

CASE REPORT

Systemic Fibrinolytic Therapy in the Presence of Absolute Contraindication; a Case Series

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Abstract: In massive pulmonary embolism (PE), fibrinolytic therapy is a potential lifesaving treatment; therefore, if other treatments are not available, the physicians encounter this question: can we accept the risk of complications from fibrinolytic therapy, especially intracranial hemorrhage, in the presence of absolute contraindication, in order to save the patient's life? Here, we describe three cases of massive PE with absolute contraindication for fibrinolytic therapy who presented to emergency department following dyspnea. Since, surgical or catheter embolectomy were not available and patients were very high risk for transferring to another hospital, systemic fibrinolytic was administered. The patients improved clinically and were discharged from hospital. It seems that, if no other acceptable treatments are available, physicians could consider fibrinolytic therapy, even at the presence of contraindication, to save the patient's life.

Keywords: Massive Pulmonary embolism; fibrinolytic therapy; anticoagulant; absolute contraindication.

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1. Introduction

Pulmonary embolism (PE) is the most common cause of preventable death in hospitalized patients. Massive PE accounts for 5-10 % of PE cases and has a high mortality rate (up to 30 – 50%) (1, 2). Massive PE affects at least half of the pulmonary vessels, leading to right ventricular (RV) dilation and dysfunction, and low blood pressure that is resistance to fluid therapy and inotrope administration (3, 4). Hallmarks of massive PE are hypotension, dyspnea and cyanosis. Hemodynamic collapse and syncope can be the initial presentation and the most common cause of early death in first days (5-7). Fibrinolytic therapy can be lifesaving and prevent complications such as RV failure, cardiogenic shock, and multi system organ failure. Contraindication exclusion is necessary for minimize bleeding risk. Although the risk of bleeding due to fibrinolytic therapy is low (10 %) (8-10), fibrinolytic administration in patients with absolute contraindication and no other available acceptable treatment is a challenging de-

cision. Here we describe three cases of massive PE with absolute contraindication for fibrinolytic therapy who were discharged from hospital after successful treatment.

2. Case presentation:

Case 1

A 54-year-old man presented to our emergency department because of sudden onset of dyspnea and an episode of loss of consciousness for 2 minutes. He had a history of ischemic cerebrovascular accident (CVA) 20 days before and was bedridden after that. Initial physical examination revealed blood pressure (BP): 75/45 mmHg, heart rate (HR) 160/minute, respiratory rate (RR) 35/minute, O₂ saturation 60% in room air that increased to 90% when using nasal O₂. He was afebrile without any signs and symptoms of pulmonary edema but jugular vein pressure (JVP) was elevated. No edema was detected in lower limbs and color Doppler ultrasonography didn't show any evidence of thrombus. A bedside electrocardiogram showed sinus tachycardia with negative T wave in VI - V3.

The result of arterial blood gas (ABG) analysis was as follows: pH=7.19, PCO₂=30, Base excess (BE) =-15. Trans-thoracic echocardiography (Figure 1.1) revealed severe RV dilation

