Usefulness of electrocardiographic changes in accurate and urgent diagnosis of pulmonary embolism due to renal cell carcinoma

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ABSTRACT
Pulmonary embolism (PE) is a clinical entity with a high mortality rate and hence requires accurate, urgent diagnosis and emergency therapy. We report a case of successful treatment of PE in a patient with renal cell carcinoma (RCC) with tumor thrombosis of the renal vein and the inferior vena cava (IVC). PE was diagnosed using electrocardiography (ECG), echocardiography, D-dimer level elevation and contrast-enhanced computed tomography. First, ECG showed a new sinus tachycardia and T wave flattening in the inferior leads (II, III, aVf) in contrast to routine ECG performed previously at a medical health check-up. Second, echocardiography revealed a dilated right ventricle, tricuspid regurgitation, and elevation of systolic pulmonary artery pressure. We emergently inserted a temporary IVC filter at the proximal end of the tumor thrombus under serial echocardiographic evaluation, followed by thrombolytic therapy and anticoagulation therapy. After 3 days, we performed radical nephrectomy and thrombectomy of the IVC. After surgery, the temporary IVC filter was removed, and the anticoagulation therapy was continued. The patient remained symptom free 3 years after surgery. For the diagnosis of PE, it is important to compare the previous ECG obtained on routine medical health check-up and the ECG results at diagnosis. In conclusion, during a medical health check-up in clinical practice, despite its rare occurrence, a life-threatening PE should be ruled out in a patient with risk factors, symptoms, and ECG findings such as tachycardia and ST-T change in the inferior leads and patients with such findings should be urgently referred to a cardiovascular specialist.

Key words pulmonary embolism, renal cell carcinoma, electrocardiographic change, transthoracic echocardiography

Introduction
Pulmonary embolism (PE) is a clinical entity that presents with sudden-onset chest pain and dyspnea. PE must be considered in the differential diagnosis of sudden-onset chest pain and dyspnea. The newly electrocardiography (ECG) findings, transthoracic echocardiography (TTE) findings, D-dimer level elevation, and contrast computed tomography (CT) findings are essential for the diagnosis of PE. Reports on PE due to renal cell carcinoma (RCC) are relatively rare. Furthermore, the diagnostic process and the detailed clinical course of PE due to RCC have been rarely reported. We report a case of successful treatment of a woman with PE due to RCC. We also describe the usefulness of comparing new and previous observations of ECG and TTE in the accurate, emergency diagnosis of PE due to RCC. Furthermore, we describe the key findings of ECG and TTE in detailed diagnostic process of PE. This case showed that electrocardiographic change comparison to previous ECG contribute to diagnose PE urgently and precisely.

