Fatal pulmonary tumour micro-emboli in a young woman with no history of cancer

Introduction

Pulmonary tumour embolism is a rare condition with an incidence of 2.4–26% in patients with known solid tumours (Jorens et al, 2009). Clinically it is almost indistinguishable from pulmonary thromboemboli, making it difficult to diagnose antemortem (Brock et al, 2002).

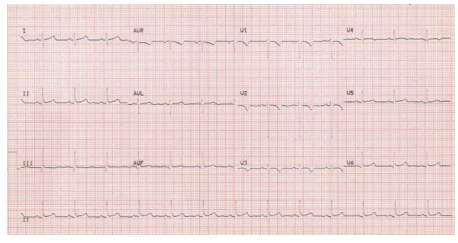
Discussion

Floating cancer cells and their clusters can lead to micro-emboli that trigger an endothelial reaction, intimal proliferation and fibrosis, resulting in occlusion of small arterioles and capillaries of lungs (Nakamura et al, 2004). Neoplastic cells are also known to trigger the coagulation cascade causing an occlusion consisting of a mixture of thrombus and tumour cells (Bassiri et al, 1997). Progressive occlusion of pulmonary microcirculation leads to increased vascular resistance, pulmonary hypertension and right ventricular dysfunction (Chan et al, 1987). The risk of tumour emboli appears to be higher with mucin-secreting adenocarcinomas and tumours of liver and kidney (Roberts et al, 2003).

Dyspnoea is the most common symptom of pulmonary tumour emboli – this can be sudden in cases of large tumour emboli, and subacute and progressive in patients with microvascular disease (Masoud et al, 2017). Accurate diagnostic investigations are limited. Computed tomography pulmonary angiogram may show filling defects in major blood vessels and, in addition, may also reveal the primary tumour or metastases (Lammi et al, 2010). Ventilation–perfusion mismatch on ventilation–perfusion scan with no filling defect on computed tomography angiography may suggest the presence of micro-emboli in the pulmonary circulation. Echocardiogram can help in assessing right heart function and pulmonary artery pressures, and can also reveal an 'embolus in transit', albeit very rarely. Sampling of blood, by pulmonary artery catheterization and lung biopsy, may confirm the presence of malignant cells (Jorens et al, 2009).

Anticoagulation with low molecular weight heparin is the standard practice; thrombolysis and clot retrieval can be considered for large tumour emboli causing a haemodynamic collapse. Treatment options for extensive micro-embolic disease are very limited. Surgical resection of the primary

Figure 1. 12-lead electrocardiogram showing normal sinus rhythm with deep S waves in lead I, Q waves and flattening of T waves in lead III and T-wave inversion in precordial leads V1–V4 in keeping with right ventricular strain.



CASE REPORT

A 25-year-old woman was admitted to the acute medical unit with breathlessness. Seven months previously, as a primigravida she had given birth to a healthy baby via caesarean section, following which she developed bilateral pulmonary emboli. She was initially treated with warfarin. However, 2 months later, she developed a left lower limb deep vein thrombosis and was switched to dalteparin. She had no other known medical conditions.

On presentation, she had normal vital signs with a resting oxygen saturation of 99% on room air, dropping to 83% on walking 20 yards. Physical examination was unremarkable. Blood results showed mild normocytic anaemia, normal renal and liver function tests, and normal cardiac troponin T level. D-dimer was raised at 6.5 mcg/litre (normal range <0.5 mcg/litre). Electrocardiogram revealed sinus rhythm, deep S waves in lead I, Q waves and flattening of T waves in lead III and T-wave inversion in leads V1–V4, suggestive of right ventricular strain (*Figure 1*). Chest X-ray was normal.

Computed tomography pulmonary angiogram showed dilatation of the pulmonary trunk and right ventricle but no pulmonary emboli (*Figure 2*). Transthoracic echocardiogram showed a dilated akinetic right ventricle with raised estimated pulmonary arterial systolic pressure (45 mmHg). Thrombophilia screen was negative.

