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Spontaneous Pulmonary Hemorrhage Following Thrombolytic Therapy for Acute Myocardial Infarction

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Abstract | **Case Report**

Systemic thrombolysis in the setting of acute myocardial infarction (AMI) remains an effective treatment. However, it exposes to a non-negligible bleeding risk Diffuse pulmonary hemorrhage is a of the rare complication of thrombolysis, it can cause a serious medical emergency potentially leading to fatal acute respiratory failure. We present four cases of diffuse pulmonary hemorrhage following administration of intravenous thrombolytic therapy (Tenecteplase), the Lack of recognition that the lungs too may be a site of spontaneous hemorrhage during thrombolytic therapy may lead to a considerable diagnostic and therapeutic delay. Pulmonary hemorrhage should be considered in the differential diagnosis of patients who receive thrombolytic therapy in whom new roentgenographic pulmonary infiltrates present accompanied by decreases in hematocrit value.

Keywords: acute myocarduak infarction, thrombolysis, hemoptysis, spontaneous.

INTRODUCTION

Systemic thrombolysis in the setting of acute myocardial infarction (AMI) remains, in the absence of contraindications, an effective treatment. However, it exposes to a non-negligible bleeding risk that remains its major adverse event. Most of the latter occur at sites of vascular access and are mild, though patients may also present with other locations such as gastrointestinal, retroperitoneal, genitourinary, and cerebral bleeding [1].

Diffuse pulmonary hemorrhage is a rare complication of thrombolysis, and serious medical emergency potentially leading to fatal acute respiratory failure with only a few cases reported in the literature." We present three cases of diffuse pulmonary hemorrhage following administration of intravenous thrombolytic therapy, we discuss in this article, through our cases and a literature review [2].

CASES PRESENTATION

Patient I

A 24-year-old man, Besides smoking nicotine and cannabis, he did not have any other cardiovascular risk factors, was admitted to our emergency department due to persisting angina for seven hours. his ECG showed normal sinus rhythm with ST segment elevation in leads V1-V6 and I, aVL and reciprocal ST segment depression in leads II, III and aVF, at presentation, her vital signs were stable, the physical and cardiovascular examination revealed no abnormalities, bedside echocardiography depicted a anterior hypokinesia with a LVEF of 45%, Immediately, systemic fibrinolytic therapy and loading doses of aspirin plus clopidogrel were administered, after 4 hours, he became 's breathless and hypoxic, his oxygen saturation in room air fell to 87% from an initial value of 99%, at examination revealed crackles in both lung fields without any other signs of congestion, a chest X-ray revealed bilateral alveolar infiltrates. Based on the clinical presentation, a diagnosis of acute pulmonary oedema was made and the patient was traited with diuretics and ventilation with a high oxygen concentration mask, Because of systematic suspicion of COVID-19 in patients with respiratory failure, polymerase chain reaction was performed and returned negative, blood tests showed a biological inflammatory syndrome and drop of hemoglobin level, High-resolution computed tomography (HRCT) of thorax

showed bilateral multiple alveolar lesions strongly suggesting a diffuse AH.

Because of the severity of the hemorrhage and respiratory condition, we maintained a single antiplatelet (clopidogrel), while a anticoagulation and aspirin withdrawal

Respiratory condition of the patient deteriorated 2 days laters required need for non-invasive ventilation, after 1 week, the patient's respiratory condition significantly improved.

After two weeks of hospitalization and close monitoring, we proceeded to coronary angiography, revealing a critical subocclusion of the left anterior descending artery with TIMI grade 3 flow successfully treated with the implantation of a stent. He was discharged on guideline-directed medical therapy and discharged home 2 days later.

