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Case report

Fade to black!

A 71-year-old man presented to the emergency room with chest pain, dry cough, shortness of breath and night sweats for 10 days. He had no fever, flu-like symptoms, sputum production or haemoptysis. There was no history of recent travel or sick contacts. A general review of systems was remarkable for subjective weight loss and malaise. He was an active smoker with a 100 pack-years smoking history and a past medical history of rectal squamous cell carcinoma (SCC). His cancer was treated with chemoradiotherapy and had been in remission for 8 years before the presentation. He was also known to have COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) category B, well-controlled, with no recent hospitalisations or exacerbations over the past year.

Upon initial examination, arterial blood pressure was 123/75 mmHg, heart rate was 81 beats per min, respiratory rate was 24 breaths per min, and oxygen saturation was 93% on room air. Arterial blood gases showed partial oxygen pressure 73 mmHg, carbon dioxide tension 45 mmHg and pH 7.43. There were decreased breath sounds on the right side, up to the upper lung zone with dull percussion note and reduced tactile vocal fremitus on chest examination. The physical examination was unremarkable otherwise. The patient had a chest radiograph, which showed a right-sided pleural effusion (figure 1).

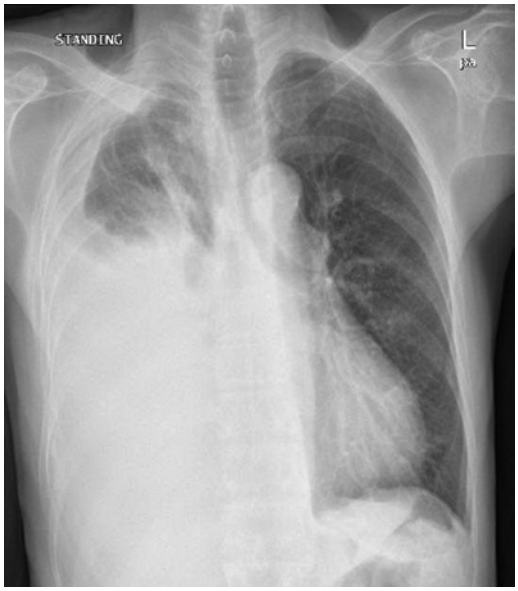

Figure 1 *Chest radiograph depicting right-sided pleural effusion.*

Task 1
What is the most likely diagnosis?

a) Community-acquired pneumonia (CAP)
b) Malignancy
c) Tuberculosis (TB)
d) Pulmonary embolism

Cite as: Yousaf Z, Jamshaid MB, Khan D, *et al*. Fade to black! *Breathe* 2020; 16: 200221.

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Black pleural effusion is a rare entity and may be a diagnostic dilemma. This interactive case discusses the various steps involved to reach the diagnosis. https://bit.ly/3dFJPTS

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Answer 1
b.

The most likely diagnosis is malignant pleural effusion due to significant smoking history and prior history of malignancy. CAP and pulmonary TB are differentials. The patient received intravenous antibiotics for possible CAP.

Task 2
What is the most appropriate investigation to undertake next?

a) Thoracentesis
b) Order a computed tomography (CT) scan
c) Perform bronchoscopy
d) Quantiferon Gold for TB

Answer 2
a.

A diagnostic thoracentesis is needed to establish appropriate diagnosis. Under ultrasound guidance, a diagnostic and therapeutic thoracentesis yielded 1200mL of fluid. Shortness of breath and tachypnoea improved post-procedure.

The fluid analysis results showed straw-coloured lymphocytic, exudative effusion, a negative Gram stain, and malignant cells, consistent with malignant pleural effusion (table 1). The pleural fluid analysis was not suggestive of complicated parapneumonic effusion or empyema.

On day 2 of admission, the patient developed worsening shortness of breath and desaturation. A follow-up examination revealed tracheal deviation to the left side, with decreased vocal fremitus and reduced breath sounds on the right side.