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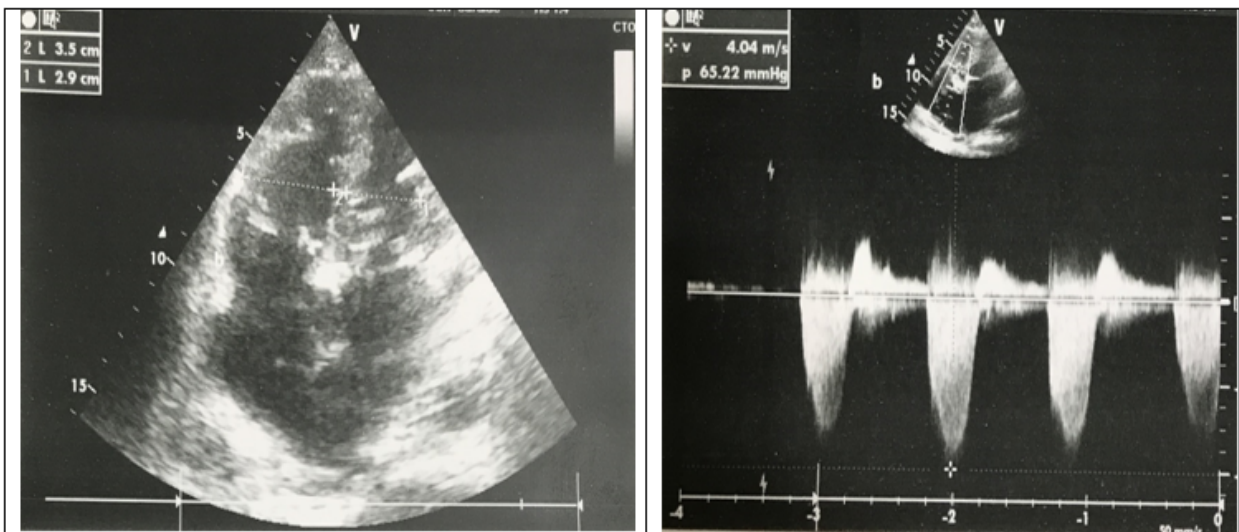


Figure 1. 1: Trans-thoracic Echocardiography showing severe right ventricular (RV) enlargement and high pulmonary artery pressure (PASP: 45 mmHg).

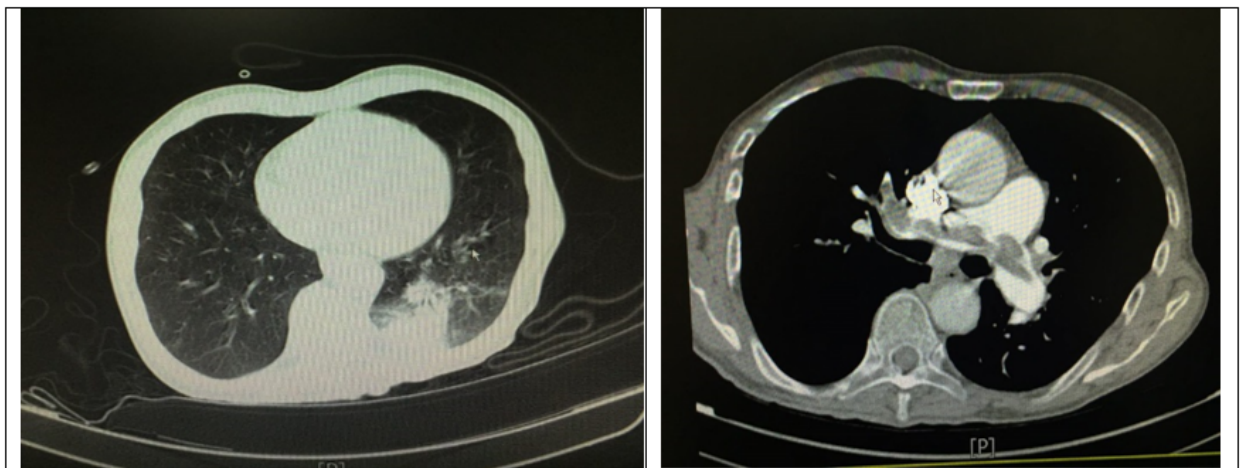


Figure 1. 2: Left: Chest computed tomography (CT) image showing a wedge consolidation in left lower lobe of lung, Right: Chest CT Angiography demonstrating large filling defect in main pulmonary artery and both main bronchi

and moderate RV dysfunction with moderate tricuspid regurgitation and elevated pulmonary artery systolic pressure (pulmonary artery systolic pressure (PASP): 45 mmHg).

A chest computed tomography (CT) scan showed a wedge consolidation in left lower lobe of lung (Figure 1.2 left). According to the above findings, PE was diagnosed for the patients and chest CT angiography was done, which demonstrated a large filling defect in main pulmonary artery and both main bronchi (Figure 1.2 right).