Case report
A 59-year-old woman presenting with sudden-onset chest pain and dyspnea at rest was referred to our hospital. She had a history of hypertension. She had no macrohematuria or abdominal pain. Physical examination on admission revealed a blood pressure of 122/96 mmHg, with a heart rate of 115 beats/min. Palpation revealed no abdominal mass. The respiratory rate was 35/min and SpO₂ was 98% on O₂ 5 L/min oxygen therapy (through a face mask). Laboratory findings revealed a hemoglobin concentration of 10.9 g/dL, a serum lactate dehydrogenase (LDH) level of 286 IU/L, and a platelet count of 237 × 10⁹/L; the white blood cell count was 7.39 × 10⁹/L, with neutrophil, lymphocyte, eosinophil counts of 83.7%, 10.8%, and 0.3%, respectively. Arterial blood gas analysis showed a pH 7.42, PaO₂ of 147 mmHg, PaCO₂ of 35.1 mmHg, a bicarbonate level of 23.3 mmol/L, and a −2.6 base excess on supplemental oxygen at O₂ 5 L/min through a face mask. The D-dimer level was elevated to 37.6 μg/mL. ECG was normal on routine medical health check-up. In contrast to the previous ECG during a routine medical health check-up, an ECG showed a new sinus tachycardia and T wave flattening in the inferior leads (II, III, aVf) (Fig. 1). TTE revealed a dilated right ventricle (Fig. 2a-c), tricuspid regurgitation, and elevation of systolic pulmonary artery pressure (Fig. 2c). The tricuspid regurgitation pressure gradient was 32 mmHg (Fig. 2e). The right atrial pressure was estimated to be 15 mmHg; based on an inferior vena cava (IVC) diameter of 21 mm and the absence of...
inspiratory collapse, the systolic artery pressure was estimated to be 47 mmHg. TTE revealed an elevation of right ventricular (RV) systolic pressure, RV enlargement, and a D-shaped configuration of the left ventricular (LV) cavity in the short-axis view (Fig. 2a-c). These findings were consistent with right ventricular dysfunction (RVD). Moreover, contrast enhanced CT revealed filling defects in the main trunk of the right pulmonary artery (Fig. 3a), inferior branch of the left pulmonary artery (Fig. 3a), and the IVC (Fig. 3b). The filling defect in the IVC was localized to 3.5 cm of the upper left renal vein (Fig. 3c). Furthermore, the CT scan revealed a heterogeneous mass in the inferior pole of the left kidney (Fig. 3d). These findings of ECG, TTE, D-dimer test and contrast enhanced CT were strongly consistent with pulmonary embolism (PE) presenting with a left renal tumor. Consequently, she was diagnosed with PE due to RCC. According to the guidelines of the Japanese Circulation Society (JCS) for the treatment of PE\(^1\), we emergently inserted a temporary IVC filter at the proximal end of the tumor thrombus to avoid progression of the pulmonary embolus. Because neither tumor embolism nor thrombotic embolism could be definitively diagnosed, we administered an intravenous bolus of recombinant tissue plasminogen activator (160 × 10⁴ units) and started intravenous heparin infusion, given the possibility of both tumor embolism and thrombotic embolism. Three days after starting anticoagulation therapy, serial TTE evaluation revealed that pulmonary hypertension was not worsening and gradually improved. Moreover, contrast-enhanced CT showed a decrease in embolus size in the right pulmonary artery.
TTE and CT showed a gradual, general improvement of the patient’s condition; therefore, we decided to perform surgical therapy. Radical nephrectomy and IVC tumor thrombus removal were performed. The pathological findings revealed clear cell carcinoma, expansive, G3>G2, solid type, pT3b, infγ, ly(−), v(+). After the surgery, the temporary IVC filter was removed and the anticoagulation therapy was continued. The patient was maintained on weekly interferon administration (300 × 10^4 units). She could walk without oxygen therapy, with no complaint of dyspnea. As her general condition was gradually improving, heparin infusion therapy was switched to oral warfarin therapy. The side-effect of bleeding was not observed. ECG and TTE after therapy showed resolution of tachycardia and pulmonary hypertension, respectively. She was symptom free without recurrence on the 3-year follow-up evaluation.

Discussion

PE requires urgent diagnosis and treatment because of the high mortality. In our patient, we diagnosed PE due to RCC using new ECG findings that were in contrast with previous findings from routine medical check-ups and TTE, D-dimer, and contrast CT findings.

First, in the diagnosis of PE, it is important to compare the previous routine ECG and new ECG findings. Co et al. reported a total of 352 cases known as PE have examined ECG changes in these patients when compared with their previous ECGs; they reported that ECG changes were noted in 75.9% (new T wave inversions, commonly in the inferior leads, 34.4%; new T wave flattening commonly in the inferior leads, 29.5%; a new sinus tachycardia, 27.3%) and no new ECG changes were noted in 24.1% of patients. According to the JCS guidelines, the significance of sinus tachycardia (>100 bpm) was described by adding 1.5 points in Wells score and 1 points in Geneva score, respectively. In our patient, new sinus tachycardia and T wave flattening in the inferior leads (II, III, aVf) were noticeable. These findings are consistent with those of Co et al. and the JCS guidelines.

