Acute Pericarditis Following Acute Pulmonary Thromboembolism

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Summary
We describe the case of a 45-year-old Japanese man who developed acute pericarditis following an acute pulmonary thromboembolism. He had developed shortness of breath 7 days prior to hospitalization and was admitted with severe dyspnea. Echocardiography and laboratory results were compatible with acute pulmonary thromboembolism, which was confirmed by contrast-enhanced chest computed tomography. On the third hospital day, he experienced chest pain exacerbated by inspiration. On the fourth hospital day, his body temperature increased to 39°C and echocardiography revealed circumferential pericardial effusion. A diagnosis of acute pericarditis was made and the patient was treated with colchicine and aspirin. On the fifth hospital day, his symptoms largely subsided. Auscultation revealed pericardial friction rub. Electrocardiography demonstrated diffuse ST-segment elevations. Twenty-four days later, computed tomography revealed the disappearance of both the pericardial effusion and pulmonary arterial emboli. This case was thought to be one of acute pericarditis following acute pulmonary thromboembolism.

Key words: Post-cardiac injury syndrome, Dressler syndrome, Pericardial effusion, Friction rub

Acute pericarditis can be caused by infection, myocardial infarction, malignancy, trauma, and autoimmune diseases. Acute pericarditis due to pericardial injury is termed post-cardiac injury syndrome. Post-cardiac injury syndrome was first described after myocardial infarction by Dressler.1) Pericarditis after the incision of the pericardium is termed post-pericardiotomy syndrome. The development of post-cardiac injury syndrome following pulmonary thromboembolism has been reported in the literature, although it is considered rare,2) especially in Japan. We present a case of acute pericarditis following acute pulmonary thromboembolism.

Case Report
The patient was a 45-year-old Japanese man. He developed shortness of breath 7 days prior to the hospital admission. His symptoms worsened by the day of admission, and he was transported to the emergency department with severe dyspnea. His body temperature was 36.0°C, his heart rate was 87 beats per minute, his blood pressure was 105/62 mmHg, his respiratory rate was 24 breaths per minute, and his pulse oximetry showed 98% oxygen saturation on 5 L/minute oxygen via a non-rebreather mask. The heart sounds were normal, and breath sounds were clear in both lung fields. The abdomen was flat and soft without tenderness. No edema was noted in the extremities.

Electrocardiography revealed sinus tachycardia (rate 136/minute), with an S1Q3T3 pattern and T-wave inversion in the right precordial leads (Figure 1A). Bedside echocardiography revealed a dilated right ventricle. The tricuspid regurgitation pressure gradient (TRPG) was 53 mmHg (Figure 2) and the diameter of the inferior vena cava was 24 mm.

Blood test results were as follows: white blood cell (WBC) count, 6,800 /μL; red blood cell count, 444 × 107 /μL; hemoglobin, 14.3 g/dL; prothrombin time (international normalized ratio), 1.05; activated partial prothrombin time, 42.1 s; D-dimer, 12.6 μ/mL; creatine kinase, 123 IU/L; aspartate aminotransferase, 91 IU/L; alanine aminotransferase, 73 IU/L; lactate dehydrogenase, 321 IU/L; troponin T, negative; low-density lipoprotein cholesterol, 117 mg/dL; creatinine, 1.2 mg/dL; C-reactive protein (CRP), 1.54 mg/dL; brain natriuretic peptide, 152.6 pg/mL; antinuclear antibody, < 40; and rheumatoid factor, < 3.0. Blood test results of the coagulation system were as follows: protein C activity, 95 %; protein S activity, 76%; lupus anticoagulant dilute Russell viper venom time ratio, 1.2; and anti-cardiolipin β2-glycoprotein I complex antibody, < 1.3 U/mL (Table). From these results, no parameter clearly showed coagulation system abnormality. Arterial blood gas analysis on 5 L/minute oxygen inhalation via a non-rebreather mask showed a pH of 7.407, pCO2 of 28.8 mm Hg, and pO2 of 75.5 mm Hg.