Considering clinical presentation, unstable hemodynamics, and pulmonary CT angiography findings, massive PE was diagnosed. Hypotension didn't correct with fluid resuscitation and vasopressor therapy. Hypoxemia and tachycardia persisted and the patient was lethargic. In brain CT scan, hemor-

rhagic transformation in territory of prior CVA was reported (Figure 1.3 left). Fibrinolytic therapy was contraindicated due to history of CVA 20 days before and surgery or embolectomy by catheter were choice treatments but they were not available and transferring him to another hospital was not possible.

Considering patient's critical situation and the risk of developing intracranial hemorrhage, Alteplase was administered with dose (50 mg during 2 hours) then heparin infusion was started after normalization of PTT (after 4 hours). Within 2 hours of thrombolysis, level of consciousness, hypotension, and hypoxemia improved (Saturation $O_2 = 95\%$ and BP = 120/85 mmHg).

The findings of repeated trans-thoracic echocardiography

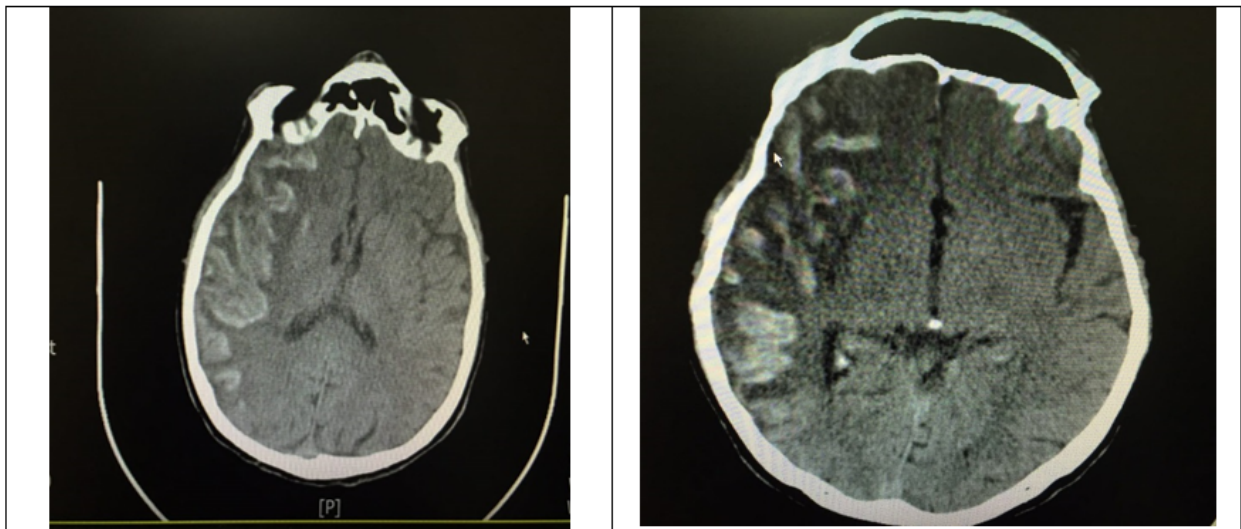


Figure 1. 3: Brain CT scan before (Left) and after (Right) fibrinolysis showing hemorrhagic transformation in territory of prior CVA without change.



Figure 1. 4: CT angiography after treatment showing reduction of thrombus bulk and RV size

showed significant improvement in RV size and RV function. PASP had dropped to 28 mmHg. Pulmonary CT angiography was done 24 hours after treatment and showed reduction of thrombus bulk and RV size (Figure 1.4).

Two control brain CT scans (4 h and 24 h after treatment) didn't show any new intracranial hemorrhage (figure 1.3 right). The patient was discharged from the hospital after 5 days with prescription of Rivaroxaban 15 mg twice a day and he was in a good condition.

Case 2

A 52-year-old man was admitted to our emergency depart-

ment with complaint of syncope. The patient also complained of dyspnea. He had a history of recent surgery for cervical discopathy 18 days before.

