Can you identify this uncommon cause of pleural effusion?

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Case report

A 51-year-old female was admitted with a history of breathlessness, pain in the left shoulder and difficulty swallowing. A malignant melanoma had been removed from her epigastrium in 1982; in 2002, another pigmented lesion was removed from her cheek. This lesion was benign (Lentigo simplex). On examination, the patient had distended neck veins on the left side and showed clinical signs of left pleural effusion. She also had a highly pigmented lesion over the malar area, present for about 12 months, which was not investigated.

Initial investigations showed haemaglobin 11.4 $g \cdot dL^{-1}$ with mean corpuscular volume 86.2 fL and C reactive protein of 60 $mg \cdot dL^{-1}$ (normal range 0–10 $mg \cdot dL^{-1}$). Renal function, liver function, calcium, phosphorus and serum electrophoresis were normal. Serum lactate dehydrogenase (LDH) was raised to 1,855 IU (normal range 0–400 IU). Chest radiography showed left-sided pleural effusion along with widened mediastinum. The patient went on to undergo a diagnostic pleural aspirate (figure 1).

Figure 1
Pleural fluid aspirate.

Task 1
Comment on the pleural aspirate.

Answer 1

The fluid is milky white in colour, very characteristic of chylous effusion. Pleural fluid was exudative according to Light's criteria, with protein of 47 $g \cdot L^{-1}$, LDH 1,488 IU, cholesterol 2.9 mM and triglyceride 9.7 mM (normal range <0.56 mM or 50 $mg \cdot dL^{-1}$). Fluid analysis showed numerous lymphocytes but no malignant cells. Bronchoscopy was normal and bronchial washings were negative for malignant cells.

The patient underwent a computed tomography (CT) scan of chest and abdomen (figures 2 and 3).

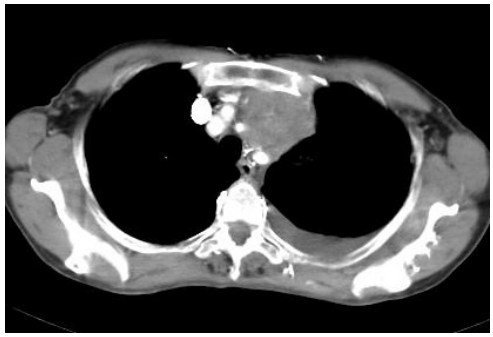

Figure 2
CT scan of the chest.

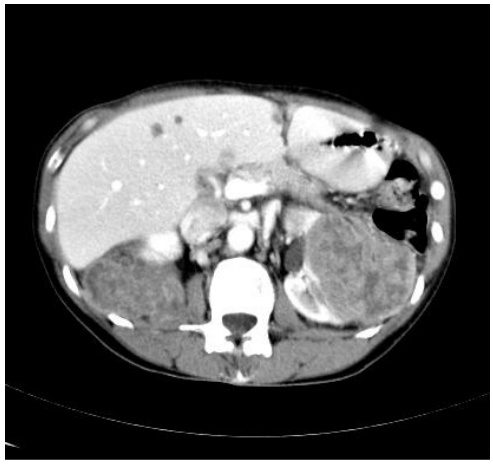

Figure 3
CT scan of the abdomen.

Task 2
Interpret the CT scans.

Answer 2

CT showed a mediastinal mass occluding the left brachiocephalic vein with collaterals and left pleural effusion. The abdominal scan showed a large mass in the right pararenal area and left kidney with deposits in the liver.

Pleural fluid analysis confirmed chylothorax and with the radiological findings of anterior-superior mediastinal mass and high serum LDH, lymphoma was first in the list of differential diagnoses. However, malignant melanoma is also likely, given the patient's history of previous melanoma 22 years previously.

The patient underwent ultrasound-guided biopsy of the right-sided pararenal mass (figure 4).

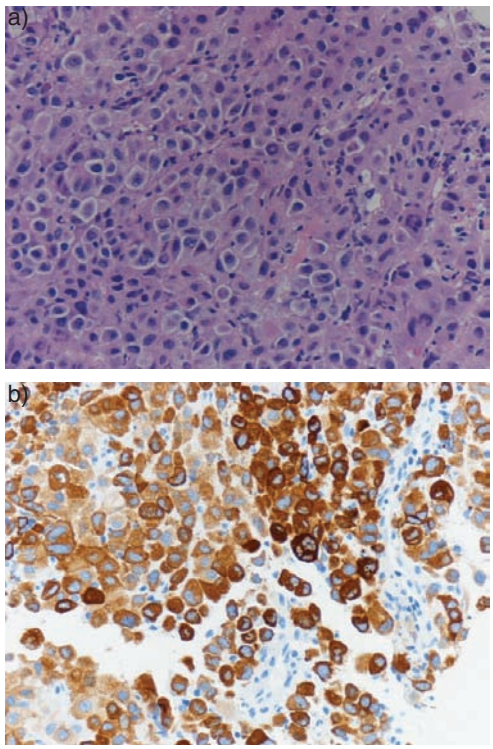

Figure 4
Biopsy from the right-sided pararenal mass stained with: a) haematoxylin and eosin; and b) melan-A.