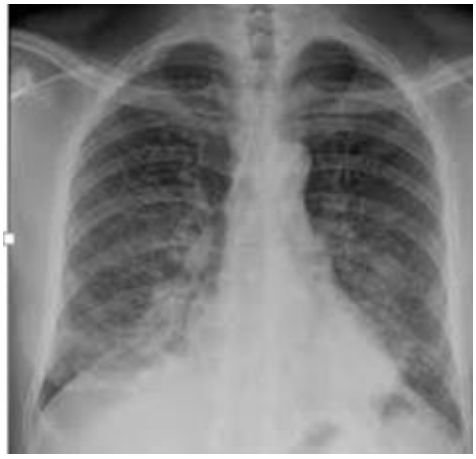

Figure 1: Chest X ray showing diffuse and bilateral lung infiltrate

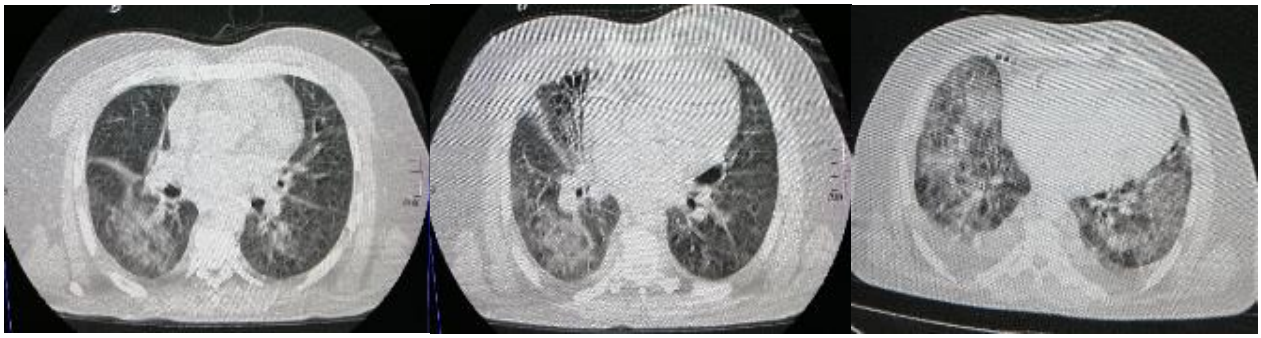

Figure 2 (A-C): Computerized tomogram of the chest (lung window) showing bilateral partially homogenous opacities and pleural effusions

Patient II

A 64-year-old male patient, he had several cardiovascular risk factors, including type-2 diabetes mellitus, hypertension, dyslipidaemia, with coronary heart disease history, presented with acute chest pain for last 11 hours, the electrocardiogram showed an anterolateral ST-elevation myocardial infarction (STEMI) ST segment elevation myocardial infarction (STEMI). He received, immediately, loading doses of aspirin and clopidogrel, and then had successful thrombolysis with Tenecteplase (Metalyse).

Five hours later, the patient developed massive hemoptysis and became severely breathless and hypoxic ($Sp0_2$ 85%), physical examination showed normal cardiac murmurs, tachypnoea, and crackles in both lung fields without any other signs of congestion. No significant repolarization abnormality was observed on electrocardiogram (ECG), An echocardiography showed anterior and inferior wall hypokinesia with left ventricular ejection fraction of 30%. His platelet counts, renal and liver function tests were normal with a significant drop of hemoglobin level, The chest X-ray revealed bilateral alveolar infiltrates. A CT scan was performed and showed bilateral ground glass opacities suggestive of diffuse pulmonary haemorrhage.

In view of the severity diffuse pulmonary haemorrhage, he was continued on a single antiplatelet (clopidogrel), while aspirin and heparin were stopped.

The indication of a coronary angiography was evident; however, we decided to delay the procedure because of the severity of the hemorrhage and respiratory condition.

Unfortunately, few days later, the respiratory state of the patient deteriorated with persistent and

refractory hypoxaemia despite ventilation with a high oxygen concentration mask, required sedation, intubation for mechanical ventilation and died 3 days later.

