

Case Report

Two case reports of cancer with acute pulmonary embolism in young adults

Zi-Kai Song, Hai-Di Wu, Hong-Yan Cao, Ming-Long Tang, Shuo Yang, Ling Qin

Department of Cardiology, The First Hospital of Jilin University, Changchun, China

Received May 9, 2018; Accepted December 8, 2018; Epub April 15, 2019; Published April 30, 2019

Abstract: Pulmonary embolism (PE) is the second leading cause of death in cancer patients. Despite publication of major consensus guidelines laying out recommendations for diagnosis and treatment of PE in cancer, PE remains misdiagnosed or undiagnosed due to its diverse clinical manifestations, a paucity of literature, and low morbidity in young adults. In order to improve recognition of PE in younger individuals with malignance and bridge the gulf between guidelines and clinical practice, reported here are two young men with PE and cancer. Case 1 had a history of right femoral osteosarcoma resection and presented at the hospital with gradually worsening dyspnea and cough over a 2-week period. Although there was no abnormality at the surgical site, and no obstacle to movement, his clinical symptoms, hypoxemia, and high D-dimer level prompted our attention to the recurrence of cancer and occurrence of PE. Nuclear magnetic resonance imaging and computed tomography pulmonary angiography (CTPA) confirmed both the cancer and PE. He accepted anti-coagulant therapy immediately. Thirty days later, the patient had no obvious discomfort and received anti-tumor therapy. Case 2 presented with syncope at home without any other clinical manifestations. Similarly, hypoxemia, high D-dimer level, and a dilated and hypokinetic right ventricle upon transthoracic echocardiography strongly indicated PE, with CTPA confirming the diagnosis. Testicular cancer and a metastatic tumor were also found by ultrasonography and abdominal enhanced CT. Unfortunately, during anti-coagulation therapy, massive PE occurred and the patient died. Thus, although the incidence of cancer among young adults is lower, it is not rare. Clinicians should be alert to presentations of dyspnea, chest pain, syncope, hypoxemia, and high D-dimer level in younger individuals in order to reduce the misdiagnosis of PE.

Keywords: Pulmonary embolism, young individual, cancer, venous thromboembolism

Introduction

Pulmonary embolism (PE) is one of the manifestations of VTE, which is now the third most common cardiovascular disease with an overall annual incidence of 100-200 per 100,000 inhabitants [1]. Epidemiology of PE is difficult to characterize as PE may be asymptomatic, detected only as an incidental finding, or remain undiagnosed over a person's life. Similarly, the prevalence of PE with cancer among young people is poorly documented. Current guidelines provide little information regarding the diagnostic workup for PE in young adults with cancer.

Patients with cancer are six times more likely to develop venous thromboembolism (VTE) than their counterparts without cancer, and account for more than 20% of all newly diagnosed cases of VTE [2]. Cancer is associated

with thrombin and fibrin formation, directly through the release of pro-coagulants by neoplastic cells, and triggering the release of cytokines and production of factor X-activating cysteine, proteases, mucinous glycoproteins, and circulating tissue factor-bearing microparticles, which lead to the activation of platelets, leukocytes, and endothelial cells, resulting in hypercoagulability [3].

Here, two cases are presented of young people with cancer and PE, suffering from osteosarcoma and testis cancer, respectively. One of the patients died of acute massive PE.

Case 1

A 16-year-old male was admitted to the hospital due to a gradually worsening cough and dyspnea over the course of 2 weeks. At the age of

