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Non-cardiogenic acute pulmonary edema in elderly patient with Dressler syndrome associated pulmonary embolism

Hui-Chun YU[1], Xiao-Bing MA[2, 3], Zhen-Qing WANG[1], Hui-Jun XU[1], Ping WANG[1], Feng-Ping AN[1], Yu-Chuan HU[4], Guang-Bin CUI[4], Xu-Fang BAI[5], He LI[2,*]

[1]*Department of Gerontology, Xiqing Hospital, Tianjin, China*
[2]*Cardiovascular Division of Gerontology, Pingjin Hospital, Logistic University of CAPF, Tianjin, China*
[3]*Postgraduate School of Tianjin University of Traditional Chinese Medicine, Tianjin, China*
[4]*Department of Radiology, Tangdu Hospital, the Fourth Military Medical University, Xi'an, Shaanxi, China*
[5]*University of Ottawa Heart Institute, Ottawa, ON, Canada*

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Pulmonary embolism (PE) is a common cardiovascular and cardiopulmonary illness and the incidence increases exponentially with age.[1] Because the clinical signs and symptoms are non-specific, its diagnosis is always difficult.[2] It also may develop a complicating pericardial syndrome resembling that described by Dressler in myocardial infarction, which is far less common,[3] simultaneous PE with pericardial syndromes and non-cardiogenic acute pulmonary edema (NCAPE) was an unusual event.[4] Herein, we reported a rare case of elderly woman with functional limitations associated with knee osteoarthritis for several years, developed progressive exertional dyspnea and exercise intolerance two months, diagnosed NCAPE and Dressler syndrome associated PE.

An 82-year-old female was admitted to the geriatric ward due to gradually worsened exertional dyspnea and exercise intolerance, which progressed gradually from New York Heart Association (NYHA) classes II–III over the course of two months, she was bed bound with knee joints limitation of functional performance due to knee osteoarthritis for three years. She had no history of chronic respiratory disease. On admission, she had a heart rate of 105 bpm and blood pressure of 130/80 mmHg. Body mass index (BMI) was 30. Physical evaluation revealed mild lips, and fingers cyanosis, arterial blood gas on room air showed that the patient was severe hypoxic with a pO2 45 mmHg. The cardiac examination was normal, without distention of the jugular veins. The pulmonary examination was remarkable only for bilaterally diffuse, easily audible, fine inspiratory basal crackles without wheezes. She had no pitting edema in her lower extremities.

Laboratory findings revealed the increase of markers of hemostasis and fibrinolysis and right ventricular dysfunction: D-dimer was 1630.0 μg/L (normal range: 0–500 μg/L), B-type natriuretic peptide (BNP) 388.730 pg/mL (normal range: < 50 pg/mL). There were no elevations of markers of myocardial injury (troponin-T and creatine kinase-MB), and leukocyte count was normal, C-reactive protein (CRP) was 13.73 mg/L (normal range: 0–10 mg/L). ECG on admission showed sinus tachycardia, an S1Q3T3 pattern in the limb leads, and incomplete right bundle branch block in V1 to V3 and T-wave inversions seen in leads V1 to V4 (Figure 1). Transthoracic echocardiography performed and demonstrated that right- sided heart strain, which characterized by enlarged right ventricle (RV) and atria, there was mild tricuspid and pulmonary valve regurgitation, a systolic pulmonary arterial pressure of 65 mmHg and pericardial effusion (Figure 2). Lower extremity venous ultrasound confirmed absence of proximal deep vein thrombosis. Chest CT showed the presence of ground-glass density in bilateral lung field (Figure 3A & B), representing interstitial pulmonary edema, considerable pericardial and bilateral pleural effusion with high attenuation on pre-contrast image (Figure 3C & D), and CT angiography (CTA) showed lower right pulmonary artery widened and low-attenuation filling defects in right lower pulmonary artery (Figure 3E).

We diagnosed that she developed NCAPE and Dressler syndrome secondary to PE, which clinically defined submissive and risk assessment with intermediate-low- risk.[5,6] She was treated with nasal cannula oxygen, warfarin, low molecular weight heparin and intravenous diuretics. The