Task 3
What is expected on a repeat chest radiograph?

a) Reaccumulating pleural effusion
b) New consolidation
c) Lung collapse
d) Pneumothorax

Table 1 *Pleural fluid analysis*

	Day 1 (at admission)	Day 16 (immediately post-thoracoscopy)
Colour	Straw-coloured	Black
Appearance	Turbid	Black
pH	7.46	7.29
Glucose mmol·L^{-1}	4.5	
Protein g·L^{-1}	40.2	
Serum protein g·L^{-1}	71	
Albumin g·L^{-1}	20.6	
LDH U·L^{-1}	358	980
Serum LDH U·L^{-1}	271	
WBC cells·µL^{-1}	328	1125
Neutrophils %	3	87
Lymphocytes %	93	7
Monocytes %	4	6
RBC cells·µL^{-1}	613	15375
Gram stain	Negative	Gram-negative bacilli
Culture	Negative	*Pseudomonas aeruginosa* and *Klebsiella pneumoniae*
Fungal culture	Negative	Negative
TB PCR, smear, and culture	Negative	Not done
Cytology	Abnormal large cohesive cells with nuclear polymorphism and vacuolated cytoplasm suspicious of malignant infiltration	Malignant cells present
Special characteristics	Abundant mesothelial cells present	Prominent RBCs[#]
Effusion characterisation	Lymphocytic, exudative, malignant effusion	Empyema in a malignant effusion

LDH: lactate dehydrogenase; WBC: white blood cell; RBC: red blood cell; [#]: RBC content declined successively over the following days.

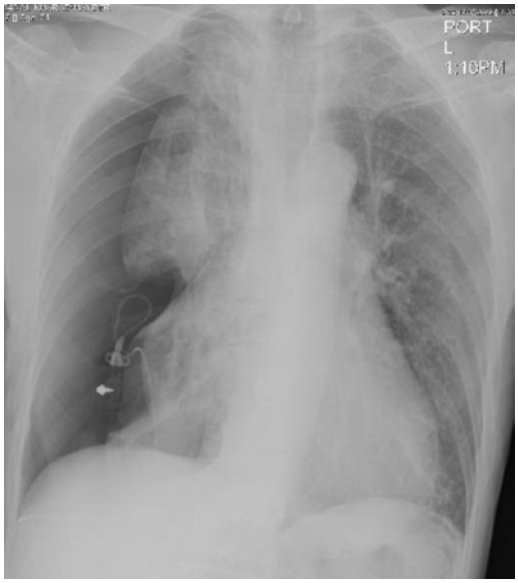

Figure 2 *Chest radiograph depicting right-sided pneumothorax.*

Answer 3
d.

A repeat chest radiograph revealed iatrogenic pneumothorax on the side of the pleural effusion (figure 2).

Task 4
What should be the next step in the management of the patient?

a) Oxygen supplementation and observation
b) Needle aspiration
c) Chest tube insertion
d) High-flow nasal oxygen

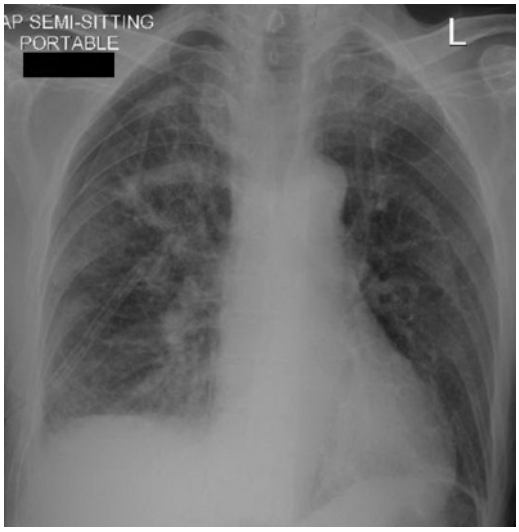

Figure 3 *Chest radiograph showing a right-sided chest tube and partial lung re-expansion.*

Answer 4
c.

The patient has a >2 cm iatrogenic pneumothorax and is symptomatic. Hence a chest tube was inserted and connected to the underwater seal (figure 3).

The patient's shortness of breath progressed despite chest tube insertion. The chest tube was functioning appropriately, as evidenced by swinging fluid levels and bubbling. CT of the chest was performed (figure 4).

