Rare disease

An older patient with bilateral non-traumatic haemothoraces

Fatema Photowala,¹ Umur Sevkett Hatipoglu,² Carlos Garcia³¹Section of Pulmonary, Critical Care, Sleep and Allergy, University of Illinois at Chicago, Chicago, Illinois, USA;²Respiratory Institute, Cleveland Clinic, Cleveland, Ohio, USA;³Pathology Department, Mercy Hospital and Medical Center, Chicago, Illinois, USA**Correspondence to** Dr Umur Sevkett Hatipoglu, hatipou@ccf.org**Summary**

This is the case of a patient who presented with bilateral spontaneous haemothoraces. Video-assisted thoracoscopic surgery was performed bilaterally to evacuate the haemothorax and perform biopsies. The patient was diagnosed with bilateral malignant epithelioid hemangioendothelioma of the pleura and pericardium. To our knowledge, this is the first description of bilateral malignant epithelioid hemangioendothelioma of the pleura presenting with haemothoraces and without obvious pulmonary involvement. Malignant epithelioid hemangioendothelioma is a rare form of malignancy that can present with unilateral or bilateral haemothoraces.

BACKGROUND

To our knowledge, this is the first case of bilateral spontaneous haemothoraces due to malignant pleural epithelioid hemangioendothelioma without distinct pulmonary involvement. We also posit that whenever bilateral effusions are present and haemothorax is documented on one side, diagnostic thoracentesis is recommended to determine aetiology on the contralateral side.

CASE PRESENTATION

An older patient was transferred to our medical intensive care unit from an outside hospital for evaluation of hypoxemia, bilateral pleuritic chest pain and left leg swelling for 3 weeks. The patient reported his chest pain as sudden onset, associated with shortness of breath and pain on deep inspiration but not associated with fever, chills or cough. Evaluation at the outside hospital consisted of normal laboratory values, negative cardiac enzymes and a CT chest, which showed presence of small to moderate bilateral pleural effusions. The patient's medical and surgical history were not contributory. There was no history of known asbestos or radiation exposure.

On physical examination, the patient was in respiratory distress with a respiratory rate of 30/min, heart rate of 110/min and oxygen saturation of 90% on 2 litres of oxygen. Auscultation revealed normal alveolar breath sounds with decreased air entry to both lungs. Percussion note was dull halfway up the bases bilaterally. The remainder of the physical examination was unremarkable.

CT of chest/abdomen and pelvis showed bilateral large pleural effusions with lower lobe atelectasis. Chest x-ray (figure 1) and CT chest (figure 2) are shown below. There was no evidence of pulmonary embolism or abdominal aortic aneurysm. The initial haemoglobin and haematocrit were 10.9 g/dl and 30%, respectively.

A right-sided thoracentesis yielded 900 ml of bloody fluid. Pleural fluid analysis yielded haematocrit of 14% concurrently with peripheral blood haematocrit of 25.8%, consistent with a haemothorax. Chemistry studies were canceled once haemothorax was confirmed. AFB, fungal,

bacterial and viral cultures in pleural fluid were all negative. Pleural fluid cytology revealed few clusters of atypical cells. A subsequent left-sided thoracentesis was performed retrieving 40 ml of bloody fluid. Pleural fluid analysis revealed a haematocrit of 20.9%. The patient was referred to thoracic surgery for therapeutic drainage and diagnostic sampling of the pleura. During bilateral thoracotomy, the parietal and visceral pleura were observed to be studded with tumour and large amount of blood was seen in both pleural cavities.

INVESTIGATIONS**Histopathology**

Tissue sections showed a malignant proliferation of epithelioid and spindle cells in a solid pattern with areas of necrosis and acute inflammation with associated congestion and haemorrhage. The process was localised to the pleura bilaterally and pericardium. The lungs were spared.

Figure 1 Chest x-ray: bilateral large pleural effusions.