She was started on higher dose enoxaparin (1 mg/kg, subcutaneous twice daily) and supplementary inhaled oxygen. Two days later, she developed severe breathlessness and hypoxia. Arterial blood gas analysis confirmed type I respiratory failure. Repeat computed tomography pulmonary angiogram showed a small filling defect in the right sub-segmental pulmonary artery, but the enlargement of central pulmonary arteries and the right ventricle was disproportionate to the clot burden. Within the next 24 hours, her condition worsened rapidly with hypoxia and hypotension. She was thrombolysed with intravenous alteplase but went into cardiopulmonary arrest, from which she could not be revived despite prolonged resuscitation.

Post-mortem histological examination of lung tissue (*Figure 3*) demonstrated extensive embolization of small pulmonary arterioles with tumour cells arising from a low-grade adenocarcinoma of the uterus.

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Figure 2. Computed tomography pulmonary angiogram showing **(a)** significant dilatation of the main pulmonary trunk (arrow) with no visible filling defects and **(b)** dilatation of the right ventricle (arrow).

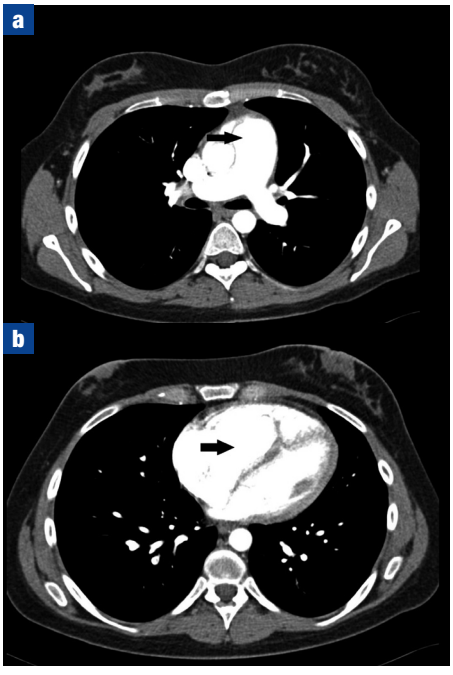
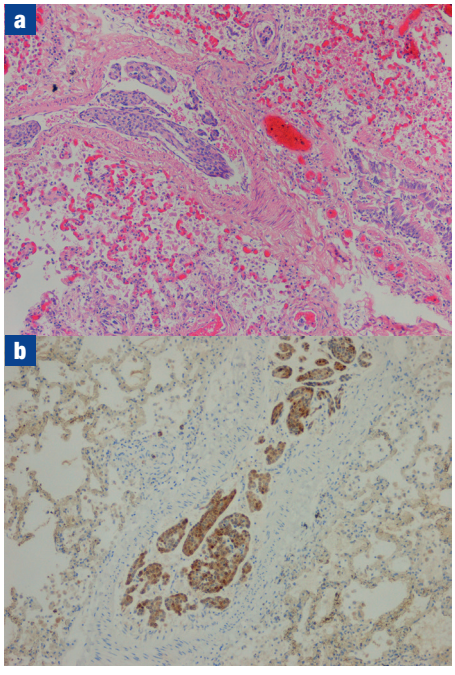


Figure 3. **a.** Haematoxylin and eosin staining (20x), showing a blood vessel containing tumour embolus. **b.** P16 immunohistochemistry staining confirms tumour cells within the vessel lumen.



LEARNING POINTS

- Pulmonary embolism can rarely be caused by migration of non-thrombotic material.
- Pulmonary tumour micro-emboli can lead to progressive dyspnoea with no filling defects on computed tomography angiography.
- Progressive pulmonary hypertension on echocardiography, negative computed tomography pulmonary angiogram and mismatched perfusion defects on ventilation–perfusion scan may point towards micro-embolic disease.
- Prognosis is usually poor although targeted chemotherapy may offer some benefit.

tumour and targeted chemotherapy may reduce the risk of further embolism in patients with some cancers (Sperling et al, 2002). Prognosis is generally poor and symptom management with supportive measures is the mainstay of treatment. **BJHM**

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