldesmon, cytokeratin (CK) AE1/AE3, CK7, CK20, thyroid transcription factor-1, calretinin, GATA3, p40, LCA, p63, S100, and CD31 staining were all negative.

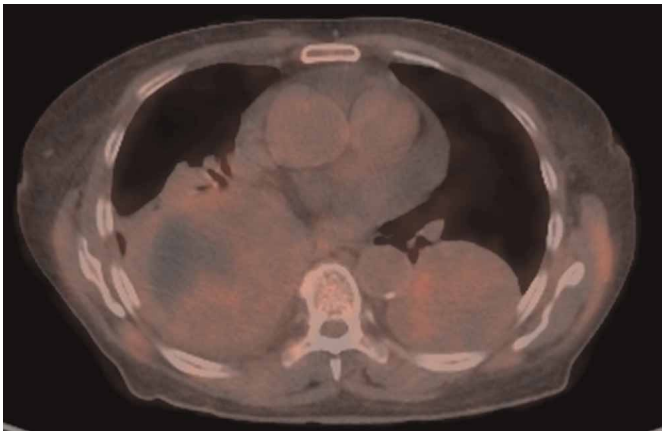

FIGURE 3 Lung positron emission tomography scan.

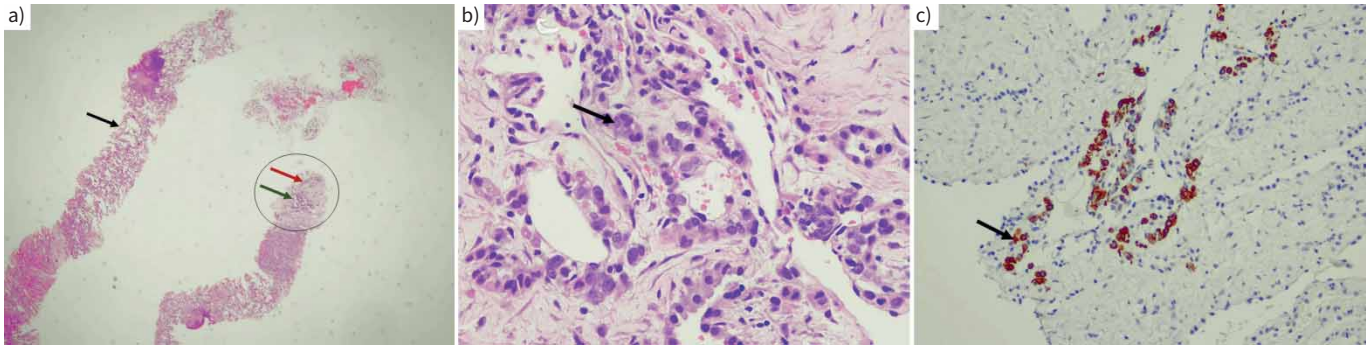

FIGURE 4 a) Lung mass biopsy histopathological examination shows a strip of lung tissue composed of alveolar spaces lined by single layer of pneumocytes (black arrow). There is present of focal area exhibiting epithelioid cells differentiation (green arrow), surrounded by mildly oedematous stroma (red arrow). Haematoxylin and eosin (H&E) staining, ×5 magnification. b) Further magnification of black circle in panel a shows a focal area of epithelioid cells with smooth muscle differentiation (black arrow), exhibiting rounded, hyperchromatic nuclei with inconspicuous nucleoli (H&E staining, ×40 magnification). b) Immunohistochemistry staining shows positivity towards Desmin (black arrow) (×20 magnification).

Task 4

What is the most likely differential diagnosis?

Go to Answers >>

Task 5

What is the best treatment option for this patient?

a) Close observation
b) Hormonal therapy
c) Surgical resection
d) Systemic artery embolisation

Go to Answers >>

A repeat transabdominal ultrasound by the gynaecological team shows no evidence of pelvic mass. A multidisciplinary discussion with the cardiothoracic surgery team took place and video-assisted thoracic surgery (VATS) assisted pulmonary leiomyoma resection was planned for this patient.

Discussion

PBML is a rare disease that develops months to years after a diagnosis of uterine myoma with a history of myomectomy or hysterectomy. The prevalence is highest among women in the late childbearing age, with a mean age of 46 years [1]. Various theories have been proposed to explain the possible mechanisms of tumour spread. These include haematogenous or lymphatic spread of uterine leiomyoma, *in situ* proliferation of smooth muscle induced by hormonal stimulation, metastasis of low-grade uterine leiomyosarcoma, peritoneal seeding after surgery for uterine leiomyoma and metaplastic transformation [2]. Rader *et al.* [3] reported a case of uterine leiomyoma that caused massive lower gastrointestinal haemorrhage and required exploratory laparotomy, hysterectomy, and bowel resection. By contrast, Abell and Littler [4] described a case of histologically benign pelvic and para-aortic lymph node metastases that resulted from fragments of leiomyoma that had entered dilated lymphatic channels at the time of endometrial curettage. Nishiwaki *et al.* [5] reported a case of intravenous leiomyomatosis that originated from the uterus and extended into the right pulmonary artery. These cases highlight the theory of haematogenous and lymphatic spread that may result in extraperitoneal cavity involvement, such as lung metastasis.