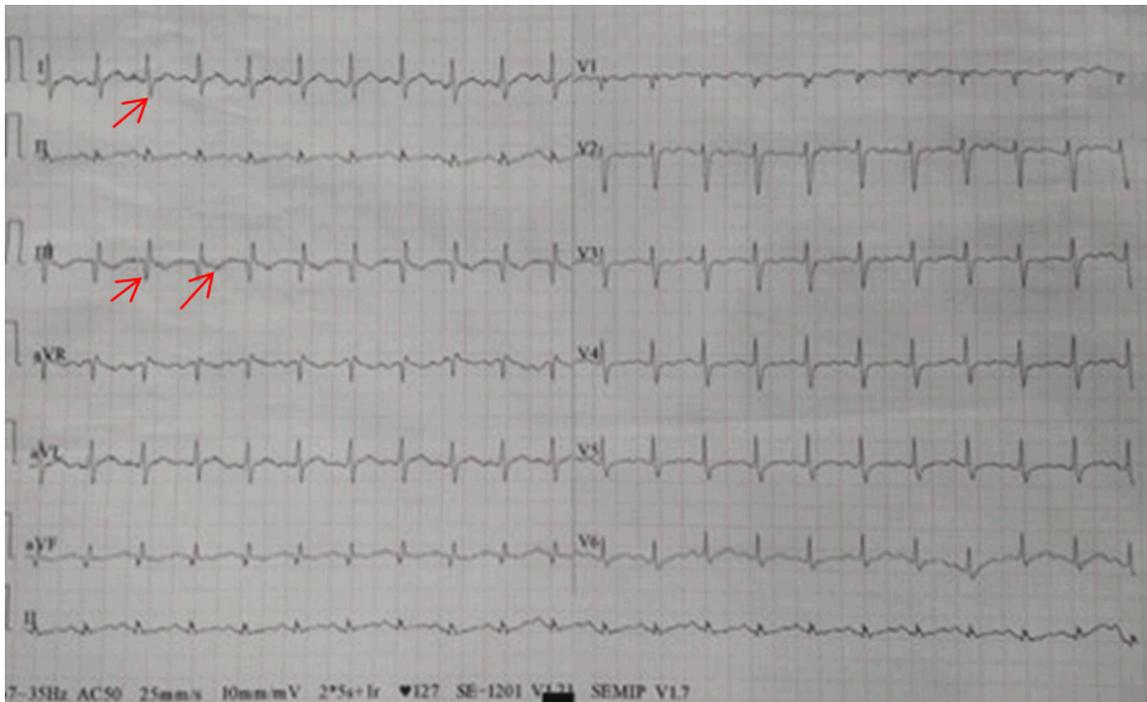


Figure 1. Case 1 electrocardiogram showing sinus tachycardia with $S_1Q_3T_3$.

14, right femoral osteosarcoma was diagnosed and resected. Upon arrival at the hospital, the patient had a blood pressure of 103/63 mmHg, a heart rate of 90 beats/min, and a respiratory rate of 22 breaths/minute. The cardiovascular and respiratory physical examinations were unremarkable. There was surgical scar visible in the middle of the right femur, but no other abnormalities. Complete blood cell count (CBC), electrolytes, liver function tests, and renal function tests were unremarkable. Cardiac troponin-T and N-terminal pro-brain natriuretic peptide (NT-proBNP) levels were also normal. However, the D-dimer level was >20 $\mu\text{g/ml}$ (reference, 0.001-0.50 $\mu\text{g/ml}$), serum alkaline phosphatase concentration was 612 U/L (reference, 45-125 U/L), arterial blood gas analysis indicated PaCO_2 was 28.8 mmHg (reference, 35.0-45.0 mmHg), and PaO_2 was 77.4 mmHg (reference, 80-100 mmHg). Electrocardiogram (ECG) showed sinus tachycardia with $S_1Q_3T_3$ (**Figure 1**). A chest radiograph and trans-thoracic, echocardiography, and lower extremity venous compression ultrasound results were normal. Magnetic resonance imaging (MRI) T2 weighted imaging indicated an uneven high signal indicative of suspected osteosarcoma recurrence. A 161 \times 119 mm inhomogeneous

mass was found between the liver and kidneys and a 104 \times 36 mm hypoechoic mass was detected in the inferior vena cava near the right atrium entrance utilizing abdominal ultrasonography (**Figure 2**), which was considered metastatic cancer.

Due to the patient's history of femoral osteosarcoma, combined with clinical presentation, hypoxemia, high D-dimer level, and MRI and ultrasonography results, femoral osteosarcoma with PE was suspected. In order to confirm this diagnosis, computed tomography pulmonary angiography (CTPA) was performed, showing intraluminal filling defects in the lower lobe of the left and right pulmonary arteries (**Figure 3**). PE risk stratification was then conducted and ascertained the simplified PE severity index (sPESI) to determine the appropriate treatment strategy. The patient's initial stratification was "not high-risk" and his sPESI score was 0. Therefore, the patient was immediately prescribed anti-coagulant therapy with low molecular weight heparin for one week. Following discharge, the patient was unable to adhere to the low molecular weight heparin, but 20 mg oral rivaroxaban once daily was managed. Thirty days later, the patient had no

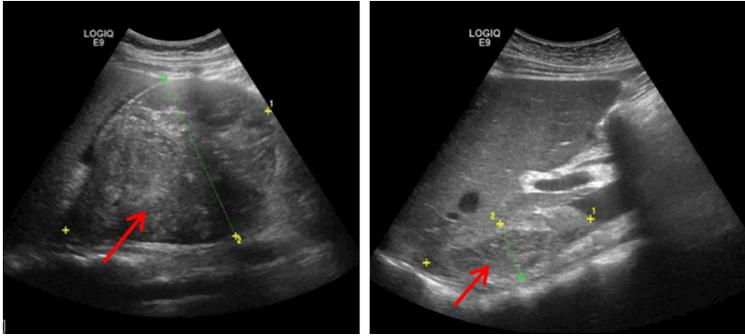


Figure 2. Case 1 had a 161 × 119 mm mixed mass of inhomogeneous interior echoes between the liver and kidney and a 104 × 36 mm hypoechoic mass detected in the inferior vena cava near the right atrium entrance utilizing abdominal ultrasonography.

