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Case report

Pulmonary embolism developing after therapeutic drainage of malignant pleural effusions

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ABSTRACT

We reported three cases of pulmonary embolism which presented acutely and was confirmed shortly after therapeutic drainage of malignant pleural effusion. The temporal association may suggest that massive pleural effusion can be a risk factor for pulmonary embolism arising from venous thrombosis of lower limbs in patients with malignancies. This association can be related to the intra-thoracic pressure changes related to therapeutic pleural drainage. In case patient developed paradoxical dysnoea and hypoxemia after drainage of malignant pleural effusion, alternate cause such as pulmonary embolism should be considered.

1. Introduction

Pleural effusion and pulmonary embolism are common causes of dyspnoea in patients with thoracic malignancies. With drainage of malignant pleural effusions, symptomatic relief and reduction in oxygen requirement is usually expected. Paradoxical worsening of dyspnoea and hypoxemia without evidence of re-expansion pulmonary oedema, however, could suggest the presence of underlying pulmonary embolism. It would be advisable to search for alternate cause for worsening dyspnea and hypoxia after drainage of malignant pleural effusion, including pulmonary embolism.

1.1. Case 1

A 58-year-old lady had Stage IV adenocarcinoma of lung with bone, brain, skin metastases. The epidermal growth factor receptor (*EGFR*) mutation test detected L858R mutation in exon 21 She was treated with Gefitinib for 14 months. With clinical disease progression, her anticancer treatment was switched to systemic chemotherapy with Pemetrexed-Carboplatin doublet for 4 cycles but the disease further progressed together with progressive accumulation of right pleural effusion. The patient opted not for further chemotherapy. She was later admitted for dyspnoea due to massive right pleural effusion. An intercostal drain (ICD) was inserted. There was initial improvement of dyspnoea and reduction in oxygen requirement after drainage of effusion, but she developed acute worsening of hypoxemia on day four of ICD insertion. The chest radiograph (CXR) showed that the amount of pleural effusion has significantly decreased. A computer tomography (CT) of the thorax with contrast revealed intraluminal filling defects at lobar arteries of left upper lobe, lingula and left lower lobe; there was also evidence of further disease progression with intrapulmonary metastases. Low molecular weight heparin (LMWH) was started for the pulmonary embolism. She was stabilized after commencement of LMWH and was eventually weaned off oxygen supplementation. However, she succumbed 5 weeks afterwards with further progression of lung cancer.

1.2. Case 2

A 72-year-old lady had Stage IV adenocarcinoma of lung with right-sided malignant pleural effusion, left adrenal and multiple bone metastases. The *EGFR* mutation L858R in exon 21 was found. She had right-sided trapped lung and an indwelling pleural catheter (IPC) was inserted for symptomatic palliation. Several litres of pleural fluid was drained with suction bottles via the IPC. She developed worsening of dyspnoea 2 days after IPC insertion. CXR showed that IPC was in-situ and right pleural effusion had much reduced in amount with trapped lung. A CT scan of thorax with contrast showed filling defects in the apico-posterior segmental artery and inferior segmental artery of left upper lobe, and lateral basal segmental artery of left lower lobe. She was started on LMWH and was then switched to warfarin for maintenance. Gefitinib was also started. Her condition improved and she was discharged 2 weeks later. Her lung cancer remained in partial response to Gefitinib for the subsequent 11 months.

1.3. Case 3

A 69-year-old lady has stage IV non-small cell lung cancer with

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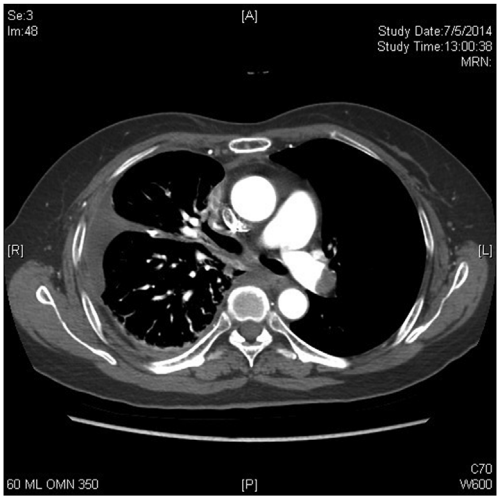

