Chest wall pain in an active 75-year-old retired machinist

M. Thirumaran
M.F. Muers

Dept of Respiratory Medicine, Leeds General Infirmary, Leeds, UK.

Correspondence:
M. Thirumaran
Dept of Respiratory Medicine
Leeds General Infirmary
Great George Street
Leeds LS1 3EX
UK

Case report

A 75-year-old female presented with a history of chest discomfort, but denied any respiratory symptoms. She had an active lifestyle, which included playing golf and dancing in her spare time. She had hypertension, but no other co-morbidities. The patient was a retired machinist in the textile industry, who had stopped smoking 20 years previously.

A clinical examination was unremarkable, and spirometry results and blood investigations were normal. Chest radiography showed a left-sided ill-defined opacity (figure 1).

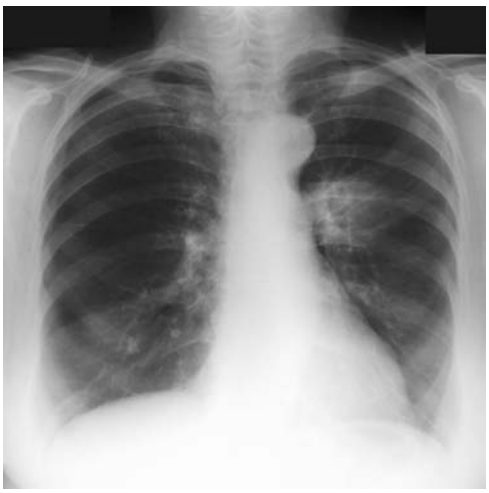

Figure 1
Chest radiograph.

Task 1
Which of the following should be the next investigation of choice and why?

a) **Computed tomography (CT) of the thorax.**
b) **Fibreoptic bronchoscopy (FOB).**
c) **Positron emission tomography (PET) scan.**

Answer 1
A CT of the thorax should be performed. By carrying out the CT scan first, unnecessary FOBs can be avoided and this will also improve the yield from FOB [1].

The patient underwent a FOB, which was normal, and the samples were negative for infection and malignancy. CT of the thorax (figure 2) revealed a 5.2-cm mass between the second and third ribs anteriorly on the left side. Mediastinal nodes were normal and there was no evidence of metastasis elsewhere.

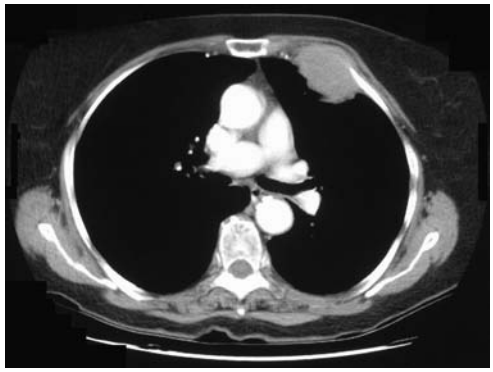

Figure 2
CT scan of the thorax.

Task 2
At this stage, what is the most likely diagnosis?
a) Primary bronchogenic carcinoma.
b) Metastasis.
c) Primary bone tumour.

Answer 2
Primary bronchogenic carcinoma is a possibility, but the CT scan of the thorax did not show any obvious involvement of the lung parenchyma. In view of the location, it is more likely to be a metastasis or a tumour arising from the bone.

The investigations proceeded to CT-guided trucut biopsy of the mass. The mass was felt to be very hard when it was biopsied. Histology revealed a tumour composed of large epithelioid cells and was immunopositive for cytokeratin and vimentin. The tumour was immunonegative for S100 protein, leukocyte common antigen, CA 125, carcinoembryonic antigen, thyroid transcription factor (TTF) and oestrogen receptor. It was concluded that the tumour was a poorly differentiated large cell carcinoma of unknown primary.

Task 3
How would you progress with the management of this patient?
a) Seek the primary.
b) PET scan.
c) Chemotherapy.
d) Radiotherapy.
e) Obtain surgical opinion regarding resection.