Contrast-enhanced chest computed tomography showed multiple filling defects in the bilateral pulmonary arteries and left popliteal vein (Figure 3). A diagnosis of acute pulmonary embolism was made and the patient was hospitalized after intravenous unfractionated heparin was...
commenced. On the second hospital day, 60 mg per day of edoxaban was started. On the third hospital day (11 days after symptoms onset), the patient developed chest pain exacerbated by deep inspiration. The WBC count and CRP level were 9,100/μL and 3.24 mg/dL, respectively. There was no clear pericardial friction rub on auscultation. On the fourth hospital day, his body temperature increased to 39°C and echocardiography revealed circumferential pericardial effusion (Figure 4). TRPG was 40 mmHg and the inferior vena cava diameter was 23 mm, both of which were lower than at the time of admission, and no findings indicating the deterioration of right heart failure were observed. A diagnosis of acute pericarditis was made and the patient was prescribed 1 mg per day of colchicine and 1.5 g per day of aspirin. On the fifth hospital day, his symptoms largely subsided, and auscultation revealed pericardial friction rub. Electrocardiography demonstrated ST-segment elevations in all leads except V1 and aVR (Figure 1B). All virus titers for coxsackie B1, B2, B3, B4, B5, B6 measured on the eighth hospital day were < 4. Eleven days after admission, the pericardial friction rub disappeared. Twenty-four days later, echocardiography revealed the disappearance of the pericardial effusion and electrocardiography showed improved ST deviation (Figure 1C). Computed tomography showed the disappearance of both the pericardial effusion and pulmonary arterial emboli (Figure 5).

This patient had no clinical symptoms or signs suggesting connective tissue diseases, and antinuclear antibody and rheumatoid factor test results were negative. He had no history of cardiac surgery. Myocardial infarction was ruled out by electrocardiography, echocardiography, and cardiac enzyme level results. He was not uremic and had no thyroid disease. Bacterial pericarditis was ruled out during the clinical course, and symptoms resolved without the use of antibiotics. Viral pericarditis could not be ruled out completely, but the time course of pericarditis in the 11 days after the onset of symptoms of acute pulmonary thromboembolism indicated a higher probability of a complication due to acute pulmonary thromboembolism than that of incidental viral pericarditis.

We reviewed the medical records of patients admitted to our hospital with acute pulmonary thromboembolism between 2006 and 2016. Of 172 cases of acute pulmonary thromboembolism, pericarditis developed only in one case (the present case).

Discussion

Post-cardiac injury syndrome occurs following pericardial or myocardial injury. Dressler syndrome occurs following myocardial infarction, and post-pericardiotomy syndrome occurs following cardiac surgery. Although it is believed to be an autoimmune phenomenon, the exact pathogenesis of pericarditis remains unclear. Rarely, in days to weeks after a pulmonary embolism, acute pericarditis may appear with symptoms closely resembling post-myocardial infarction syndrome. There are several case reports of acute pericarditis after acute pulmonary thromboembolism.7,8)

Jerjes-Sanchez et al. described 6 patients who developed acute pericarditis among 195 with pulmonary thromboembolism.9) The authors reported in another study that pericarditis after pulmonary embolism is not unusual, and occurred in 3.48% of cases in a series of 402 cases.9) These reports are from North America, Europe, and the Middle East. The mechanism of acute pericarditis after pulmonary embolism is unclear; however, the mechanism may be the same as that in post-myocardial infarction syndrome, and anatomical vicinity and hypersensitivity may play a role.10) In the present case, the clinical findings were fever, chest pain, pericardial friction rub, and leukocytosis in association with an elevated serum CRP level, and based on the biochemistry data and pericardial effusion, the case resembled Dressler syndrome.

