

Incidental Multiple Pulmonary Nodules in a Middle-Aged Woman

A 54-year-old lady underwent a screening cardiac computed tomography (CT) scan for coronary calcium which found incidental multiple sub-centimetre pulmonary nodules of varying sizes present in both lungs. This finding was confirmed on a CT of the chest (Fig. 1). Plain chest radiography was not done before surgery. She was a lifelong non-smoker with a history of total hysterectomy 15 years ago for menorrhagia secondary to fibroids. Her father had colon and lung cancer. Her mother had pulmonary tuberculosis, colon, lung and breast cancer. The patient had no cough, dyspnoea or constitutional symptoms including fever, night sweats, loss of weight and appetite. Physical examination was unremarkable. She had a recent mammography which was normal. Positron emission tomography-computed tomography (PET-CT) scan was performed to evaluate for the presence of malignancy elsewhere with lung metastases, but no hypermetabolic primary malignancy was detected. Autoimmune workup was negative.

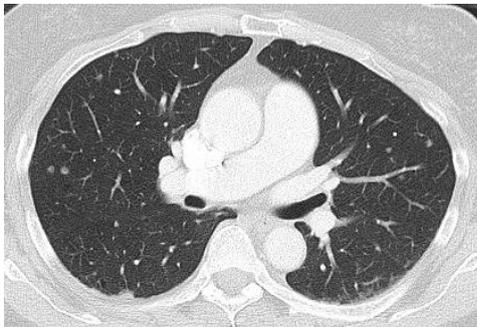


Fig. 1. Computed tomography scan of the chest demonstrates multiple sub-centimetre pulmonary nodules in both lungs.

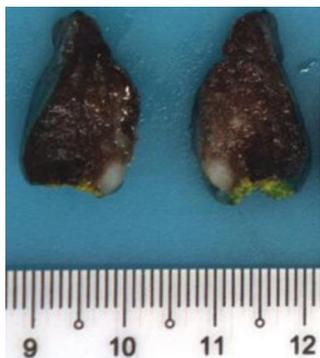


Fig. 2. Cut sections of the lung showing circumscribed whitish nodules.

The patient eventually underwent a video-assisted thoracoscopic (VATS) wedge resection of the right middle and lower lobes, which showed multiple small circumscribed firm whitish nodules (Fig. 2). Histologic findings showed circumscribed nodules with surrounding lung parenchyma (Fig. 3A), composed of a proliferation of interlacing fascicles of bland spindle cells featuring cigar-shaped nuclei with eosinophilic fibrillary cytoplasm, accompanied by a few entrapped tubules (Fig. 3B). Immunohistochemistry showed strong and diffuse staining for smooth muscle marker caldesmon (Fig. 3C) and oestrogen receptor (Fig. 3D) in the spindle cells. Ki-67 immunolabelling highlighted a very low proliferation index (F).

What is the diagnosis?

- A. Miliary tuberculosis
- B. Metastatic lung cancer
- C. Sarcoidosis
- D. Benign metastasising leiomyoma
- E. Nodular pulmonary amyloidosis

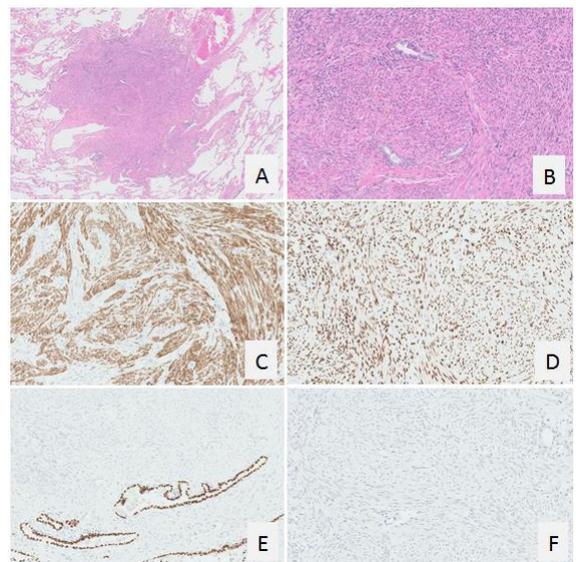


Fig. 3. A) Hematoxylin and eosin stain, x1; B) Hematoxylin and eosin stain, x10; C) Immunohistochemical stain positive for smooth muscle marker caldesmon and D) oestrogen receptor in the spindle cells; E) Entrapped tubules lined by TTF-1 positive bronchial epithelial cells; and F) Ki-67 immunolabelling demonstrated a very low proliferation index.

Answer: D

Discussion

Multiple pulmonary nodules in a patient with a strong family history of cancer and previous exposure to a close contact with pulmonary tuberculosis raised suspicion for an undiagnosed malignancy with lung metastases, or infections like tuberculosis. The PET-CT scan did not reveal any primary malignancy. The resected lung specimen was negative for bacterial, mycobacterial and fungal cultures. There was no evidence from the history or physical examination to suggest other differentials including inflammatory processes like sarcoidosis, rheumatoid nodules, nodular pulmonary amyloidosis and granulomatosis with polyangiitis.

A final diagnosis of benign metastasising leiomyoma (BML) was established based on the histopathological findings of multiple smooth muscle nodules found in the lungs. Leiomyosarcoma is not likely given the bland nature of the spindle cells, absence of necrosis and mitotic activity, as well as a low Ki-67 index. BML may closely resemble lymphangioliomyomatosis (LAMS), but can be differentiated from the latter using immunohistochemical stain with melanocytic markers such as human melanoma black (HMB-45), which was negative in our patient. Multiple pulmonary fibroleiomyomatous hamartomas is another consideration with similar histopathological features, but the given history of a previous hysterectomy for fibroids would favour a diagnosis of BML in our patient.

Several hypotheses have been proposed to explain the pathogenesis of BML, the most widely accepted of which refers to these lesions as haematogenous metastases from histologically benign uterine tumours. A majority of women with BML underwent previous myomectomy or hysterectomy, raising the possibility of surgically induced vascular spread. Some authors suggest BML represents lung metastases from low grade leiomyosarcoma. Others postulate a multifocal smooth muscle proliferation theory, but the presence of oestrogen and progesterone receptors, as well as positive bcl-2 expression in most reported cases of BML does not support this notion. Moreover, studies have demonstrated that BMLs and uterine leiomyomas are clonally related.¹

Most patients with BML remain asymptomatic although some rapidly progress to respiratory failure and death. Management would depend on the extent and progression of disease, hormone receptor positivity and age of the patient. Asymptomatic patients with stable lung lesions may not require treatment. Patients with solitary enlarging lung lesions are recommended for primary surgical excision. Those with progressive disease or unresectable lesions with positive expression of oestrogen receptors should be considered for hormonal manipulation via

surgical oophorectomy or pharmacological means, such as selective oestrogen receptor modulator therapy, long acting gonadotropin releasing hormone (GnRH) analogues in combination with aromatase inhibitors.² Spontaneous regression of lesions due to the effects of natural hormonal changes after menopause has been reported.³ Our patient received no further treatment but she remained on surveillance with 3-monthly chest radiographs, and was scheduled for a repeat CT chest after 12 months.

This case illustrates benign metastasising leiomyoma as an important differential to consider in patients with a history of fibroids and uterine surgery who present with multiple pulmonary nodules. VATS wedge resection of the lung is a useful means to obtain tissue for diagnosis. Although most cases follow an indolent course of progression, there is potential for some to develop progressive respiratory failure especially in premenopausal patients. Surgical resection and anti-oestrogen hormonal therapy are recommended treatment options for patients with progressive disease.

REFERENCES

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