Commonly, the diagnosis of PBML is incidental to routine imaging of an asymptomatic patient, while some patients present with dyspnoea and respiratory distress. Despite the benign nature of the tumour, there are cases with rapid progression leading to local compressive effects such as the narrowing of the right main bronchus that is seen in our case [6]. The most common radiological finding in PBML is described as multiple solid nodules in the lungs. Other rare features include a solitary nodule, small miliary nodules, or mediastinal mass [7]. It is important to consider leiomyosarcoma as a potential diagnosis in cases with rapid tumour progression. An ^{18}F-FDG-PET scan is useful to evaluate the possibility of

aggressive malignant tumour [8]. Although a lung biopsy may indicate a benign nature, it is important to note that leiomyosarcoma can exhibit a heterogenous nature. Therefore, relying solely on the results of a lung biopsy may not provide a comprehensive assessment of the tumour's behaviour. VATS is often considered the gold standard for obtaining a definitive diagnosis [9]. As our patient refuses VATS, a multidisciplinary approach involving a team of respiratory physicians, oncologists, radiologists and pathologists may be necessary to collectively diagnose and decide further management.

There is no standard clinical practice guideline for the treatment of this disease. Main modalities of treatment include close observation, surgical resection and/or hormonal therapy, such as progestin inhibitors and luteinising hormone-releasing hormone analogues [10]. The treatment of PBML varies depending on the symptoms and compressive effect of the tumour. Surgical resection has been the mainstay of treatment for tumours with mass effect [11]. Surprisingly, a growing number of reports indicate that some tumours continue to progress despite surgical resection, indicating that hormonal therapy might be a vital adjunct to treatment [11, 12]. The presence of oestrogen and progesterone receptors in these tumours support their origin from uterine smooth muscle, and more importantly supports the use of hormonal therapy, especially in unresectable metastatic disease [13]. Progesterone and selective oestrogen receptor modulation therapy such as tamoxifen has shown regression of tumour size due to its ability to suppress the hypothalamic–pituitary–gonadal axis and reduce ovarian oestrogen production [14].

Conclusion

PBML should be considered as one of the differential diagnoses for female patients with multiple pulmonary tumours and a history of uterine leiomyoma. A biopsy for histopathological examination is critical for distinguishing between benign and malignant diseases. A combination of hormonal therapy and surgical resection should be considered in the management of progressive and symptomatic lesions.

Answer 1

A well-defined mass at the medial aspect of the right hemithorax. The inner border of this mass is not visualised. The right heart border is seen clearly. There is also another lesion of similar appearance at the medial aspect of left hemithorax, at the left hilar region. The left heart border and the left hilar structures are seen clearly through the lesion. The radiographic features suggest that the masses are located posterior to the heart.

<< Go to Task 1

Answer 2

CT thorax in the mediastinal window (figure 2a) and the lung window (figure 2b) shows a heterogeneously enhancing lesion at the posterior aspect of the right hemithorax, posterior to the right pulmonary vessels. It compresses onto the right lower lobe bronchus; however, the airway is still patent. This lesion shows an acute angle with the chest wall. There is mild adjacent pleural thickening. Another smaller, similar lesion is seen at the left posterior hemithorax. Due to the acute angulation with the chest wall, the lesions are more likely to be peripherally located intrapulmonary masses rather than arising from the pleura or the chest wall.

<< Go to Task 2

Answer 3

PET-CT revealed mild 2-fluoro-2-deoxy-D-glucose (FDG) avid bilateral peripherally located intrathoracic masses with well-defined border. This may represent benign tumours.

<< Go to Task 3

Answer 4

The presence of smooth muscle differentiation with positive smooth muscle actin and oestrogen receptor supports the diagnosis of pulmonary benign metastasising leiomyoma (PBML).

<< Go to Task 4

Answer 5

c. Surgical resection is the mainstay of treatment for this symptomatic patient due to rapid progression of the tumour causing compression to the right main bronchus and pulmonary veins. Preoperative embolisation can be considered for a mass with significant systemic vascularisation to reduce bleeding risk during surgical resection. Hormonal therapy can be used as adjunct therapy if the tumours continue to progress despite surgical resection.

<< Go to Task 5

Author contributions: Y.S. Wong initiated the idea for case reporting and prepared the final copy of the manuscript with M.Z. Siti Kaamilah. J. Bushra reported the radiological findings and N.M. Nik Ahmad Fadhil reported the histopathological results. M. Aisya Natasya was involved in the overall management of the patient. All authors read and approved the final manuscript.

Conflict of interest: The authors have no conflicts of interest to declare.

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