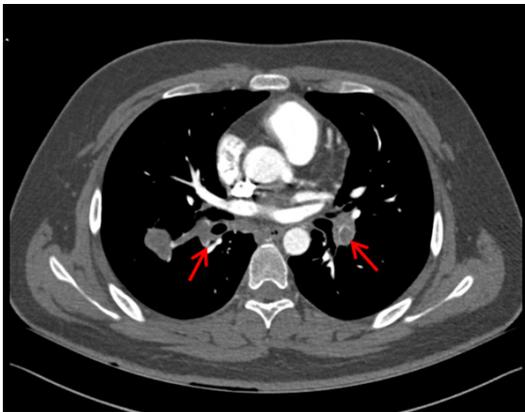


Figure 3. Case 1 had intraluminal filling defects present in the lower lobe of the left and right pulmonary arteries by computerized tomography pulmonary angiography.

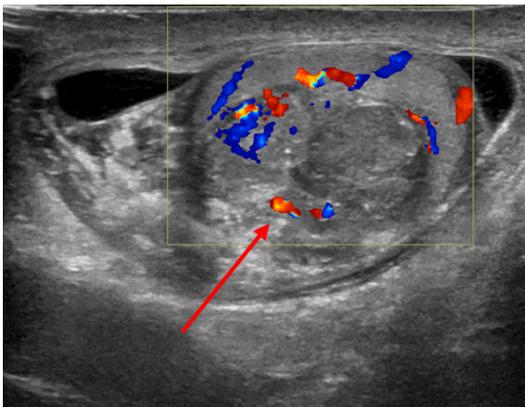


Figure 4. A 22 × 21 mm solid mass of irregular shape was found in the right testis by ultrasonography in Case 2.

obvious discomfort and received anti-tumor therapy.

Case 2

A 21-year-old male presented with a syncopal attack at home. Upon admission, the patient had a blood pressure of 118/70 mmHg, a heart rate of 96 beats/min, a respiratory rate of 20 breaths/minute, clear bilateral lungs, and regular cardiac rhythm on auscultation. Abdominal examination was unremarkable. Laboratory tests showed CBC, electrolytes, liver function tests, and renal function tests were not

abnormal. Cardiac troponin-T and NT-proBNP levels were also normal. The D-dimer level was forty times higher than normal (reference, 0.001-0.50 µg/ml), arterial blood gas analysis revealed a PaCO₂ of 29.1 mmHg (reference, 35.0-45.0 mmHg) and a PaO₂ of 58 mmHg (reference, 80-100 mmHg). Transthoracic echocardiography revealed a dilated and hypokinetic right ventricle combined with pulmonary hypertension, and lower limb venous compression ultrasonography revealed no abnormal findings. However, a 22 × 21 mm solid mass of irregular shape was found in the right testis by ultrasonography (**Figure 4**), which was considered testicular cancer. Abdominal enhanced CT revealed a low-density shadow in the right lobe of the liver, which was considered a metastatic tumor (**Figure 5**). Further, CTPA revealed thromboembolism in the upper, middle, and lower lobes of the right pulmonary artery and left main pulmonary artery (**Figure 6**). PE risk stratification was “not high-risk” and sPESI score was 0. The patient received low molecular weight heparin therapy. Six days later, the patient experienced syncope again accompanied by loss of pulse, requiring advanced cardiopulmonary life support. Cardiopulmonary resuscitation was performed for approximately 20 minutes, however, spontaneous circulation was not achieved and the patient died.

