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Case Report

Thrombolysis for Submassive Pulmonary Embolism

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Abstract

We describe a case of Submassive Pulmonary Embolism treated with Alteplase. We discuss the treatment plan and controversies in management of similar cases in our clinical setting.

Introduction:

Pulmonary Embolism (PE) is a common condition characterized by thrombi obstructing the pulmonary arteries or one of its branches. In a multinational registry, the 3 months mortality rate of Acute PE was 15.3% (1). In a study that reviewed CT scans positive for PE, the 10-year survival was 37.4%. Untreated PE is fatal in up to 30% of patients, with the risk of death greatest within the first 30 days (2).

PE is classified according to severity & hemodynamic stability into: Massive PE (hemodynamically unstable – high risk), Submassive PE (hemodynamically stable – intermediate risk – with Right ventricular (RV) strain) and low-risk PE (hemodynamically stable – with no evidence of RV strain). PE can also be classified according to the anatomic location of the PE into Saddle (obstruction of the both right and left main pulmonary arteries), Lobar, Segmental and Subsegmental.

Massive PE or “high-risk” PE is characterized by sustained hypotension (systolic BP < 90 mmHg or requiring vasopressors) without another cause of hypotension. Submassive PE is characterized by normal blood pressure or non-sustained hypotension with either RV dysfunction or myocardial necrosis. RV dysfunction is defined by the presence of at least one of the following: RV dilatation by echocardiography or computed tomography (CT), elevation of Brain Natriuretic Peptide (BNP) blood level, elevation of N-terminal pro-BNP blood level, or electrocardiographic changes suggestive of RV strain.

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Myocardial necrosis is defined as elevation of troponin level in the blood.

There is expert consensus that systemic thrombolysis is beneficial in patients with Massive PE (3). Normotensive patients with RV dysfunction have a worse short-term outcome when compared to normotensive patients with no RV dysfunction (4). In one clinical trial of 256 patients with Submassive PE, Alteplase resulted in less clinical escalation (requirement for vasopressors, etc..) but no mortality benefit (5). When compared to Alteplase, Streptokinase was found to have similar efficacy in patients with Massive PE (6, 7). A metanalysis showed that thrombolysis in Submassive PE patients is associated with lower rates of all-cause mortality but with increased risk of major bleeding and intracranial hemorrhage (8). The PIETHO trial demonstrated that Tenecteplase prevented hemodynamic decompensation in patients with Submassive PE but increased the risk bleeding and intracranial hemorrhage (9). A recent metanalysis identified four risk factors for intracranial hemorrhage following thrombolytic therapy (PE-CH) score: Prior Cerebrovascular accident with residual deficit, prior myocardial infarction, age greater than 65 and peripheral vascular disease (10).

Case presentation:

A 42-year-old male with no significant past medical history presented with 5-day history of recurrent syncope. It initially occurred with moderate exertion, and then with only mild exertion. He had a dry cough with no haemoptysis and no chest pain. He had no risk factors for Deep Vein Thrombosis (DVT) or PE.

On physical examination, his heart rate was 128/min, respiratory rate was 37/min, BP 120/80 with no other abnormal findings on physical examination. He developed brief episodes of hypotension which promptly resolved with intravenous fluid administration and did not require vasopressors. ECG showed sinus tachycardia, with no ST changes; Chest X-ray showed clear lung fields. Laboratory tests showed elevated Creatinine at 1.4 mg/dl, Troponin was mildly increased at 0.06 ng/ml (0.04 ng/ml is the upper limit of normal for laboratory), CRP at 16 mg/l (1 mg/l is the upper limit of normal for laboratory). The remaining blood tests were unremarkable. Due to elevated troponin

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and suspicion of acute coronary syndrome, a bedside echocardiogram was performed. It showed a dilated RV with reduced function, severe pulmonary hypertension, and severe tricuspid regurgitation (TR) (**Video 1)**. CT pulmonary angiography confirmed Saddle PE (**Photo 1)**.

Alteplase 100mg infusion was administered intravenously, in addition to anticoagulation with Enoxaparin before and after the infusion. The patient's symptoms subsided shortly after administration of Alteplase, with no recurrence of hypotension or syncope. Three days later, a follow up echocardiogram demonstrated reduction in the size of the right ventricle, improvement in right ventricular function, reduction in severity of tricuspid regurgitation and reduction in pulmonary arterial pressure. He was transitioned from enoxaparin to oral Rivaroxaban at discharge. A search for a cause of the PE (Lower extremity Venous Doppler Ultrasound, Abdominal Ultrasound, etc...) did not yield any abnormal findings. The plan was to continue Rivaroxaban for life. No abnormalities were detected on thrombophilia screening.

At 3 months, the patient remained without symptoms, echocardiogram showed a normal sized right ventricle with normal function, normal right ventricular systolic pressure, and only mild tricuspid regurgitation **(Table 1), (Video 2)**.