Task 5
Can you identify the finding on the chest CT image (figure 4)?

a) Pneumothorax
b) Apical bleb
c) Sub-pleural nodules
d) All of the above

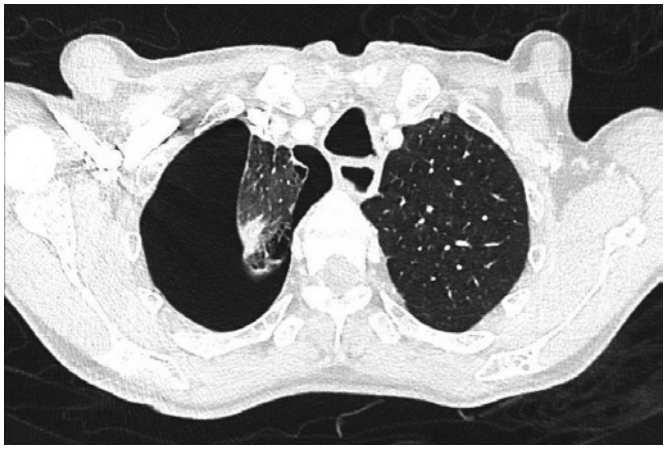

Figure 4 *Chest CT.*

Answer 5
d.

The right lung shows a sizeable pneumothorax, apical subpleural blebs and subpleural nodules. Other cuts of CT revealed multiple spiculated nodules throughout both lung fields.

Task 6
Considering the persistent air-leak, what is the most appropriate next step in management?

a) Perform bronchoscopy
b) Pleurodesis
c) Thoracoscopy
d) Bilateral chest tube insertion

Answer 6
c.

The patient underwent right-sided video-assisted thoracoscopy. There was an upper lobe scar with surrounding nodules and continuous air leak. The thoracic surgery team performed an upper lobe wedge resection to fix the air leak and inserted a chest tube connected to an underwater seal. The colour of the fluid draining from the chest tube noted immediately post chest tube insertion was black (figure 5).

Task 7
What is the most common cause of this finding?

a) Crack cocaine use
b) Malignancy
c) Fungal infection
d) Pancreatic pseudocyst rupture with pancreaticoplural fistula