Answer 3

Following discussions at a regular multidisciplinary lung cancer meeting, it was decided that a radioisotope bone scan should be carried out, and the patient should be referred for surgical resection. The CT scan did not show any evidence of malignancy elsewhere. PET scanning is valuable in mediastinal staging [2], although its value in extrathoracic staging or chasing an extrathoracic primary is debatable. A PET scan would have been ideal in this case, but this facility was not available locally so it was decided to proceed with surgical resection to avoid a time delay.

The radioisotope bone scan revealed an increased uptake in the left 2nd and 3rd ribs, which was suggestive of infiltration. The patient had a left anterior thorocotomy and the mass was observed along the 4th rib, extending into the pectoralis major and the lingula. A chest wall resection and lingulectomy was performed. The patient recovered well without any complications.

Histologically, the rib was expanded and infiltrated by a malignant epithelioid tumour extending into the lung. The tumour showed epithelioid and spindle morphology. It was strongly positive for calretinin, cytokeratin (CK)5/6 and CK7; borderline positive for epithelial membrane antigen (EMA); and negative for other markers including CD56, ER, BerEp4, AUA1, MelanA, alpha-foetoprotein, CK20, CD31, CD34, S100, BRST2 and hepR1. These features were in keeping with a diagnosis of mesothelioma.

Task 4

Would you agree with the diagnosis of mesothelioma?

a) Yes.
b) No.
c) Not sure.

Answer 4

The immunohistochemistry would fit with a diagnosis of mesothelioma. In view of the localised nature of the tumour, a diagnosis of **localised malignant mesothelioma (LMM)** was reached.

A histological diagnosis in malignant mesothelioma (MM) is often difficult due to complex structural variability among the histological subtypes. Epithelioid MM is often difficult to differentiate from adenocarcinoma. Immunohistochemistry is valuable in diagnosing and differentiating MM from metastatic adenocarcinomas of various origins. It is worth noting that no single stain is diagnostic of MM. The commonly used stains are listed in table 1.

The patient denied any history of asbestos exposure. She lived >2 miles away from the local asbestos factory in the 1970s.

Task 5

What would you do next?

a) Observe.
b) Chemotherapy.
c) Local radiotherapy.

Table 1 Commonly used stains

Immunostains	*Mesothelioma*	*Other carcinomas*
TTF-1 (epithelial marker)	*Usually negative*	*Positive in adenocarcinoma of lung origin and thyroid carcinomas*
Calretinin	*Usually positive (epithelioid)*	*Occasionally positive in pulmonary adenocarcinoma*
CK5/6 (epithelial marker)	*Usually positive*	*Useful in differentiating mesothelioma from adenocarcinoma, can be positive in squamous cell carcinomas too*
CK7	*Usually negative*	*Positive in adenocarcinomas of lung, breast and ovary. Negative in squamous carcinomas*
CK20	*Negative*	*Positive in adenocarcinomas of gastrointestinal, pancreatic, ovary and breast carcinomas*
Thrombomodulin	*Usually positive*	*Rarely positive in adenocarcinoma, frequently positive in squamous cell carcinomas*
LeuM1 (CD15)	*Rarely positive*	*Positive in most adenocarcinomas and Hodgkin's disease*
CEA (epithelial marker)	*Rarely positive*	*Strongly positive in pulmonary and gastrointestinal adenocarcinomas*
BerEp4 (epithelial marker)	*Mostly negative*	*Positive in pulmonary adenocarcinoma and to a lesser extent in renal carcinoma*
Cadherins (mesothelial marker)	*N-cadherin positive*	*E-cadherin positivity is seen in adenocarcinomas*
Vimentin (mesenchymal marker)	*Positive*	*Can be positive to a lesser extent in adenocarcinomas*
EMA (epithelial marker)	*Frequently positive*	*Can be positive to a lesser extent in adenocarcinomas. Useful in differentiating reactive mesothelium from mesothelioma*
CA125	*Usually negative*	*Positive in ovarian carcinoma*

Answer 5

Very little is known about the behaviour of these tumours. There is no evidence to suggest the use of either chemotherapy or local radiotherapy, as this tumour is rare. Therefore, the patient was observed.