Fig. 1. Computer tomography of the thorax with contrast showing filling defect is seen at left main pulmonary artery, with subtotal occlusion.

right-sided malignant pleural effusion. Exon 19 deletion was detected in the EGFR mutation test of her pleural fluid sample. She was started on Gefitinib as first-line treatment for 15 months but the disease progressed afterwards with re-accumulation of right pleural effusion. She had an IPC inserted for draining the right pleural effusion. One liter of pleural fluid was drained and the catheter was capped. She did not require oxygen supplementation initially but complained of acute dyspnoea four hours after IPC insertion. CXR showed slight reduction in right pleural effusion with IPC *in situ*. She deteriorated rapidly in subsequent hours and she required high flow oxygen supplementation. CT angiogram showed filling defects at the left main pulmonary artery, with subtotal occlusion extending to segmental and subsegmental arteries as well as the right lower lobe pulmonary artery (Fig. 1). She was started on LMWH. Thrombolytic therapy was not considered as she had undergone a recent invasive procedure IPC insertion. She improved gradually and oxygen supplementation was stopped. She was discharged one week afterwards. Her lung cancer progressed several months afterwards despite second-line anti-cancer treatment with Afatinib and she succumbed with advanced stage lung cancer eight months after the episode of pulmonary embolism.

2. Discussion

We herein reported three cases highlighting the temporal association of pulmonary embolism leading to paradoxical hypoxemia after therapeutic drainage of malignant pleural effusion. Venous thromboembolism (VTE) is common, which affects 13% of patients with newly diagnosed lung cancer undergoing imaging screening in a recent Chinese study [1]. Advanced age, pneumonectomy, disseminated disease, radiotherapy and smoking were found to be predictors of VTE in a retrospective Korean study including Asian subjects with lung cancer [2]. Malignancy is associated with pro-thrombotic states, as a result of alterations in the inflammatory and haemostatic cascades [3]. In addition to hypercoagulability, patients with malignancies are often limited in mobility as a result of cachexia, muscle atrophy, disease involvement of nervous system or side effects of medications, causing peripheral venous stasis. Of note, exertional dyspnoea subsequent to massive pleural effusion will lead to further impairment in mobility, and will give further predisposition to VTE complications. On the other hand, dyspnoea and worsening in gas exchange in massive pleural effusion has been attributed to the pressure effect on lung compression, expansion of rib cage and compression of diaphragm making it at mechanical disadvantage [4]. Large amount of pleural effusion was also reported to be associated with diastolic right atrial or ventricular collapse similar to the effects of cardiac tamponade, which should be reversible after therapeutic drainage [5,6]. The pressure effect from pleural effusion could impede venous return, atrial and ventricular filing and therefore venous stasis [5]. Hence, the presence of massive pleural effusion could add to the risk of venous clot formation in the lower limbs, which may be dislodged upon relief of increased intrathoracic pressure with therapeutic pleural drainage and improvement of venous blood flow towards the heart. Therefore, pulmonary embolism should be considered and CT angiogram be arranged timely in patients with paradoxical deterioration in hypoxemia after drainage of pleural effusion, in particular if CXR does not suggest other causes such as re-expansion pulmonary oedema.

To summarize, large amount of pleural effusion can be a risk factor for venous thrombosis in patients with malignancies. We have observed a temporal association between therapeutic pleural drainage and the development of pulmonary embolism in our series, and the underlying mechanisms including haemodynamic changes would require further research effort. Whether patients are more vulnerable to having venous clot dislodgement and pulmonary embolism subsequent to pleural drainage and intra-thoracic pressure changes requires further investigations. High index of suspicion for the presence of deep vein thrombosis in patients with both malignancy and sizable pleural effusion is warranted, in order to allow timely diagnosis of such treatable complications. Physicians should look for alternate cause for worsening dyspnea and hypoxia after drainage of malignant pleural effusion, such as pulmonary embolism.

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Conflicts of interest

I declare on behalf of my co-authors and myself that we do not (delete as needed) have any conflict of interest to declare.

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