Task 3
Interpret the histological findings from the biopsied mass.

Answer 3

Biopsy showed a cellular malignant tumour. Cells are large and round with abundant eosinophilic cytoplasm and central nuclei (figure 4a). Immunohistochemistry was negative for lymphoid and epithelial markers and strongly positive for S 100 and melan-A (figure 4b), confirming malignant melanoma.

The patient initially underwent closed pleural drainage followed by video-assisted thoracic surgery and pleurodesis. She was referred to the regional melanoma referral centre for chemotherapy and interferon treatment. However, owing to her extensive disease, she died a few months later.

Discussion

Chylothorax is an uncommon cause of pleural effusion, accounting for a small proportion of cases. It is caused by disruption or blockage of the thoracic duct anywhere along its course in the thorax, leading to leakage of chyle into the pleural space. The thoracic duct is the major lymph vessel. It begins as cisterna chyli in the abdomen and then runs behind the aorta in the diaphragm, running to the right of the vertebral column between the aorta and azygous vein. At the level of the fifth vertebra, it inclines towards the left side, continuing upwards behind the oesophagus and subclavian artery to empty into the confluence of the left subclavian and left internal jugular veins. Leakage of chyle occurs more commonly on the right, owing to its longer course and easy susceptibility to damage secondary to stretching [1].

Malignancy is responsible for ~50% of cases of chylothorax [2]; of these, lymphoma accounts for ~75% [3]. Trauma (mainly iatrogenic) during thoracic surgery is the second-most common cause [2]. Other causes include congenital or acquired lymphatic disorders (Milroy disease, congenital lymphatic hypoplasia, pulmonary lymphangioleomyomatosis or thoracic irradiation). Chylothorax may also occur secondary to chylous ascites due to primary billiary cirrhosis, primary sclerosing cholangitis, alcoholic cirrhosis or hepatitis C infection. In a small proportion of cases, the cause is unknown or idiopathic.

Diagnosis is suggested by a chylous/milky appearance of the pleural fluid and is confirmed by a pleural fluid triglyceride level >1.24 mM (or >110 $mg \cdot dL^{-1}$). In the absence of such high triglyceride levels, the presence of chylomicrons will help in confirming the diagnosis [4]. As far as the authors are aware, the present report is the first published case where chylothorax has resulted from the direct spread of malignant melanoma. A case of chylothorax in a melanoma patient due to thoracic duct ligation during surgery has been reported [5]. In the present patient, thoracic duct blockage occurred on the left side as a result of mediastinal spread of the melanoma, leading to left chylothorax.

Another important, but rare, disorder in which pleural fluid appears chylous is pseudochylothorax. It is characterised by cholesterol-rich pleural fluid that lacks triglycerides and chylomicrons and is surrounded by thick pleural tissue [5]. This is seen in conditions associated with chronic pleural thickening and effusion, such as chronic rheumatoid pleural effusion, tubercular effusion and traumatic effusion.

Treatment of chylothorax is aimed mainly at managing the cause along with repeated thoracocentesis and chest drain, with or without pleurodesis. In ~50% of metastatic carcinomas and 68% of lymphomas, significant resolution occurred after radiotherapy [6]. A fat-restricted diet with medium chain triglyceride supplementation or total parenteral nutrition helps in reducing the synthesis of chyle [7]. Surgical intervention is warranted if: conservative management fails after 2 weeks; daily chyle leak exceeds 1 L; the lungs do not re-expand; loculated chylothorax or postesophagectomy chylothorax occur; or if significant nutritional imbalances ensue [8, 9]. Early surgery is indicated in iatrogenic causes, as delays lead to increased mortality and morbidity. The standard surgical procedure is thoracic duct ligation. Other interventions include pleurodesis with tetracycline or talc or pleuroperitoneal shunting.

Patients with chylothorax are more prone to secondary infections owing to impaired immunity, nutritional depletion and the presence of a chest drain. High mortality and morbidity are associated with this disorder, hence if conservative management fails or the conditions discussed above arise, early surgical intervention should be considered.

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