Pleural biopsy findings are shown in figure 3. The tumour cells displayed significant mitotic activity, prominent nucleoli and mild cytological atypia. Acid-fast bacilli, Grocott's methenamine silver and periodic acid-schiff stains were negative for mycobacteria, fungi, including pneumocystis. Immunohistochemical stains showed positive reactivity of tumour cells with antibodies to cytokeratins AE1/3 and CAM 5.2 (epithelial markers) (figure 4) and CD31 (vascular marker) (figure 5). Tumour cells were negative for calretinin, cytokeratin-5/6, cytokeratin-7, cytokeratin-20, CD30, CD117 and CD34 (figure 6).

Diagnosis

Bilateral malignant epithelioid hemangioendothelioma of the pleura.

Figure 2 CT chest with contrast – massive bilateral pleural effusions with lower lobe atelectasis. The exam was negative for pulmonary embolism.

DISCUSSION

Haemothorax is diagnosed when pleural fluid haematocrit is equal to or greater than 50% of the peripheral blood haematocrit. Most common causes of haemothorax are penetrating or non-penetrating chest trauma. Iatrogenic injuries during placement of central venous catheters in the subclavian or internal jugular veins and thoracentesis comprise a significant proportion of traumatic haemothoraces.

Non-traumatic spontaneous haemothoraces occur infrequently. The most common aetiologies are spontaneous haemopneumothorax, conditions associated with coagulopathy (acquired or congenital), vascular causes (eg, Osler-Weber-Rendu disease, ruptured thoracic aorta), malignant pleural disease (eg, vascular tumours, germ cell tumours, lung cancer and mesothelioma) and other infrequent aetiologies such as catamenial haemothorax, extramedullary haematopoiesis and pulmonary sequestration. Spontaneous bilateral haemothoraces are exceedingly rare. In a recent review, only nine cases were identified over the last 50 years.¹ Spontaneous bilateral haemothorax has been reported in association with pulmonary angiosarcoma, subclavian artery aneurysm, endometriosis, iatrogenic coagulopathy and of idiopathic aetiology.

Epithelioid hemangioendotheliomas (EHE) are uncommon tumours, with intermediate characteristics between haemangioma and angiosarcoma. Features of epithelioid or histiocytoid endothelial cell proliferation are typical. Dail and Leibow² were the first to publish a case series of 20 patients with EHE who presented with bilateral nodular lesions in the lungs. The entity was described as an intravascular bronchioloalveolar tumour (IVBAT). In 1982, Weiss and Enzinger³ reported 41 patients with soft tissue tumours whose histology was similar to IVBAT. Kitaichi *et al*⁴ reported 21 patients with pulmonary EHE in 1998. Similar to Dail and Leibow's series, most patients presented with pulmonary nodules and presence of pleural effusion conferred a worse prognosis. The tumour arose at any site – soft tissue, solid organs and serous membranes. Lung and liver were the most commonly affected organs. Symptoms associated with EHE were non-specific such as cough, dyspnoea, pleuritic chest pain and haemoptysis.

Figure 3 Pleural biopsy. Left: malignant proliferation of epithelioid and spindle cells in a solid pattern with areas of necrosis and acute inflammation with associated congestion and haemorrhage. Right: the tumour cells displayed significant mitotic activity, prominent nucleoli and mild cytological atypia.

Figure 4 Immunohistochemical stains performed showed positive reactivity of tumour cells for epithelial marker with cytokeratin – Cam 5.2.

Figure 5 Immunohistochemical stains were positive for CD-31 in tumour cells, an endothelial marker.

Evidence of the tumour's vascular origin is corroborated by the presence of Weibel-Palade bodies (organelles specific to endothelial cells) and immunoreactivity for Factor VIII-related antigen in the cell cytoplasm. Immunohistochemical stains are usually positive for vascular endothelial markers (eg, CD31, CD34) and negative for epithelial markers (eg, cytokeratin). In our patient, the immunohistochemical staining was positive for cytokeratin antibodies (AE1/AE3 and CAM 5.2) and CD31 and negative for CD34. The lesion corresponds to the epithelioid sarcoma-like variant of hemangioendothelioma (due to the lack of reactivity with CD34).

Figure 6 Immunohistochemical stains were positive for CD-34 in blood vessels but not in tumour cells.