Discussion

LMMs are rare, and the term has been used to define focal pleural and peritoneal fibrous tumours in the past. These tumours are well circumscribed and have all the histological and immunocytochemical features of diffuse MM, but do not exhibit any evidence of spread [3]. LMMs have a different biological behaviour, but far better prognosis when compared with diffuse MMs.

Often, LMMs are diagnosed incidentally as these patients have very minimal symptoms. There have been a few case reports of LMMs arising from the pleura, pericardium, peritoneum or the chest wall [4–8], but the pleura tends to be the most common site. Rarely, LMMs can present as a pulmonary [9], mediastinal [10], small intestine [11] or hepatic [12] mass. Clinical signs such as hypoglycaemia and pulmonary osteoarthropathy have been reported [13, 14]. LMMs can be pedunculated or sessile. In some cases, they exhibit calcification or cystic changes [15]. It is often difficult to differentiate by various imaging modalities, but magnetic resonance imaging can be useful in assessing the extent of the lesion.

Commonly, they are epithelial in origin. The other histological patterns seen are mixed or biphasic and sarcomatous type. In addition, most of these patients have limited or no history of asbestos exposure. Unlike diffuse MMs, where the epithelioid type favours a better prognosis, the histological pattern does not predict survival in LMMs [3]. The important aspect of diagnosing LMM is that it is curable by surgical resection. When these tumours recur, they follow a similar pattern to sarcomas.

References

1. *Laroche C, Fairbairn I, Moss H, et al. Role of computed tomographic scanning of the thorax prior to bronchoscopy in the investigation of suspected lung cancer. Thorax 2000; 55: 359–363.*
2. *Lung cancer: diagnosis and treatment. NICE Guidelines. London, NHS National Institute for Health and Clinical Excellence, 2005.*
3. *Allen TC, Cagle PT, Churg AM, et al. Localized malignant mesothelioma. Am J Surg Pathol 2005; 29: 866–873.*
4. *Tarao M, Sakamoto K, Fukuchi T, Sumi Y, Ichihashi M, Gotou A. [A case of malignant localized chest wall mesothelioma accompanying with abdominal aortic aneurysm]. Kyobu Geka 1994; 47: 149–152.*
5. *Erkilic S, Sari I, Tuncozgur B. Localized pleural malignant mesothelioma. Pathol Int 2001; 51: 812–815.*
6. *Hirano H, Takeda S, Sawabata Y, et al. Localized pleural malignant mesothelioma. Pathol Int 2003; 53: 616–621.*
7. *Kerrigan SA, Cagle P, Churg A. Malignant mesothelioma of the peritoneum presenting as an inflammatory lesion: a report of four cases. Am J Surg Pathol 2003; 27: 248–253.*
8. *Matsukuma S, Aida S, Hata Y, Sugiura Y, Tamai S. Localized malignant peritoneal mesothelioma containing rhabdoid cells. Pathol Int 1996; 46: 389–391.*
9. *Ojeda HF, Mech K Jr, Hicken WJ. Localized malignant mesothelioma: a case report. Am Surg 1998; 64: 881–885.*
10. *Erdogan E, Demirkazik FB, Gulsun M, Ariyurek M, Emri S, Sak SD. Incidental localized (solitary) mediastinal malignant mesothelioma. Br J Radiol 2005; 78: 858–861.*
11. *Gourtsoyiannis N, Bays D, Missas S, Gallis P. Solitary malignant mesothelioma of the small intestine: radiological appearances. Abdom Imaging 1996; 21: 258–260.*
12. *Imura J, Ichikawa K, Takeda J, et al. Localized malignant mesothelioma of the epithelial type occurring as a primary hepatic neoplasm: a case report with review of the literature. Apmis 2002; 110: 789–794.*
13. *Kishimoto T. [A case of benign localized mesothelioma with occupational history of asbestos exposure]. Nihon Kyobu Shikkan Gakkai Zasshi 1991; 29: 1603–1607.*
14. *England DM, Hochholzer L, McCarthy MJ. Localized benign and malignant fibrous tumors of the pleura. A clinicopathologic review of 223 cases. Am J Surg Pathol 1989; 13: 640–658.*
15. *Luo D, Shi M. [Imaging diagnosis of localized pleural mesothelioma]. Zhonghua Zhong Liu Za Zhi 1995; 17: 36–38.*