***Correspondence to:** hli.tianjin@ yahoo.com

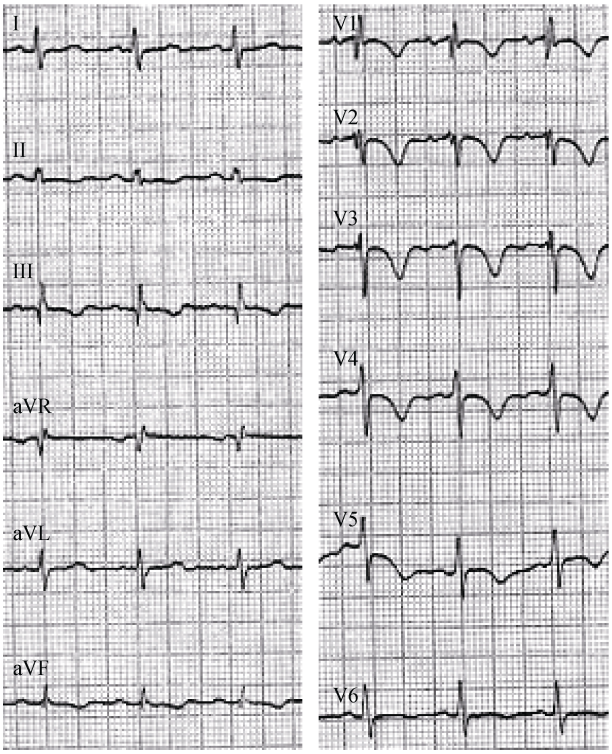

Figure 1. ECG abnormalities obtained at admission. Electrocardiography showed sinus rhythm with a heart rate of 96 beats/min, S1Q3T3 pattern in the limb leads, incomplete right bundle branch block in leads V1–V3, T-waves inversion in V1–V5.

patient remained on the treatment for the next three days. She continued to improve clinically, accompanied by alleviating hypoxia and decreasing alveolar infiltrates. She was discharged after 10 days. After discharge, she discontinued their medication without consulting the physician. A month later, repeat ultrasound examination underwent and showed that both pericardial and pleural fluid did not relieve. She died in her home two months afterwards.

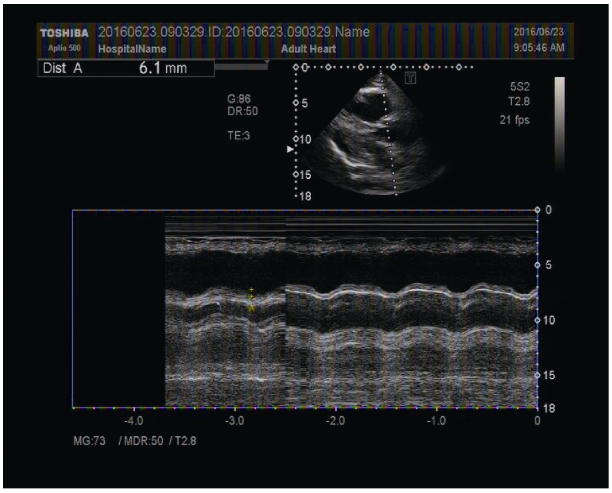

Figure 2. Enlarged image of right ventricle. Small amount of pericardial effusion is observed in front of the right ventricular free wall and below the left ventricular posterior wall.

