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Case Report / Olgu Sunumu

A successful thrombolysis with tissue-type plasminogen activator in a case of pulmonary embolism after failed streptokinase therapy

Başarısız streptokinaz tedavisi sonrası pulmoner embolili bir olguda doku tipi plasminojen aktivatör ile başarılı tromboliz

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A 76-year-old male patient diagnosed with acute, massive pulmonary embolism due to deep vein thrombosis of a lower extremity developed significant cardiovascular and respiratory instability. Subsequently, streptokinase infusion was administered over two hours. Spiral computed tomography was performed due to the persistent hemodynamic instability following the thrombolytic therapy. Computed tomography showed persistent massive pulmonary embolism. In the light of literature data, the patient was recommended for surgical pulmonary embolectomy, however he refused surgery. Therefore, he was administered intravenous recombinant tissue type plasminogen activator over two hours. Clinic status of the patient and radiological findings were significantly improved following therapy. The patient was discharged with effective anticoagulant therapy.

Key words: Computed tomography; pulmonary embolism; thrombolytic therapy.

Alt ekstremite derin ven trombozuna bağlı oluşan akut, masif pulmoner emboli tanısı konmuş 76 yaşında erkek hastada ciddi kardiyovasküler ve solunumsal instabilite gelişti. Takiben hastaya iki saat süreyle streptokinaz infüzyonu verildi. Trombolitik tedavi sonrası hemodinamik kararsızlığın devam etmesi üzerine, spiral bilgisayarlı tomografi çekildi. Bilgisayarlı tomografi, masif pulmoner embolinin sebat ettiğini gösterdi. Literatür verileri ışığında hastaya cerrahi pulmoner embolektomi önerildi; ancak hasta cerrahiyi reddetti. Bunun üzerine hastaya iki saat süreyle intravenöz rekombinant doku tipi plazminojen aktivatörü verildi. Tedavi sonrasında hastanın klinik durumu ve radyolojik bulguları belirgin olarak düzeldi. Hasta efektif antikoagülan tedavi ile taburcu edildi.

Anahtar sözcükler: Bilgisayar tomografi; pulmoner emboli; trombolitik tedavi.

Despite many advances in medical science, the mortality rate for acute pulmonary embolism (PE) remains high, The estimated mortality rate is 10-15% within three months of diagnosis.[1] The main therapy in PE is based on risk stratification. High-risk PE therapy includes anticoagulant therapy and thrombolysis. Results from randomized trials have shown that thrombolytic agents rapidly resolve thromboembolic obstruction and have favorable hemodynamic effects. Thrombolytic treatment is strongly recommended in patients with acute PE associated with shock. The use of streptokinase, urokinase and a recombinant tissue-type plasminogen activator (rt-PA) has been approved for this indication.[2,3] The management of patients with acute massive PE who do not respond to fibrinolytic therapy remains unclear. This is partly due to the difficulty of defining "failed" thrombolysis in this setting, unlike cases of myocardial infarction which do not have this problem. The therapeutic options in patients with persistent hemodynamic instability who do not respond to thrombolysis rely on two different strategies comprised of either rescue surgical embolectomy or repeat thrombolysis.[4]

This report presents a successful recurrent thrombolysis with rt-PA in a patient with persistent massive PE after failed thrombolysis with streptokinase. This serves as an alternative treatment option in the event that surgery cannot be performed.

CASE REPORT

A 76-year-old man, who was previously prescribed medications for hypertension and Parkinson's disease,

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presented to the emergency department complaining of severe shortness of breath which had occurred abruptly. The patient was a bit confused and had associated symptoms of chest pain and diaphoresis at admission. While questioning relatives about the patient's background, it was learned that his arterial blood pressure had not been under control, with values of between approximately 140/90 mmHg and 180/110 mmHg. The patient was also being seen by the neurology department due to his previous diagnosis of Parkinson's disease. He had been admitted to the cardiovascular surgery department with swelling and pain in his right leg five days earlier, and a diagnosis of deep vein thrombosis (DVT) had been made after an evaluation. The patient was prescribed an empirical anticoagulation treatment, but he had not taken this medication.