Discussion

PE is a serious life-threatening disease that affects all age groups [4, 5]. Studies commonly focus on adults or the elderly, and reports involving young people are rare. An increasing number of studies have found that PE may precede or coincide with a diagnosis of cancer,

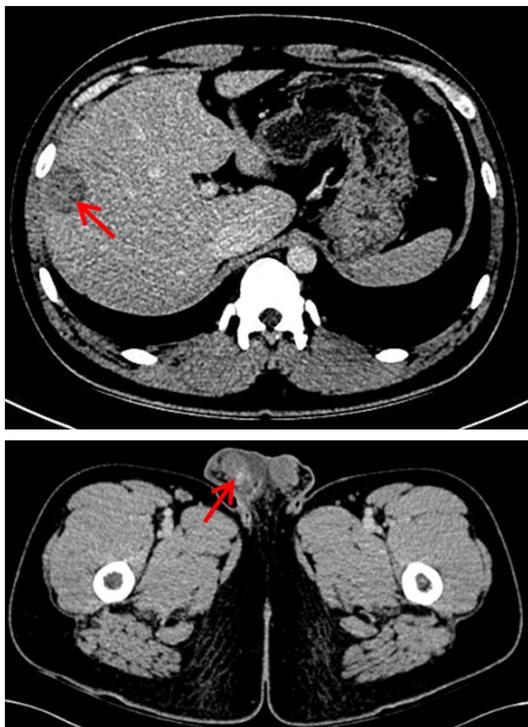


Figure 5. Case 2 abdominal ultrasonography revealed a low-density shadow in the right lobe of the liver, which was considered a metastatic tumor, and a 22 × 21 mm solid mass of irregular shape in the right testis, in which visible blood flow supported a diagnosis of a malignant tumor.

and thromboembolic events frequently complicate the course of malignancy.

Cancer cells exert a pro-thrombotic effect on their microenvironment through direct and indirect mechanisms, which can manifest systemically and present clinically as thrombosis. Dysregulation of the coagulation cascade is common in patients with cancer and has a significant impact on treatment, prognosis, and quality of life [3], and approximately 25% of patients with malignancy require readmission due to VTE recurrence [6].

The occurrence of venous thrombotic events generally requires three basic conditions: vascular endothelial injury, slow blood flow or stasis, and a hypercoagulable state. Although a variety of triggers can induce a hypercoagulable state and coagulation, malignancy is one of the most common. The first patient, Case 1, presented with dyspnea and cough as primary symptoms and had a history of osteosarcoma surgery. The ECG changes in $S_1Q_3T_3$ are commonly present in acute pulmonary artery occlusion, pulmonary artery hypertension, and right

cardiac overload. The patient's subsequent hypoxemia and high D-dimer level significantly enhanced the possibility of PE, and CTPA finally confirmed the diagnosis of PE. Based upon the patient's high serum alkaline phosphatase concentration, abdominal ultrasonography, and MRI, osteosarcoma was determined to be recurrent and the cancer metastasized to the abdominal and inferior vena cava. The second patient, Case 2, was considered healthy, with syncope the only symptom. Syncope is commonly of a neurologic etiology. Therefore, the probability of PE was ignored. However, in a series of studies, patients hospitalized for their first episode of syncope had a high prevalence of PE [7-9]. Transthoracic echocardiography revealed a dilated and hypokinetic right ventricle combined with pulmonary hypertension. Therefore, increased right ventricular diameter is associated with adverse effects in patients with acute, symptomatic, cancer-associated PE.

Based on the American College of Chest Physician guidelines-10 [10] and PE risk stratification, both cases received low molecular heparin as an anti-coagulation therapy. Although the first patient, Case 1, continued to be treated, the second patient, Case 2, died during treatment.

In our experience, young adults with cancer and PE are not rare, but they are not taken seriously. For young individuals who have symptoms such as dyspnea and syncope, the initial assessment generally includes anamnesis, clinical exploration, blood gases, ECG, and specific biomarkers. Transthoracic echocardiography is useful to assess the prognosis. Signs of increased diameter or dysfunction of right ventricular have been related to poor prognosis in cancer patients with PE.

Acknowledgements

We thank all participants for their support and participation.

Disclosure of conflict of interest

None.

Address correspondence to: Ling Qin, Department of Cardiology, The First Hospital of Jilin University, Changchun 130021, China. Tel: +86 15843073203; Fax: +86 0431 84841049; E-mail: 15043022401@163.com