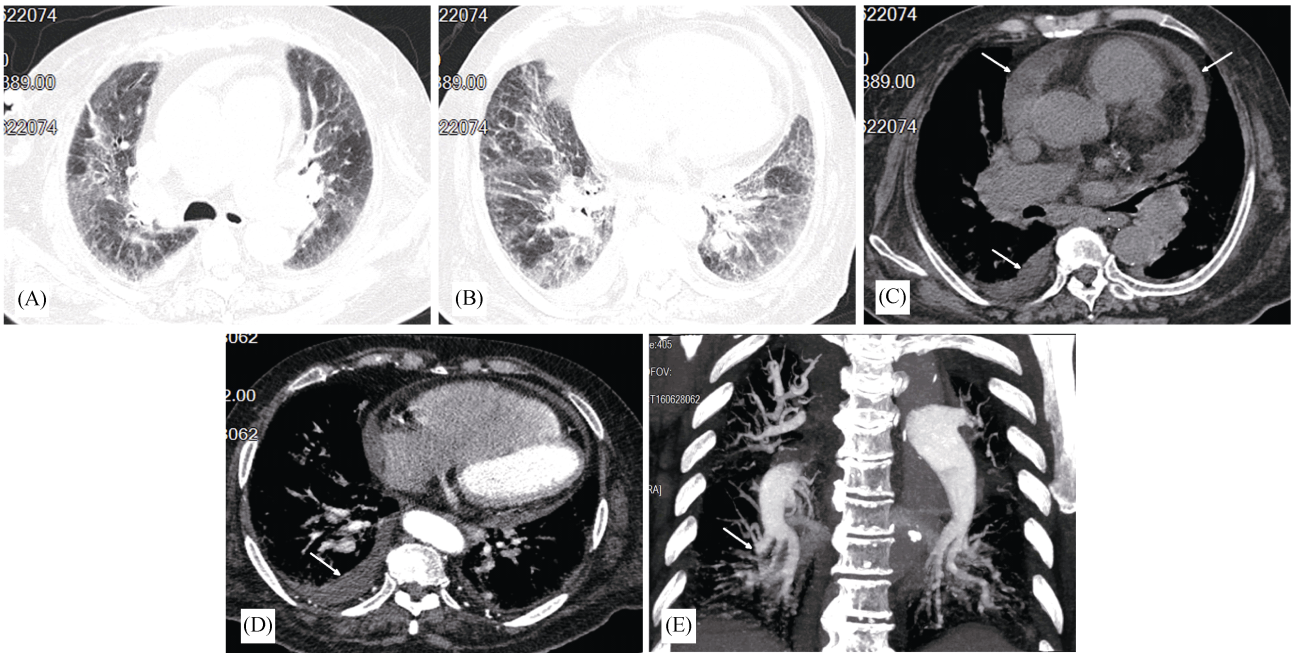

Figure 3. Chest CT and CT angiography in a 82-year-old woman with right lower pulmonary artery embolism. (A&B): Axial CT images shows ground-glass density in bilateral lung field, representing interstitial pulmonary edema; (C&D): axial CT plain scan and contrast enhanced images shows the presence of pericardial and bilateral pleural effusion (arrow); lower right pulmonary artery widened; (E): coronal maximum intensity projection image from pulmonary artery CT angiography scan shows contrast filling defects and an abrupt cutoff at segmental branches of right lower pulmonary artery (arrow).

The present case reported a combination of both NCAPE and Dressler syndrome after PE. Dressler syndrome is described "a post-infarct syndrome", including myocardial infarction (MI) and pulmonary infarction/embolism, which is characterized by pericarditis with or without pericardial effusion, pleuritis and/or pneumonitis with or without pleural effusion, cardiac arrhythmias, fever, leukocytosis, and increased red blood cell sedimentation rate; NCAPE also described in this syndrome after MI and PE.[3,7,8] This syndrome had been found in as many as 3.48% in a series of 402 patients after PE, but those combined with NCAPE was only about 0.9%.[3] Although the pathogenesis of the syndrome is not clear, an immunopathological genesis has been considered.[3,7,8] In this patient, there was no evidence of myocardial injury, even though right ventricle strain and subendocardial ischemia, but mild CRP elevated, which could be considered an inflammatory response associated with immune mechanisms.

NCAPE is a syndrome, which may be resulted from various causes, usually secondary to a more systemic severe medical or surgical pathology that triggers the event. The mechanism of NCAPE remains to clarify, which usually is thought to be due to pre-capillary vasodilatation resulting in excessive pulmonary capillary transudate secondary to pressure effect.[4,9–16] But in PE, hypoxemia as an prominent clinical finding not only is one of diagnostic cretiaria,[5] but actually also paly an important role on pulmonary vascular endothelial permeability, capillary hydrostatic pressure, and alveolar fluid clearance, which promote development of pulmonary edema and alters pulmonary vascular tone and causes pulmonary vasoconstriction. In turn, pulmonary edema further exaggerates alveolar hypoxia as a consequence of alveolar flooding.[17–21]

It is well known that hypoxia as a critical factor contribute to develop pulmonary edema, such as high altitude pulmonary edema, which is a physiological response to hypoxia.[20–23] Our patient developed NCAPE related to PE, had a normal LV function on echocardiography suggested that pulmonary edema was not attributed to left heart failure. Severe hypoxia was one of main clinical findings in the patient, which might be a central role for development of the NCAPE through pathways above mentioned that elevating vascular pressure and an increasing in lung vascular permeability resulting in the accumulation of pulmonary edema. There are clinical reports showing that the simple administration of supplemental oxygen to patients with pulmonary edema may in itself enhance the resolution of alveolar edema.[4,9,10,12,24,25] Studies have shown that hypoxia is related to interstitial pulmonary edema in acute mountain sickness[26,27] and pulmonary edema.[28,29] Additionally, hypoxia increase sympathetic nervous system activity by which may play a role in the induction of NCAPE.[30] Therefore, supplemental oxygen, the most valuable modality of therapeutic interventions, is always required in this condition.

Albeit this patient was improved clinically after the oxygen therapy, but the outcome was poor, which might be attribute to PE-related deaths including recurrent PE. Studies found that RV enlargement on chest CT predicts early death in patients with acute PE.[31,32] Toosi, *et al*.[33] used transthoracic echocardiography to assess risk stratification of patients with PE and found that RV dilation correlated with clinical severity and were significantly associated with in-hospital complications and mortality and these generally represented the best predictors of short-term outcome. PADIS-PE Randomized Clinical Trial showed that prolonged anticoagulation for secondary prophylaxis after a first episode of PE reduced the recurrent venous thrombosis, but benefit was not maintained after discontinuation of anticoagulation therapy.[34] Early discontinued anticoagulation therapy could be catastrophic for our patient.

PE induced hypoxia attribute to NCAPE resulted in the poor outcome of the patient, which should be paid high attention. As there are only few cases of the patients documented, management guidelines are limited and can only advise. Thus, identification of potential risk factors for development of thromboembolic complications and risk stratification in high risk population are required necessarily for effective prevention of venous thromboembolism and optimization of patient care.

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