His vital signs upon arrival to the emergency department showed a systolic blood pressure of 65 mmHg, a heart rate of 118 beats per minute, a respiratory rate of 28 per minute & oxygen saturation of 80% in ambient air. In physical examination, jugular veins were distended and cardiac exam showed tachycardia and a right ventricular heave. Pulmonary examination was unremarkable.

The initial electrocardiogram showed sinus tachycardia at a rate of 118 per minute, S1Q3T3 pattern and inverted T wave in V1-V3.

Bedside echocardiography showed severe RV dilation, moderate RV dysfunction, moderate tricuspid regurgitation, elevated pulmonary artery pressure (PAP: 60 mmHg), McConnell sign with no RV and RA clot. CT angiography of pulmonary arteries was performed due to suspicion of PE. The findings of CT angiography (figure 2.1) confirmed Saddle embolism in pulmonary arteries (filling defects in main, left and right pulmonary artery).

According to the above findings, massive PE was diagnosed but the patient had absolute contraindication for fibrinolytic therapy due to recent spinal surgery, so he became candidate for emergent surgery or embolectomy by catheter but this procedure was not available and critical condition of patient did not allow us to transfer him to another hospital. So we decided to administrate fibrinolytic. Alteplase was administered with a dose of 100 mg for 2 hours.

The patient felt much better and blood pressure rose after termination of Alteplase infusion. Repeated bedside trans-thoracic echocardiography showed reduction in RV size and

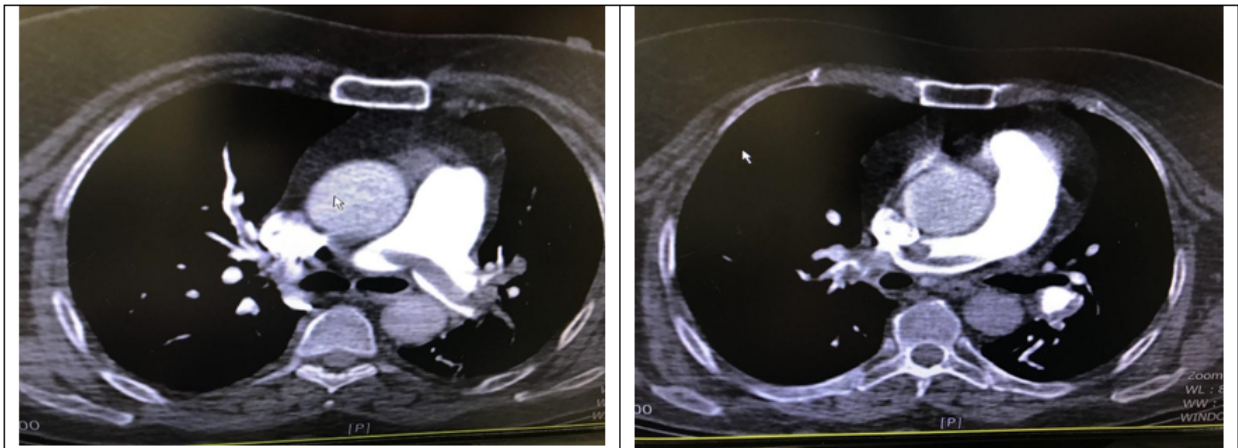


Figure2. 1: Pulmonary computed tomography angiography confirmed Saddle embolism in pulmonary arteries.