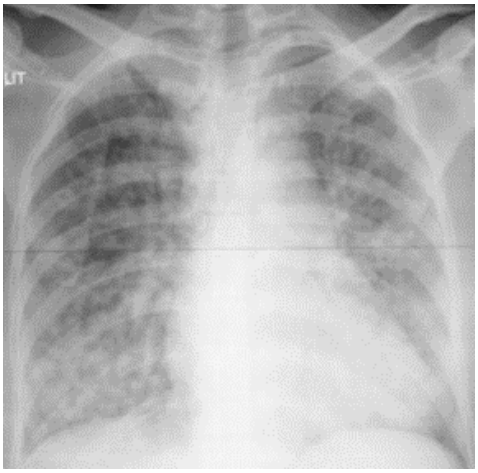

Figure 3: Chest X ray showing diffuse and bilateral lung infiltrate

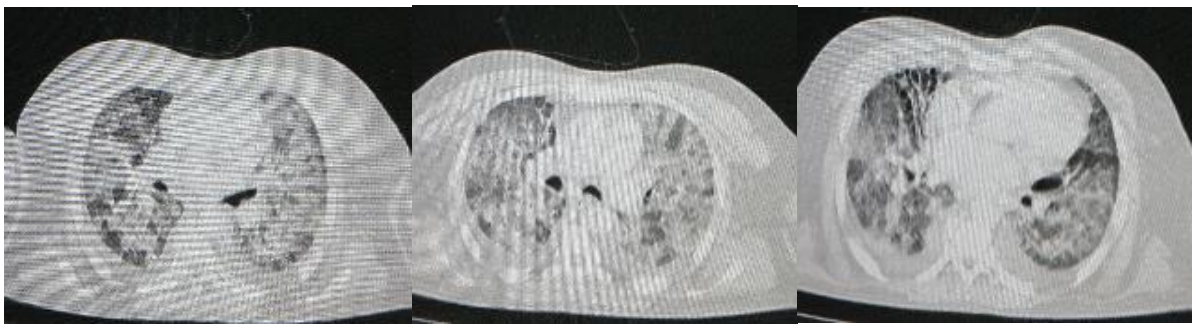

Figure 4 (A-C): Computed Tomography Scan showing Crazy paving with ground glass opacities and bilateral thickening suggesting diffuse alveolar hemorrhage

Patient III

A previously healthy 55-year-old man, heavy smoker, with no past medical history, presented to the emergency with complaint of chest pain for last 6 hours. On examination, he was hemodynamically stable, with 12 lead electrocardiogram (ECG) showing ST elevation in leads II, III and aVF, complicated with atrioventricular heart block, suggestive of acute ST elevated inferior wall myocardial infarction. 2-D echocardiography showed inferior wall hypokinesia with left ventricular ejection fraction of 38%, he was thrombolysed with Tenecteplase (Metalyse), and anti-platelets and anti-anginal drugs were administered according to standard protocol.

Few hours later , he developed a moderate hemoptysis and breathlessness, On physical examination, he was he was hemodynamically stable, however, he was polypneic with a respiratory rate at 25 cycles/minute and his oxygen saturation (SaO2) on room air had dropped from an initial value of 98% to 87%, pulmonary auscultation revealed crackles limited to the lung bases. There was no other sign of heart failure. blood tests showed a normal renal and liver function and drop of hemoglobin level, The chest X-ray revealed bilateral alveolar infiltrates. A CT scan confirmed the diagnosis of diffuse pulmonary haemorrhage

In view of the severity diffuse pulmonary haemorrhage, he was continued on a single antiplatelet (clopidogrel), while aspirin and heparin were stopped.

The patient recovered under oxygen administered via facial mask, and support of breathing through the use of non-invasive ventilation. After 1 week, the patient's respiratory condition significantly improved, and his saturation on room air increased to 97%,

We proceeded to coronary angiography revealing a critical subocclusion of the right coronary artery, left ascending coronary artery, and intermedius artery, witch were the indication of coronary artery bypass graft surgery. One month later, the patient underwent a successful operation, and he was discharged with the conventional treatment for ACS.