On admission, the patient's blood pressure was 110/70 mmHg. This value should have been considered as evidence of systemic hypotension as his pulse rate was 150 bpm, his respiratory rate was 40 pm, and the oxygen saturation was 80%. His arterial blood gas analysis taken without oxygen showed pH 7.54, pCO_2 of 23.9 mmHg, and pO_2 of 52.4 mmHg. Positive physical examination findings were jugular vein distention, bilateral crackles at the bases of the lungs, tachycardia, a wide, fixed second heart sound, and a third heart sound; however, no murmurs were heard. His extremities were cool and cyanotic with weak peripheral pulses. His legs also demonstrated a difference in diameter. Positive laboratory findings were cardiac troponin I, 0.09 ng/mL (reference <0.04) and D-dimer >1.0 (reference <0.5).

The initial electrocardiogram showed sinus tachycardia at a rate 149 bpm, incomplete right bundle branch block, right axis deviation, T-wave inversion in the precordial leads, and an S1Q3T3 pattern. Bedside echocardiography demonstrated normal left ventricular systolic function, severe right ventricular dilation, severe hypokinesis of the right ventricular free wall and the ventricular septum, and good right ventricular (RV) apical contraction (i.e. the McConnell sign). The estimated pulmonary artery systolic pressure was 70 mmHg by continous-wave Doppler.

The patient was immediately referred to the cardiology department and was hospitalized in the intensive care unit (ICU). Due to the diagnosis of high-risk PE and hemodynamic instability, the patient was immediately administered 1.500.000 IU streptokinase infusion over a two-hour period. At the end of the treatment, heparin infusion was continued in combination with warfarine until the international normalized ratio (INR) and the activated partial thromboplastin time (APTT) level were within the effective therapeutic range (2.0 to 3.0 and 50 to 70 msec, respectively). After the thrombolytic therapy, although the effective therapeutic range for APTT was accessed over the next three days, the patient's hemodynamic instability and echocardiographic findings of PE still continued. Therefore, a spiral computed tomography (CT) was performed which revealed that massive bilateral PE was persisting (Figure 1). As a result, it was believed that the patient was receiving no benefit from the streptokinase infusion, and he was referred to have an immediate surgical pulmonary embolectomy.

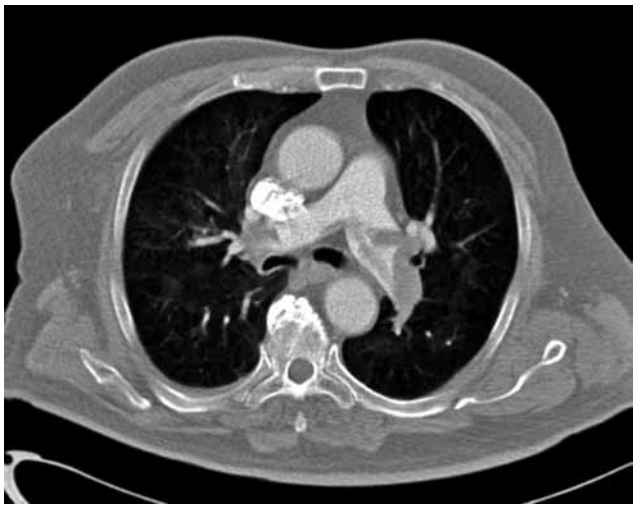

Figure 1. On pulmonary computed tomography angiography, hypodense imaging in the pulmonary bifurcation level indicates a massive pulmonary embolism being more prominent in the left pulmonary artery after thrombolytic therapy with streptokinase.

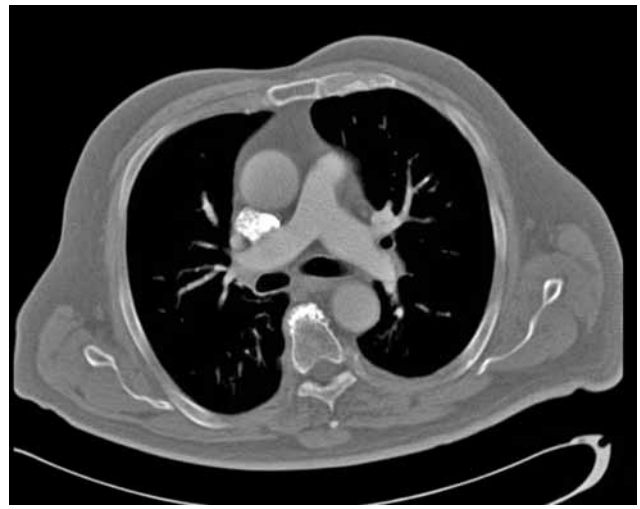

Figure 2. There is no perfusion defect seen on control pulmonary computed tomography angiography imaging performed after the second thrombolytic therapy with a tissue plasminogen activator.