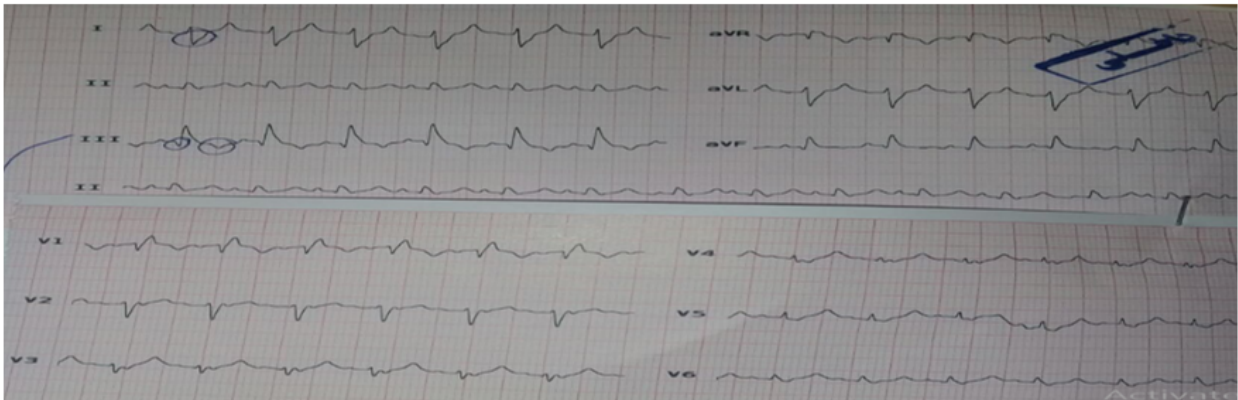


Figure3. 1: Electrocardiogram shows sinus tachycardia and right bundle branch block.

pulmonary artery pressure. During the hospital stay, the patient was continuously monitored for bleeding of the site of surgery, and no complication was observed. So, on the sixth day, he was discharged with a good general condition.

Case 3

A 48 Year-old female, with a known case of brain tumor, presented to our emergency department complaining of dyspnea and drowsiness since 4 days before. She had history of emergency department admission 4 weeks before following headache and loss of consciousness and diagnosis of brain tumor with right parietal lobe involvement and intratumoral hemorrhage. She underwent mass resection and was discharged from the hospital after 8 days of hospitalization. 24 days after discharge she presented to emergency department with complaint of severe shortness of breath.

Her vital signs upon arrival to the emergency department showed a systolic blood pressure of 60 mmHg, a heart rate of 145 beats per minute, an oral temperature of 38°C, a respiratory rate of 35 per minute, and oxygen saturation of 50% in ambient air.

Initially, due to hypotension, fever and cold limbs were diagnosed with septic shock-induced meningitis or pneumonia treated with broad-spectrum antibiotics and vasopressor. The initial electrocardiogram showed sinus tachycardia at a rate of 135 per minute, right bundle branch block with a QRS duration of 125 milliseconds and right axis deviation of 120 degrees (figure 3.1).

Both lower extremities swelling developed and subsequent compression ultrasound and Doppler studies revealed bilateral acute extensive thrombus formation in the deep veins to the level of iliac. Pulmonary CT angiography confirmed large bilateral pulmonary thromboembolic (saddle-shaped embolism with obstruction of 85% of the arterial substrate) with radiological evidence of RV strain (figure 3.2).

Fibrinolytic therapy was contraindicated due to history of brain tumor and recent surgery 28 days before and surgery or embolectomy by catheter were choice treatments but the patient's clinical condition was not suitable for surgery and transferring her to another hospital for embolectomy by catheter was not possible. Ultimately despite absolute con-