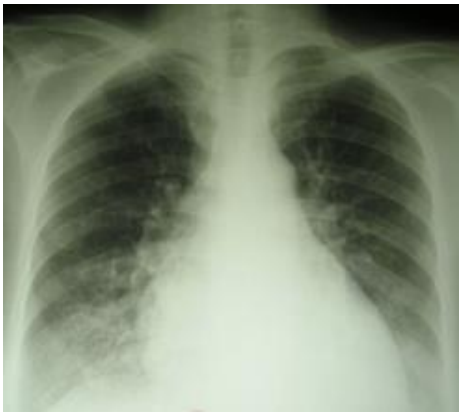

Figure 5: Chest X ray showing diffuse interstitial lung disease

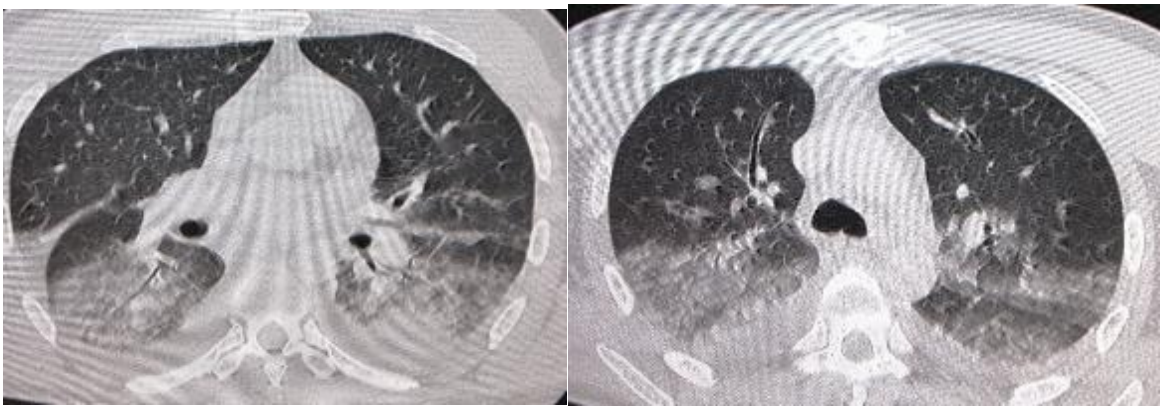

Figure 6 (A, B): Computerized tomogram of the chest showing bilateral infiltrations suggesting diffuse alveolar hemorrhage

Patient IV

A 61-year-old male patient, with coronary heart disease history (PCI of LAD and RCA one month before his admission), he was non-hypertensive, non-diabetic, and devoid of any other traditional risk factors of cardiovascular diseases including smoking, presenting with chest pain radiating to his left shoulder ten hours previously, at presentation, his vital signs were stable. The physical and cardiovascular examination revealed no abnormalities, a 12-lead electrocardiogram (ECG) was performed revealed ST-elevation in anterior and inferior leads, bedside echocardiography revealed an ejection fraction of about 40%. Immediately, systemic fibrinolytic therapy and loading doses of aspirin plus clopidogrel were administered.

After 12 hours, he became s breathless and hypoxic and developed moderate hemoptysis and breathlessness. His oxygen saturation in room air fell to 90 % from an initial value of 99%. Examination revealed bilateral fine-end inspiratory crepitations limited to lung bases, A chest X-ray revealed bilateral alveolar infiltrates. High-resolution computed tomography (HRCT) of thorax revealed bilateral alveolar patchy condensations, strongly suggestive of alveolar hemorrhage.

In front of the risque of stent thrombosis, We decided to withdraw anticoagulation, and maintain the double antiplatelet therapy.

The patient experienced progressive improvement of his respiratory parameters over the next 3 days under oxygen administered via facial mask.

A coronary angiogram performed six days after myocardial infarction revealed a significant thrombotic stenosis of the circumflex coronary artery, successfully treated with the implantation of a drug-eluting stent. He was discharged on guideline-directed medical therapy and discharged home 2 days later.

