A 75-year-old Han Chinese man presented with a 1-day history of acute shortness of breath. His medical history included lung adenocarcinoma, hepatitis B virus (carrier), hypertension, previous deep vein thrombosis (DVT), smoking for 45 years, and drinking for 35 years. He underwent dissection of his right upper and middle lobes and mediastinal lymph nodes 5 years previously and developed pleural and multiple pulmonary metastasis 3 months postoperatively. Molecular tests for epidermal growth factor receptor, KRAS, and anaplastic lymphoma kinase rearrangement were negative. He received 33 cycles of chemotherapy and 2 sessions of radiotherapy for lung metastases. However, he still developed bilateral lung metastases and multiple thoracic and lumbar vertebral metastases. Six weeks before the current presentation, he received nivolumab (3 mg/kg every 2 weeks, three cycles).

Physical examination revealed 92% oxygen saturation on room air, clubbed fingers, rales in the right lower lung, a higher second sound in the pulmonary than aortic area, and symmetrical edema of the lower limbs. Laboratory tests demonstrated a D-dimer level of 18.9 mg/L (normal, <0.24 mg/L), brain natriuretic protein level of 343 pg/ml (normal, <100 pg/ml), and cardiac troponin I level of 0.113 ng/ml (normal, <0.03 ng/ml). Platelet aggregation tests showed an increased adenosine diphosphate level of 75.36% (normal, 42–68%), Col level of 77.1% (normal, 56–75%), and Ris level of 85.9% (normal, 58–76%). Arterial blood gas analysis showed a pH of 7.405, PaCO₂ of 37.3 mmHg (1 mmHg = 0.133 kPa), and PaO₂ of 75.8 mmHg while breathing 5 L/min of oxygen by nasal cannula. Computed tomography pulmonary angiography (CTPA) showed pulmonary artery emboli at multiple left segments and right anterior basal segments [Figure 1]. Doppler ultrasound showed right popliteal vein thrombosis and left lower-limb calf vein thrombosis. Echocardiography showed an enlarged right atrium and right ventricle, and the systolic pulmonary artery pressure was 63 mmHg. Intravenous infusion of 50 mg of recombinant tissue plasminogen activator (rt-PA) followed by low-molecular-weight heparin was administered. The patient's dyspnea was significantly improved 8 h after treatment.

From days 5–7, the patient developed increasingly worsening respiratory distress. Repeat CTPA [Figure 1] on day 7 showed extensive bilateral infiltration and ground-glass attenuations, the pulmonary artery thrombosis had been significantly absorbed. Laboratory tests demonstrated a white blood cell count of 12,500/ml with 89.1% neutrophils and 3.2% lymphocytes, and a C-reactive protein level of 303.8 mg/L (normal, <3 mg/L), and lactate dehydrogenase level of 306 U/L (normal, 100–240 U/L). Piperacillin/sulbactam was initiated on day 8. Sputum smears and culture revealed no microorganisms. Cytomegalovirus DNA and Epstein–Barr virus DNA in the blood were negative, and the procalcitonin level was <0.25 ng/ml. The patient was diagnosed with acute respiratory distress syndrome (ARDS) secondary to nivolumab treatment (Grade 4). Intravenous...
reported two patients who received nivolumab. Both patients received glucocorticoids, other immunosuppressants. Nishino et al. reported nivolumab-induced Grade 4 pneumonitis in a patient with melanoma. The patient continued to worsen for 3 days after mPSL pulse therapy, and cyclophosphamide with repeat mPSL pulse therapy resolved her condition.[4] Our patient had multiple risk factors for venous thromboembolism (VTE), including end-stage lung cancer, metastasis, hypertension, old age, increased platelet aggregation, and previous DVT. A recent large cohort study in Europe showed that people with lung cancer had a 3.92% overall incidence of VTE, and independent factors associated with VTE were metastatic disease, the adenocarcinoma subtype, chemotherapy, and diagnosis via emergency hospital admission.[5] Therefore, the acute pulmonary embolism probably resulted from the primary disease (lung cancer with widespread metastasis); whether it can be an adverse effect of nivolumab requires further observation.

In summary, we have described a patient who developed late-onset Grade 4 pneumonitis after nivolumab treatment accompanied by acute pulmonary embolism; rt-PA, high-dose corticosteroid therapy, and intravenous immunoglobulin therapy were lifesaving. The association between VTE and PD-1 inhibitors requires further investigation.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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