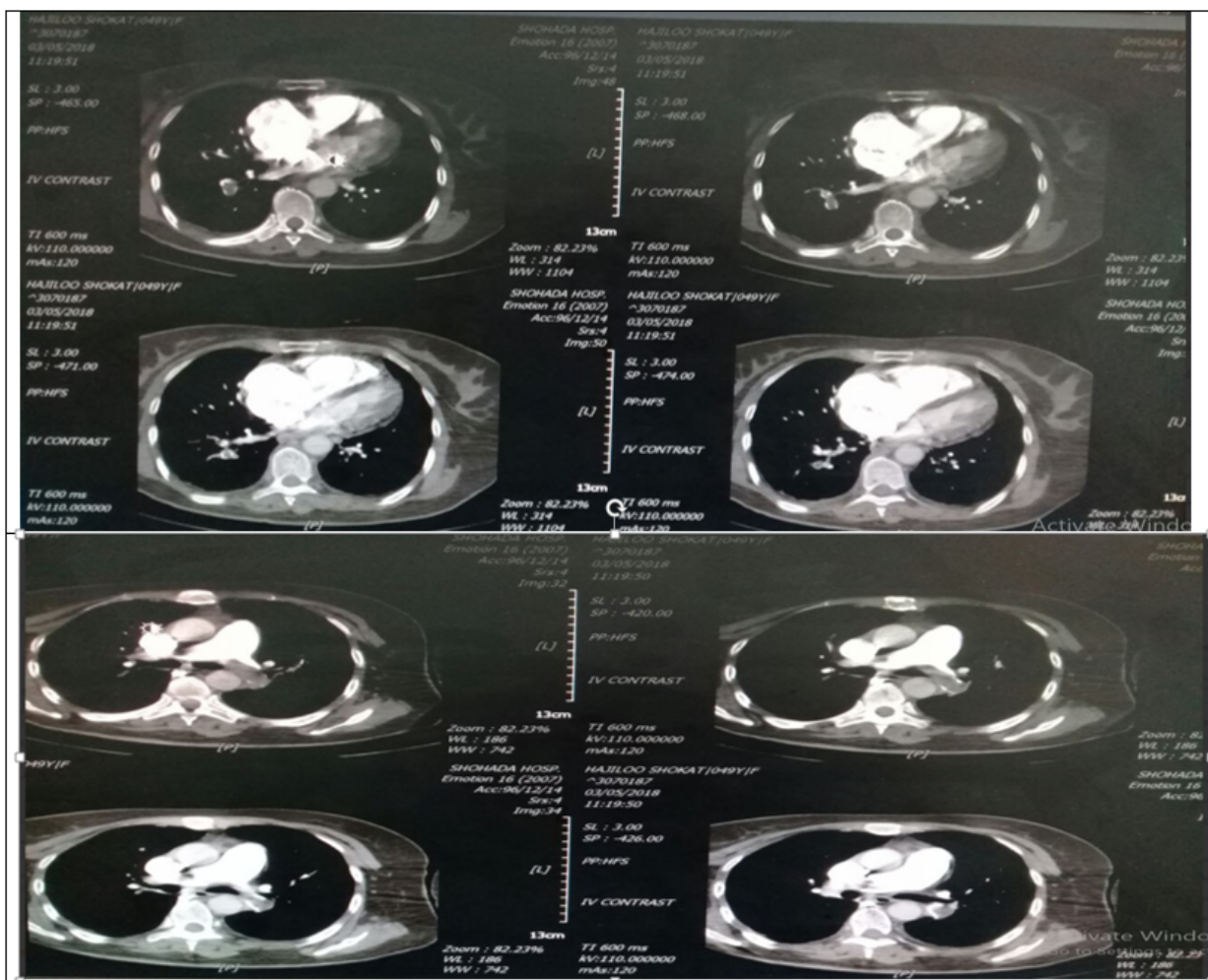


Figure 3. 2: Pulmonary CT angiography demonstrates bilateral pulmonary thromboembolism with RV dilatation.