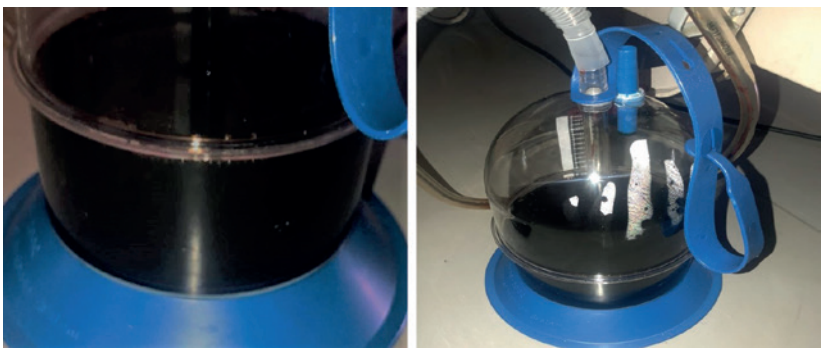

Figure 5 *Black-coloured pleural fluid draining from the chest tube.*

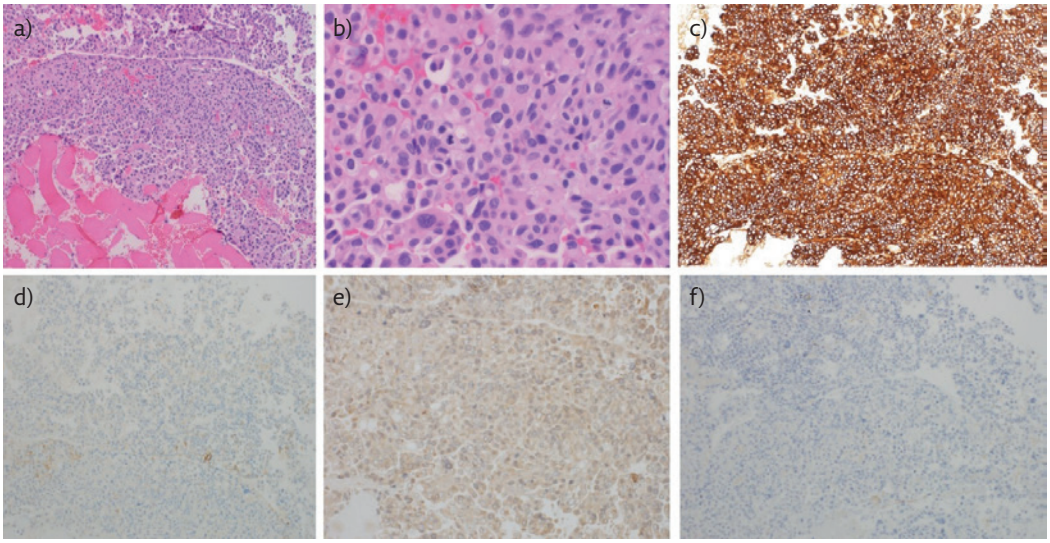

Figure 6 *Histopathology slides. a) Poorly differentiated tumour arranged in solid sheets (haematoxylin and eosin stain, magnification x100). b) Highly pleomorphic tumour cells with brisk mitotic activity (haematoxylin and eosin stain x400). c) Immunoreactive for CK-7 (immunohistochemistry x100). d) Negative for CK-20 (immunohistochemistry x100). e) Negative for TTF-1 (immunohistochemistry x200). f) Negative for napsin-A (immunohistochemistry x100).*

Answer 7

b.

The most common cause of the black pleural effusion is malignancy. The pleural fluid analysis was consistent with empyema secondary to *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* (table 1). Multiple invasive procedures, including a thoracocentesis and chest tube insertion performed before thoracoscopy on a frail, elderly patient with underlying malignancy, could have led to an iatrogenic empyema. Pyomelanin is a brown/black extracellular pigment produced by *Pseudomonas*; however, it does not cause black discolouration of body fluids.

The patient also had neutrophilic leukocytosis, a raised C-reative protein (324 mg·L^{-1}), and high procalcitonin (38.2 ng·mL^{-1}). He received piperacillin/tazobactam with a working diagnosis of empyema. Over the next 8 weeks, 8 L of pleural fluid was drained. Although the pleural fluid haematocrit was not measured, there was no drop in haemoglobin with massive fluid removal. Moreover, the fluid was free-flowing without any clots. The persisting dark colour of the fluid despite a decrease in RBC content over time without a haemoglobin drop indicates the absence of haemodynamically significant bleeding. The possibility of the black colour being secondary to haemolysis cannot be excluded entirely; however, the fact that the fluid colour turned to black immediately post-thoracoscopy without an initial red colour, which is more typical of a haemothorax, makes acute bleeding less likely as a cause. The other possibility is of bilothorax, which is usually reported secondary to a pancreaticopleural fistula. The absence of ascites and right-sided effusion makes that less likely.

Reported causes of black pleural fluid associated with malignancy are either due to pigment production by malignant cells (*e.g.* melanoma) or haemolysis. The black pleural effusion associated with most adenocarcinoma cases has been attributed to haemolysis. The authors believe that the absence of black colour from the initial pleural fluid sample, and then the appearance of this colour post-thoracoscopy, may be suggestive of the colour being attributed to the surgical intervention. However, to the best of our knowledge, such an association is not reported in the literature.

The surgical pathology report from the wedge resection showed infiltration of the lung by poorly differentiated malignant cells forming solid sheets. The tumour cells were pleomorphic with abundant eosinophilic cytoplasm, along with frequent mitotic

Table 2 *Tumour markers*

Tumour marker	Normal range	Value in patient
CEA µg·L^{-1}	5.5–6.5 (smoker) 3.8–5 (nonsmoker)	6
CA19–9 Units·mL^{-1}	0–27	256
AFP IU·L^{-1}	0–6	4