Pleural EHE manifests with pleural effusion, pleural thickening, pleural tumour or a combination of these. Recently, Márquez-Medina *et al* reviewed 22 cases of pleural fluid hemangioendothelioma published in the literature.⁵ Most cases presented with pleural effusion which was serosanguineous in nature. Only two of these cases presented with haemothorax. A case of bilateral haemothorax due to epithelioid hemangioendothelioma was recently reported in abstract form however, concomitant pulmonary involvement was also present.⁶

Prognosis of pleural hemangioendothelioma is poor with mean survival of 10–12 months. Due to the rarity of the disease, treatment has not been standardised. In the case series by Kitaichi *et al*,⁴ five patients received chemotherapy with mitomycin C, 5-fluorouracil, cyclophosphamide, vincristine and tegafur with no beneficial effect. Pinet *et al*⁷ reported a case of a patient with bilateral pleural EHE extending to the peritoneum who responded to treatment with six courses of carboplatinum and etoposide. Antiangiogenic therapy such as bevacizumab has not been successful.⁵ Surgical therapy involves pleural stripping and de-cortication, however, our patient was too ill to undergo this morbid operation.

To the best of our knowledge, bilateral spontaneous haemothoraces as a manifestation of pleural epithelioid hemangioendothelioma has not been reported in the literature. Our patient had rapid onset of symptoms and thoracentesis revealed bilateral haemothoraces. Thoracotomy revealed extensive tumour involvement of the parietal pleura and the pericardium. His hospital course was complicated with respiratory failure which necessitated tracheostomy for prolonged mechanical ventilation. His condition was not deemed optimal for chemotherapy. Five months after discharge to a long-term care facility, the patient succumbed to pneumonia and gastrointestinal bleeding.

Learning points

- ▶ Spontaneous non-traumatic haemothoraces are uncommon therefore it is essential to rule out traumatic and iatrogenic causes.
- ▶ Whenever bilateral effusions are present and haemothorax is documented on one side, diagnostic thoracentesis is recommended to determine aetiology on the contralateral side.
- ▶ Malignant epithelioid hemangioendothelioma is a rare form of malignancy that can present with bilateral haemothoraces.

Acknowledgements The authors would like to thank Dr Carol Farver from the Department of Anatomic Pathology at the Cleveland Clinic for insightful critique of the manuscript.

Competing interests None.

Patient consent Not obtained.

REFERENCES

1. **Ali HA**, Lippmann M, Mundathaje U, *et al.* Spontaneous hemothorax: a comprehensive review. *Chest* 2008;**134**:1056–65.
2. **Dail DH**, Liebow AA, Gmelich JT, *et al.* Intravascular, bronchiolar, and alveolar tumor of the lung (IVBAT). An analysis of twenty cases of a peculiar sclerosing endothelial tumor. *Cancer* 1983;**51**:452–64.
3. **Weiss SW**, Enzinger FM. Epithelioid hemangioendothelioma: a vascular tumor often mistaken for a carcinoma. *Cancer* 1982;**50**:970–81.
4. **Kitaichi M**, Nagai S, Nishimura K, *et al.* Pulmonary epithelioid haemangioendothelioma in 21 patients, including three with partial spontaneous regression. *Eur Respir J* 1998;**12**:89–96.
5. **Márquez-Medina D**, Samamé-Pérezvargas JC, Tuset-DerAbraín N, *et al.* Pleural epithelioid hemangioendothelioma in an elderly patient. A case report and review of the literature. *Lung Cancer* 2011;**73**:116–9.
6. **Ali HA**, Lippmann M, Khaleeq G. Spontaneous hemothorax secondary to epithelioid hemangioendothelioma. *Chest* 2008;**134**:c61001.
7. **Pinet C**, Magnan A, Garbe L, *et al.* Aggressive form of pleural epithelioid haemangioendothelioma: complete response after chemotherapy. *Eur Respir J* 1999;**14**:237–8.

This pdf has been created automatically from the final edited text and images.

Copyright 2012 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Photowala F, Hatipoglu US, Garcia C. An older patient with bilateral non-traumatic haemothoraces. *BMJ Case Reports* 2012; 10.1136/bcr.01.2012.5527, Published XXX

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow

Keep up to date with all published cases by signing up for an alert (all we need is your email address) <http://casereports.bmj.com/cgi/alerts/etoc>