Discussion:

Although our patient's presentation did not meet the definition of Massive PE, he was at high risk of hemodynamic compromise in the short term as his blood pressure required intravenous fluid administration and he had recurrent syncopal episodes probably due to hypotension. Echocardiographic changes were markedly abnormal with dilated RV with reduced function; and severe pulmonary hypertension. Furthermore, he was at low risk of intracranial hemorrhage with relatively young age at 42; no history of Stroke, Myocardial Infarction or Peripheral artery disease; essentially no risk factors for intracranial hemorrhage according to the PE-CH score. We felt that the balance of risk versus benefit favored systemic thrombolysis. The patient had an excellent response to Alteplase with complete resolution of symptoms, and

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objective improvement on echocardiography parameters up to 3 months from the event; and no bleeding complications. The main limitation for the widespread adoption of Alteplase in similar patients in our clinical setting is the cost of Alteplase (US$1000) and its' limited availability. A lower cost and more widely available alternative is streptokinase (US$30). The other important learning point from this case is the value of early performance of echocardiography in patients with suspected PE; in our patient this allowed early diagnosis and treatment leading to a favorable clinical outcome. Training Emergency Medicine physicians in basic echocardiography may improve the early detection of PE given the limited number of Cardiologists working outside tertiary cardiac centers. Moreover, to advance our daily practice, a registry for patients with Massive and Submassive PE would be useful to increase the utilization of early echocardiography and thrombolysis with streptokinase and hopefully improve outcomes in our patients with Massive and Submassive PE.

Conclusion:

There may be a role for Thrombolysis in patients with Submassive Pulmonary Embolism, provided that they have high risk of hemodynamic compromise and low bleeding risk.

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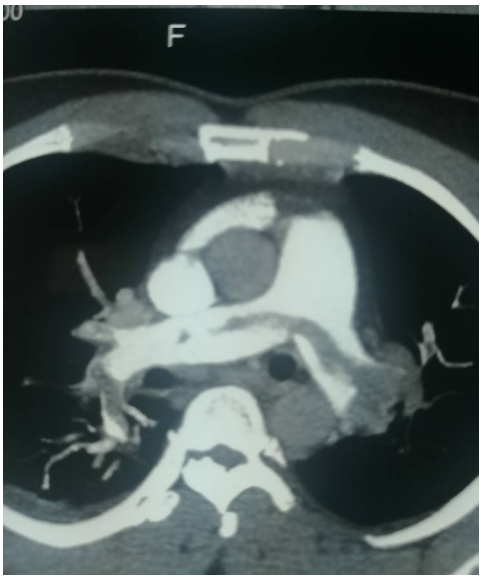
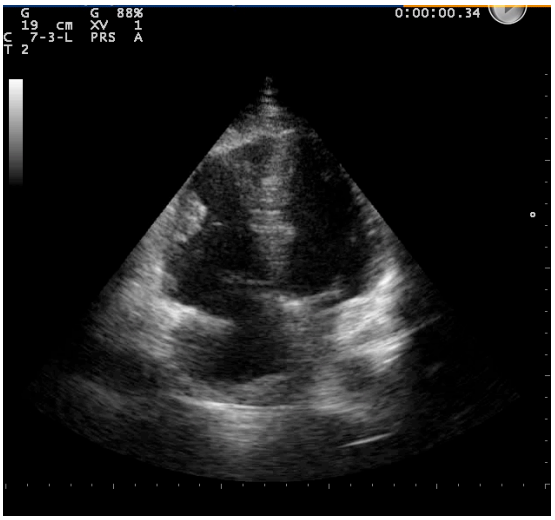


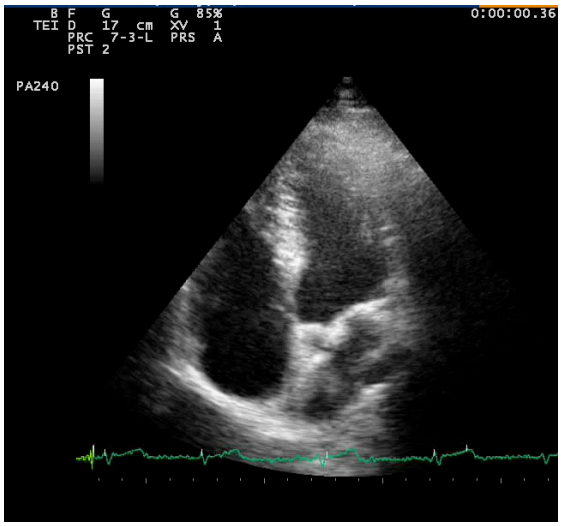
Photo 1. CT Pulmonary Angiography reveals a Saddle Embolus occluding both left and right pulmonary arteries.

Echo	Prior to Alteplase	3 days after Alteplase	90 days after Alteplase
RV basal diameter (mm)	45	43	37
RVSP (mmHg)	70-75	45-50	30-35
Severity of tricuspid regurgitation	Severe	Mild	Mild

Table 1: Marked improvement in echocardiographic parameters on follow up



Video 1. Apical 4 Chamber View, demonstrating marked dilatation of the RV with reduced function (Click on image to see video or visit https://streamable.com/nkyje)



Video 2. Apical 4 Chamber View, 3 months after thrombolysis – showing marked improvement in the size and function of the RV (Click on image to see video or visit https://streamable.com/qi9z8)