Table 3 *Previously reported cases of black pleural effusion*

Author [ref.] (year)	Diagnosis
Chhabra *et al*. [6] (2015)	Metastatic melanoma
Mohan *et al*. [7] (2010)	Metastatic melanoma
Patel *et al*. [8] (2017)	Metastatic melanoma
Mishe'el *et al*. [9] (2016)	Metastatic melanoma
Sumalani *et al*. [10] (2019)	Metastatic melanoma
Liao *et al*. [11] (2010)	Metastatic melanoma
Guo *et al*. [12] (2017)	Rupture of pancreatic pseudocyst with pancreaticopleural fistula
Ishigaki *et al*. [13] (2019)	Rupture of pancreatic pseudocyst with pancreaticopleural fistula
Kaur *et al*. [14] (2014)	Pancreatic pseudocyst with pancreaticopleural fistula
Huang *et al*. [15] (2013)	Pancreatic pseudocyst with pancreaticopleural fistula
Koide *et al*. [16] (2012)	Pancreatic pseudocyst with pancreaticopleural fistula
Mookherjee *et al*. [17] (2014)	Pancreatic pseudocyst with Pancreaticopleural fistula
Lai *et al*. [18] (2006)	*Rhizopus oryzae* empyema thoracis
Metzger *et al*. [19] (1984)	*Aspergillus niger* empyema
Koff *et al*. [20] (2020)	*Aspergillus niger* empyema
Jayakrishnan *et al*. [21] (2015)	Adenocarcinoma of pulmonary origin
Thampy *et al*. [22] (2016)	Adenocarcinoma of pulmonary origin
Fernandes *et al*. [23] (2018)	Adenocarcinoma of pulmonary origin
Rojas-Solano *et al*. [24] (2008)	Nonsmall cell carcinoma of the lung
Singh *et al*. [25] (1995) (two cases)	Crack cocaine
Mitra *et al*. [26] (2018)	Mediastinal cystic teratoma
Jacob *et al*. [27] (2014)	Rheumatoid pleurisy
Justiniani *et al*. [28] (1985)	Bronchopulmonary fistula
Hirsh *et al*. [29] (2018)	Boerhaave hydropneumothorax

figures and atypical forms. Immunohistochemistry was negative for P-40 and P-63, which are the markers for SCC. This immunoreactivity excluded the possibility of recurrence of the rectal SCC. The tumour cells' reactivity for epithelial-specific antigen (MOC-31) and BER-EP4 confirmed the epithelial origin of the tumour. Based on negative lung adenocarcinoma markers, thyroid transcription factor 1 (TTF-1) and napsin-A, a lung primary was less likely. TTF-1 immunoreactivity is highly sensitive and specific in determining pulmonary *versus* extrapulmonary origin of adenocarcinoma [1]. In extrapulmonary adenocarcinomas (except thyroid) is so low (1%) that the negativity for TTF-1 may be interpreted as definitive evidence that the tumour is a primary from an extrapulmonary source. The cells were immunopositive for cytokeratin (CK)-7 expression and immunonegative for CK-20 expression (figure 6). A definitive conclusion on the origin of the tumour based entirely on the immunostaining is challenging due to the lack of additional markers of pancreatic and hepatobiliary origin.

CT of the chest, abdomen and pelvis with contrast showed a dilated common bile duct measuring 16 mm with associated dilated intrahepatic biliary radicals. CK-7 positivity and CK-20 negativity in biliary tract carcinomas are associated with intrahepatic bile duct carcinomas. Tumour markers showed normal alpha-fetoprotein (AFP) and carcinoembryonic antigen (CEA), but a raised carbohydrate antigen 19-9 (CA19-9) (table 2). The serum alkaline phosphatase, total bilirubin and aspartate aminotransferase were also elevated. The patient's age, sex, tumour marker profile, immunohistochemical profile, liver function profile, and imaging data fit the possibility of metastasis from a hepatobiliary origin, likely intrahepatic bile duct carcinoma [2–5].

A multidisciplinary team meeting between the primary team, pulmonology, cardiothoracic surgery, oncology, onco-radiology and histopathology was conducted. The general condition of the patient made him unfit for further malignancy workup or chemotherapy. He received palliative care from thereon. He later passed away due to the progression of the disease.

Discussion

The aetiologies of pleural effusion are varied and range from infection to malignancy and

autoimmunity to drugs of abuse [6, 7]. Analysis of pleural fluid is essential to the diagnosis of underlying aetiology. The pleural fluid colour may vary from clear or straw-coloured to blood-tinged or frankly bloody [8]. It is incredibly unusual to have black coloured pleural effusion. The authors reviewed the literature on Medline, PubMed, Embase and Google scholar. Key terms used were ("black" and (("pleura" or pleural")) and "effusion"). The search duration was from 1950 to June 26, 2020. The search identified 25 reported cases of black pleural effusion (table 3).

There are 11 reported cases of black pleural fluid secondary to malignancy. What makes this case unique is the immunostaining being negative for lung markers and melanoma. Hence, it is the first reported black pleural effusion case thought to be secondary to hepatobiliary malignancy.

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Conflict of interest

None declared.

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