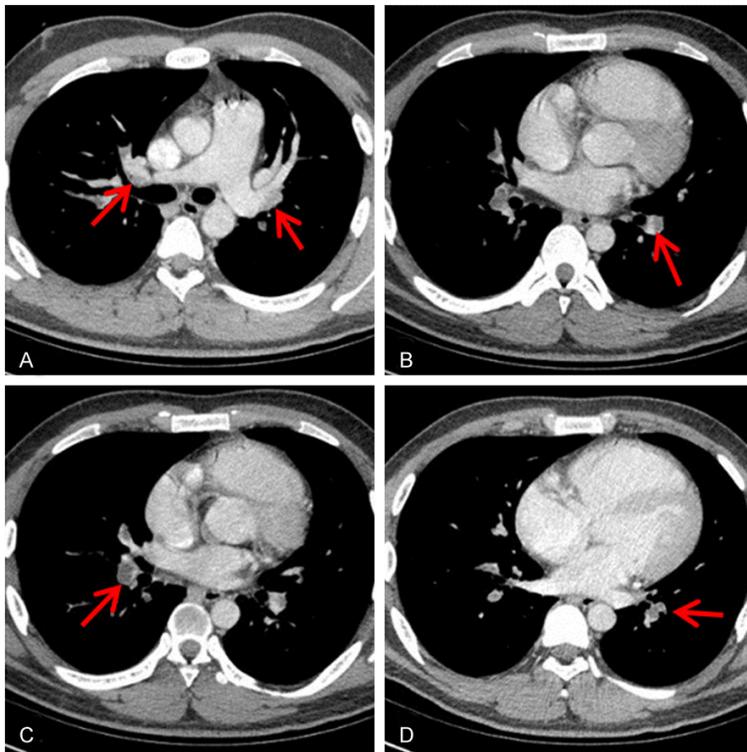


Figure 6. The upper, middle, and lower lobes of the right pulmonary artery and left main pulmonary artery embolism were detected by computerized tomography pulmonary angiography in Case 2.

References

- [1] Konstantinides SV, Torbicki A, Agnelli G, Danchin N, Fitzmaurice D, Galie N, Gibbs JS, Huisman MV, Humbert M, Kucher N, Lang I, Lankeit M, Lekakis J, Maack C, Mayer E, Meneveau N, Perrier A, Pruszczyk P, Rasmussen LH, Schindler TH, Svitil P, Vonk Noordegraaf A, Zamorano JL, Zompatori M; Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC). 2014 ESC guidelines on the diagnosis and management of acute pulmonary embolism. *Eur Heart J* 2014; 35: 3033-3069, 69a-69k.
- [2] Donnellan E, Khorana AA. Cancer and venous thromboembolic disease: a review. *Oncologist* 2017; 22: 199-207.
- [3] Donnellan E, Kevane B, Bird BR, Ainle FN. Cancer and venous thromboembolic disease: from molecular mechanisms to clinical management. *Curr Oncol* 2014; 21: 134-143.
- [4] Barrios D, Morillo R, Guerassimova I, Barbero E, Escobar-Morreale H, Cohen AT, Becattini C, Tapson V, Yusen R, Jimenez D. Sex differences in the characteristics and short-term prognosis of patients presenting with acute symptomatic pulmonary embolism. *PLoS One* 2017; 12: e0187648.
- [5] Jeong WJ, Lee JW, Yoo YH, Ryu S, Cho SW, Song KH, Park SI. Extracorporeal cardiopulmonary resuscitation in bedside echocardiography-diagnosed massive pulmonary embolism. *Am J Emerg Med* 2015; 33: 1545, e1-2.
- [6] Bullano MF, Willey V, Hauch O, Wygant G, Spyropoulos AC, Hoffman L. Longitudinal evaluation of health plan cost per venous thromboembolism or bleed event in patients with a prior venous thromboembolism event during hospitalization. *J Manag Care Pharm* 2005; 11: 663-673.
- [7] Khorana AA, Rubens D, Francis CW. Screening high-risk cancer patients for VTE: a prospective observational study. *Thromb Res* 2014; 134: 1205-1207.
- [8] Prandoni P, Lensing AW, Prins MH, Ciammaichella M, Perlati M, Mumoli N, Bucherini E, Visona A, Bova C, Imberti D, Camprostrini S, Barbar S; PESIT Investigators. Prevalence of pulmonary embolism among patients hospitalized for syncope. *N Engl J Med* 2016; 375: 1524-1531.
- [9] Theilade J, Winkel BG, Holst AG, Tfelt-Hansen J, Svendsen JH, Haunso S. A nationwide, retrospective analysis of symptoms, comorbidities, medical care and autopsy findings in cases of fatal pulmonary embolism in younger patients. *J Thromb Haemost* 2010; 8: 1723-1729.
- [10] Kearon C, Akl EA, Ornelas J, Blaivas A, Jimenez D, Bounameaux H, Huisman M, King CS, Morris TA, Sood N, Stevens SM, Vintch JRE, Wells P, Woller SC, Moores L. Antithrombotic therapy for VTE disease: chest guideline and expert panel report. *Chest* 2016; 149: 315-352.