However, the patient rejected any kind of surgical intervention. Eventually, 100 mg of rt-PA intravenous (i.v.) was given over two hours as an alternative as a "last chance" option. After the recurrent thrombolytic therapy, no hemorrhagic complications were seen, and the patient's clinical status improved dramatically. The arterial blood gas analysis returned to its normal values, and the estimated systolic pulmonary artery pressure was evaluated at approximately 40 mmHg in echocardiography. Control CT imaging performed on the 10th day of the follow-up showed complete resolution of the bilateral PE (Figure 2), and the fully-recovered patient was discharged with an effective anticoagulant therapy (INR: 2.9) after 15 days in the hospital.

DISCUSSION

Thrombolysis can be a life saver for patients with massive PE, cardiogenic shock, or overt hemodynamic instability. Thrombolytic agents accelerate the lysis of the PE. Currently, the Food and Drug Administration (FDA) recommends thrombolysis for the treatment of a "massive pulmonary embolism".[1]

A large, multinational, randomized trial is currently under way to determine whether normotensive patients with right ventricular dysfunction, as detected on an echocardiography or CT scan, and evidence of myocardial injury, as indicated by a positive troponine test, may benefit from early thrombolytic treatment.[2] Among the patients who underwent echocardiography, a finding of right ventricular hypokinesis was associated with a doubling of the mortality rate at 14 days and with a rate at three months that was 1.5 times higher than that of patients without hypokinesis.[5] The Management Strategy and Prognosis of Pulmonary Embolism Registry (MAPPET) of 1001 patients with PE and right ventricular dysfunction showed that the mortality rate increased as right ventricular failure worsened.[6]

Limited comparative data is available regarding different thrombolytic agents in the treatment of PE. Experimental studies of venous thromboembolism suggested that rt-PA was more potent than urokinase or streptokinase, prompting its assessment for PE.[7,8] Meneveau et al.[9] randomized 66 patients to 100 mg rt-PA over a two-hour period or 1.5 million units of streptokinase over the same amount of time. At one hour, there was significant reduction in total pulmonary resistance in the rt-PA group compared with the streptokinase group (33% versus 19%), and in the two-hour post-initiation of therapy, similar hemodynamic efficacy was noted.[9] Goldhaber et al.[10] performed a multicenter study in which 45 patients were given either 100 mg tissue plasminogen activator (t-PA) infusion over a two-hour period or a 24-hour urokinase infusion followed by heparin. After two hours of therapy, pulmonary angiographic and hemodynamic evaluations were repeatedly performed. It was demonstrated that t-PA led to significantly greater resolution of the pulmonary arterial pressure when compared with urokinase. Because of the small sample size in the study, pulmonary embolism guidelines were advised to any one of three thrombolytic agents. Also, in accordance with the policy of our institution, most of the patients are initially administered streptokinase therapy due to its low cost.

There are limited studies in the literature relating to the follow-up of patients after failed thrombolytic therapy. The most definitive and significant study in this field was conducted by Meneveau et al.[9] as a prospective single-center registry of PE patients who underwent a second thrombolytic therapy due to unsuccessful thrombolysis. They found that approximately 8% of patients do not respond to this procedure. In this situation, rescue surgical embolectomy should be preferred over repeat thrombolysis. The in-hospital course of patients who had undergone rescue embolectomy was significantly better than that of patients who were treated with a second thrombolysis. In the repeat thrombolysis group, the in-hospital mortality rate reached 38%, and one third of these deaths were caused by recurrent PE, In contrast, patients who underwent rescue surgical embolectomy had a very low in-hospital mortality rate of 7% and experienced no recurrent PE. Their results demonstrate that repeat thrombolysis is successful without adverse outcomes in only 31% of patients. Repeat thrombolysis in this study consisted of the administration of streptokinase in patients who had been previously treated with alteplase while patients who received streptokinase initially were subsequently treated with alteplase.[4]

Although it is a well-known fact in the literature that patients who do not respond to the first thrombolytic therapy should be referred for rescue surgical embolectomy instead of repeating the thrombolysis, there can be some extraordinary circumstances for which substantially limited alternatives exist. This case report has suggested that giving the second thrombolytic therapy with fibrin-specific agents like rt-PA after failed thrombolytic therapy might be favorable for a patient's "last chance" treatment. This is especially true when the procedure was first performed with non-fibrin-specific agents like streptokinase or when the patient is still hemodynamically unstable and rejects the surgical approach.

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