However, pericarditis after acute pulmonary embolism has not been reported in the English literature from an Asian country. Only one Japanese abstract reported in a congress was found relating to this condition.11) In our hospital, only this case of pericarditis was diagnosed among 172 confirmed cases of acute pulmonary thromboembolism. In Japan, the frequency of pericarditis following pulmonary thromboembolism may be low, possibly due to racial differences. Alternatively, the low frequency of pericarditis after acute pulmonary thromboembolism may be due to differences in therapeutic strategy. Early reperfusion by percutaneous coronary intervention is the current standard therapy for acute myocardial infarction.11,12) The incidence of Dressler syndrome after acute myocardial infarction has decreased in the reperfusion era, because of the extensive use of thrombolysis and coronary
The standard treatment of pulmonary thromboembolism is systemic anticoagulation. For massive acute pulmonary thromboembolism, systemic thrombolysis is a therapeutic option; however, the beneficial effect for sub-massive embolism has been reported to be limited because of the higher incidence of major complications. Another therapeutic option is catheter-directed interventions. However, for acute myocardial infarction, primary percutaneous coronary intervention is frequently performed, while catheter interventions are seldom used for acute pulmonary thromboembolism. Catheter intervention was not performed in any of the 172 cases of acute pulmonary thromboembolism. Furthermore, there has been no report of pericarditis after acute pulmonary thromboembolism before the introduction of systemic thrombolysis in Japan. It is unlikely that differences in therapeutic strategy are the cause. Therefore, this difference in frequency is likely due to genetic differences based on patient demographics. A study has shown that serositis is less common in Oriental patients with systemic lupus erythematosus, and pericarditis following acute pulmonary embolism may follow the trend. To confirm this hypothesis, accumulation of reports from other hospitals in Japan is necessary.

Figure 2. Initial two-dimensional transthoracic echocardiogram in the parasternal view (left panel) and short-axis view (right panel) showing right ventricular enlargement. The tricuspid regurgitation pressure gradient was 53 mmHg. No pericardial effusion was observed.
Table. Laboratory Data

| Variable | Value |
|----------|-------|
| WBC      | 6.8 ×10^3/μL |
| RBC      | 444 ×10^9/μL |
| Hb       | 14.3 g/dL |
| Hct      | 44 % |
| Plt      | 16.1 ×10^9/μL |
| PT (INR) | 1.05 |
| APTT     | 42.1 seconds |
| AT III   | 92.6 % |
| FDP      | 43.4 μg/mL |
| D-dimer  | 12.6 μg/mL |
| CRP      | 1.54 mg/dL |
| Na       | 139 mEq/L |
| K        | 3.8 mEq/L |
| Cl       | 107 mEq/L |
| BUN      | 18 mg/dL |
| Cre      | 1.2 mg/dL |
| UA       | 5.2 mg/dL |
| TP       | 6.7 g/dL  |
| T.bil    | 1.3 mg/dL |
| AST      | 91 U/L   |
| ALT      | 73 U/L   |
| ALP      | 261 U/L  |
| LDH      | 321 U/L  |
| γGTP     | 59 U/L   |
| CK       | 123 U/L  |
| IgG      | 1103 mg/dL |
| IgA      | 357 mg/dL |
| IgM      | 119 mg/dL |
| C3       | 148 mg/dL |
| C4       | 33.8 mg/dL |
| ANA      | < 40     |
| RF       | < 3.0    |
| CLβ2GPI  | < 1.3 U/mL |
| LAC/DRVVT| 1.2      |
| ProteinC | 95 %     |
| ProteinS | 76 %     |

WBC indicates white blood cell count; RBC, red blood cell count; Hb, hemoglobin; Hct, hematocrit; Plt, platelet count; PT (INR), prothrombin time (international normalized ratio); APTT, activated partial thromboplastin time; AT III, antithrombin III; FDP, fibrinogen degradation products; CRP, c-reactive protein; BUN, blood urea nitrogen; Cre, creatinine; UA, uric acid; TP, total protein; T. bil, total bilirubin; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; LDH, lactate dehydrogenase; γGTP, γ-glutamyl transpeptidase; CK, creatine kinase; Ig, immunoglobulin; ANA, anti-nuclear antibody; RF, rheumatoid factor; RF, rheumatoid factor; CLβ2GPI, anti cardiolipin β2-glycoprotein I complex antibody; LAC, lupus anti-coagulant; and DRVVT, dilute Russell viper venom time.
Figure 3. Contrast-enhanced chest computed tomogram on admission showing multiple thromboemboli (arrows) in the bilateral pulmonary arteries (A, B), enlargement of the right ventricle with no pericardial effusion (C), and thrombosis (arrowhead) of the left popliteal vein (D).

Figure 4. Transthoracic echocardiogram in the parasternal view (left panel) and apical four-chamber view (right panel) recorded on the fourth day of hospitalization showing circumferential pericardial effusion.
Figure 5. Computed tomogram 24 days later, showing the disappearance of both pericardial effusion and pulmonary arterial emboli.

Disclosures

Conflicts of interest: The authors state that they have no conflict of interest.

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