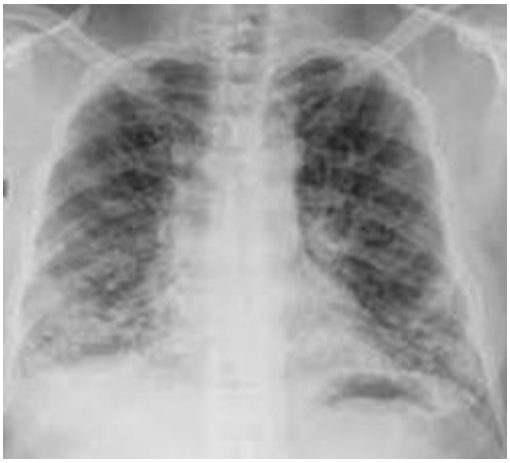

Figure 7: Chest X ray showing diffuse and bilateral lung infiltrate

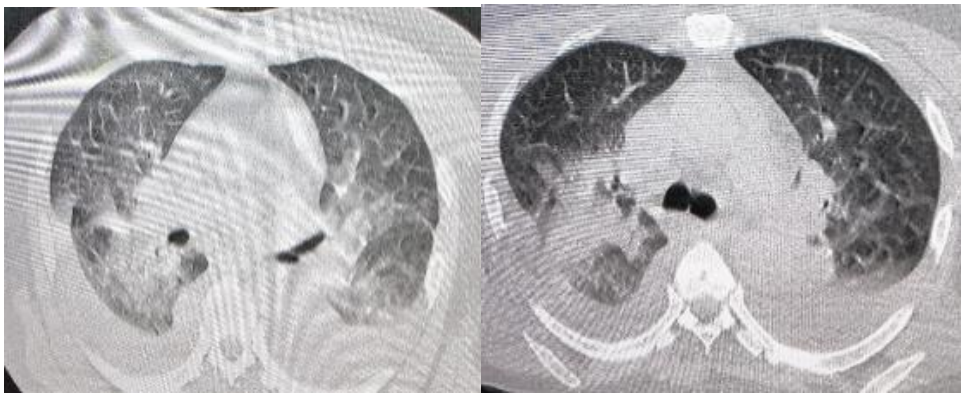

Figure 8 (A, B): Computerized tomogram of the chest showing bilateral infiltrations suggesting diffuse alveolar hemorrhage with pleural effusions

DISCUSSION

Eearly administration of thrombolytic therapy for patients with acute myocardial infarction (AMI) results in restoration of coronary flow, improvement in left ventricular function, However, it can lead to hemorrhagic complications. The most common types of thrombolyticrelated major bleeding complications are gastrointestinal tract and intracranial hemorrhages [3, 1].

Only a few cases of spontaneous pulmonary hemorrhage have been reported in the literatere Acute respiratory distress syndrome has also been described with use of streptokinase and anisoylated plasminogen streptokinase activator complex [4-6].

Spontaneous pulmonary hemorrhage after thrombolysis is a diagnosis of exclusion, although there are several factors that may augment the risk of this complication or provide clinical clues that may aid in its recognition, It usually occurs 12hours to 5 days after thrombolys

Dyspnea and tachypnea are common findings and usually are accompanied by a decrease in oxyhemoglobin saturation. Hemoptysis and a drop in hematocrit appear to be universal findings, present in both of our patients and in all of the patients in previously reported cases [7].

Chang *et al*., in a study of 2634 acute MI patients, reported 0.4% incidence of pulmonary haemorrhage following thrombolysis. Yigla et al reviewed 10 cases of pulmonary haemorrhage following MI. Ben Mrad et al reviewed 2 cases of AH associated with Tenecteplase (Metalyse), Ikeda et al reported a case in which alveolar hemorrhage occurred following dual antiplatelet therapy, sandar et al reported a case of pulmonary hemorrhage and acute respiratory failure secondary to thrombolytic treatment with tissue plasminogen activator (rt-PA) in patients with acute myocardial infarction [8, 9, 2, 10-12, 5, 2].

Although a chest X-ray helps in making the diagnosis and can reveale bilateral alveolar infiltrates, CT identifies the detailed distribution of haemorrhage and also rules out other causes of haemoptysis [2].

The predisposing factors for haemorrhage following streptokinase therapy include age >75 years, body weight 4 prior to thrombolysis and renal dysfunction.2 11–13 Prior smoking, cocaine or alcohol abuse, underlying lung diseases, chronic obstructive airway disease, recent pneumonia, heart failure, pulmonary hypertension, pulmonary catheterisation and

defibrillator use for arrhythmia increases the risk of pulmonary haemorrhage, The pathogenesis of DAH attributable to thrombolytic therapy remains uncertain and may be explained by the pre-existing fibrinolytic states, the presence of parenchymal abnormalities or an immune reaction to streptokinase causing pulmonary capillaritis as it has been proposed [13, 1, 7, 8].

Treatment includes supportive management, withholding antiplatelet and anticoagulation medications, and appropriate ventilatory support.

This rare but potentially life-threatening complication should be considered in any patient receiving thrombolysis in whom such findings are present [8, 5].

CONCLUSION

Thrombolytic therapy for myocardial infarction can result in hemorrhagic complications, the most common being bleeding from vascular access sites. Pulmonary alveolar hemorrhage is an uncommon and life-threatening complication of fibrinolytic therapy and should be considered as one of the differential diagnoses of pulmonary infiltrates or a decreasing level of hemoglobin after thrombolysis.

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