Comparison of ECG findings is not only important for diagnosis of PE, but also for speculating on its occurrence. Thus, ECG changes are key to diagnosing PE. These previous reports and our case suggest that sinus tachycardia is a strong indicator of possible PE.

Second, the key to diagnosing PE is the TTE finding of RVD. Tongyoo et al. reported that TTE parameters of left ventricular (LV) D-shape (sensitivity 61.1%, specificity 84.6%), loss of left ventricular apical triangle (sensitivity 44.4%, specificity 80%), RV systolic pressure >40 mmHg (sensitivity 77.8%, specificity 60%) and right ventricular end systolic areas: left ventricular end systolic areas (RVESA:LVESA) >0.65 (sensitivity 94.4%, specificity 39.1%) were consistent with right ventricular dysfunction (RVD). In this report, the presence of at least 2 out of 4 findings on echocardiogram correlated with RVD, with the area under the ROC curve at 0.79, with a sensitivity of 77.8% and a specificity of 67.7%. In our case, 2 out of 4 TTE parameters (left ventricular D-shape and RV systolic pressure >40 mmHg) were
present. Thus, our case was consistent with RVD. RVD strongly suggests the presence of PE. The elevation of D-dimer level further supports the diagnosis of PE. However, D-dimer level elevation may also be because of a malignant disease. TTE findings combined with D-dimer level elevation increase the likelihood of PE in malignant disease, such as in our patient.

Moreover, repeated TTE evaluation is useful in evaluating therapeutic efficacy. In our case, serial TTE evaluation was useful in monitoring the degree of pulmonary hypertension after anticoagulation therapy. TTE findings were also essential in deciding on the appropriateness of surgical intervention for RCC.

Thirdly, the major cause of PE is lower limb deep vein thrombus. According to previous reports, approximate 70% of pulmonary emboli occur as a result of lower limb deep vein thrombosis\(^3\)-\(^9\). On the other hand, abdominal lesions, such as RCC, could be the cause of PE. Therefore, abdominal abnormalities, such as RCC, are included in the differential diagnosis of PE in addition to lower limb deep vein thrombosis. Abel et al. reported that PE was identified preoperatively in 35 of 782 patients (4.4%) with RCC\(^10\). However, the incidence of PE due to RCC is relatively rare; identification of RCC as the cause is critical for deciding on the additional surgical therapy along with anticoagulant therapy. PE due to RCC was successfully diagnosed in our patient, and surgical therapy with anticoagulant therapy was performed.

Finally, we discussed the ECG findings of PE associated with RCC in our case. Takada et al. reported that the Operational Results for Electrocardiogram Emergency Reporting System in Ningen Dock and Health Check-ups ensured patient safety and enabled early treatment of emergencies\(^11\). Moreover, Takada et al. reported that among 132,577 subjects assessed between July 2012 and February 2015, 25 were in the urgent report category\(^12\). After a health check-up, 8 subjects were referred to cardiovascular hospitals\(^13\). These subjects underwent PCI, pacemaker implantation, or catheter ablation\(^14\). Although PE patients were not included in this report, Hasegawa et al. stated that patients with underlying factors of heart disease, prolonged bed rest, postoperative rest, thrombophlebitis, or malignant tumors with (i) symptoms of dyspnea, chest pain, tachycardia, or shock, or (ii) ECG findings of ST-T abnormalities such as T-wave inversion with ST elevation in V1-3, ST depression in V4-6, or sinus tachycardia, should be assessed for PE and urgently treated if diagnosed\(^15\). Thus, during a medical health check-up in clinical practice, despite its rare occurrence, a life-threatening PE should be ruled out in a patient with risk factors, symptoms, and ECG findings such as tachycardia and ST-T change in the inferior leads and patients with such findings should be urgently referred to a cardiovascular specialist.

Compliance and ethical standards

Ethical statements: This case study was conducted in compliance with Good Clinical Practices and the ethical principles of the Declaration of Helsinki.

Informed consent: Informed consent was obtained from the patient towards publication.

The authors state that they have no Conflict of Interest (COI).

REFERENCES