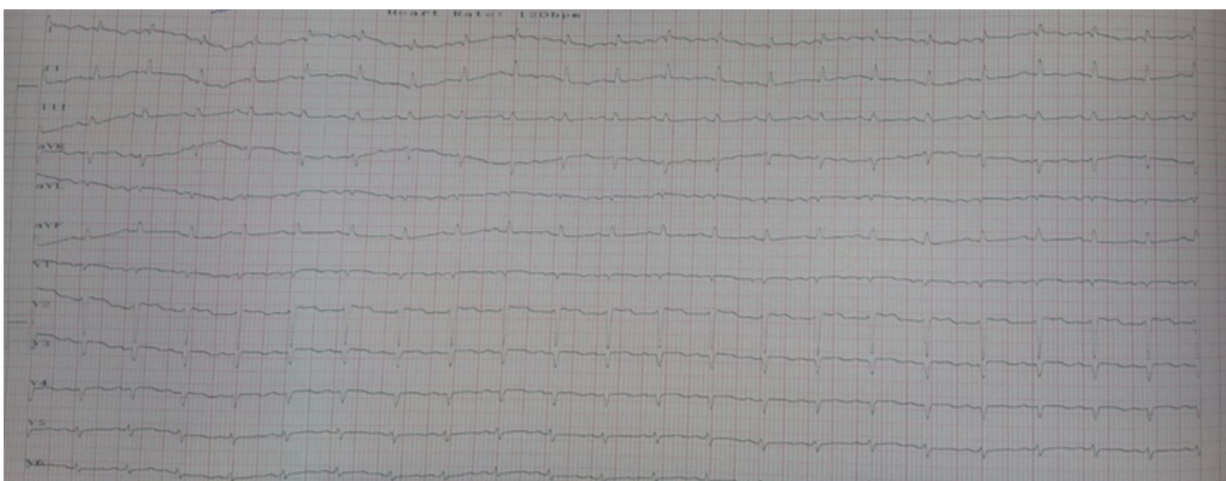


Figure 3. 3: Electrocardiogram shows normal sinus tachycardia.

trindications, Alteplase was administered with dose (25 mg during 1 hours). Approximately 24 hour after termination



of thrombolytic therapy, blood pressure returned to 115/75 mmHg, with a heart rate of 90 beats per minute and a respiratory rate of 20 per minute with an oxygen saturation of 88% in ambient air. Electrocardiogram then showed sinus tachycardia at a rate of 125 per minute, normal QRS duration and normal axis (Figure 3.3).

Control brain CT scans didn't show any new intracranial hemorrhage (48h after treatment). After 72 hours, patient's level of consciousness returned to the previous level and the patient was discharged on the seventh day with oral administration of rivaroxaban.

3. Discussion

American Heart Association (AHA) (11) and ACCP Guidelines (12) advise advanced treatments such as systemic fibrinolysis through a peripheral vein, pharmaco-mechanical catheter-directed therapy and surgical embolectomy for patients with massive PE.

Patients being considered for systemic fibrinolysis have to be screened for contraindication. The overall risk of intracranial hemorrhage in patients who receive fibrinolysis is relatively low (0.9%) (13), but studies have shown that the use of fibrinolysis has decreased by 50% in patients with massive PE over the last decade due to fear of intracranial hemorrhage (14).

Physicians when faced with patients with massive PE that concomitantly have contraindication for fibrinolysis, have to choose other treatments due to fear of complications, especially intracranial hemorrhage.

Unfortunately, other therapeutic options, such as pharmaco-mechanical catheter-directed therapy and surgical embolectomy are not available in all hospitals or, if available, may be rejected by surgeons or anesthesiologists because of the high risk of intervention.

In this case series, we presented three cases, in which diagnosis of massive PE was affirmed based on clinical presentations and images. All cases had contraindication for fibrinolytic therapy.

Due to the inability to use other treatments and patients' critical condition, as non-treatment leads to death of patients, we had to administrate fibrinolysis. Despite the risk of bleeding, fortunately, there were no fibrinolytic side effects in these patients. All cases had dramatic responses to fibrinolytic administration. They were discharged from the hospital with a good general condition.

4. Conclusion:

In some critical conditions, physicians are confronted with the question: how can I manage massive PE in the presence of absolute contraindication for fibrinolytic? It seems that, if no other acceptable treatments are available, physicians

could consider fibrinolytic therapy to save the patient's life.

5. Appendix

5.1. Acknowledgements

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5.2. Authors contribution

All authors meet the standard criteria of authorship based on the recommendations of the international committee of medical journal editors.

5.3. Conflict of interest

The authors declare that there is no conflict of interest in any phase of performing the study.

5.4. Funding

None.

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