CASE REPORT

Bleed or Clot? Managing Bleeding in Post Thrombolysis Patient with Massive Pulmonary Embolism Who Underwent Recent Major Cancer Surgery

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ABSTRACT

A 51-year-old lady with invasive left breast cancer had a syncopal attack following acute chest pain on day 1 post-mastectomy. She was hypotensive and her electrocardiogram showed ST elevation at anterior leads. She had received systemic thrombolysis therapy with an excellent initial symptomatic response and ECG resolution. However, echocardiogram and computed-tomography pulmonary angiogram later showed evidence of massive pulmonary embolism. The treatment was complicated with significant bleeding from the surgical site which required a total of 11 units of packed cells, 4 units of fresh frozen plasma, 4 units of platelet, 6 units of cryoprecipitate and prothrombin complex concentrate; in order to control the bleeding along with local compression. As the haemostasis was achieved, anticoagulation was cautiously initiated, initially with unfractionated heparin followed by low-molecular-weight heparin. Eventually, she received rivaroxaban to complete her course of treatment. She made an excellent recovery on follow-up review and is planned for further treatment for her breast cancer. This case portrayed the complexity of managing a concurrent event of massive thrombosis and significant bleeding, which required a diligent assessment of both risks to ensure the best patient's outcome.

Keywords
Pulmonary embolism, thrombolysis, bleeding, MTP

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Received: 18th September 2020; Accepted: 20th December 2021

Doi: https://doi.org/10.31436/imjm.v21i1

INTRODUCTION

Massive pulmonary embolism is a fatal post-operative complication which accounts for 6 percent of hospital deaths.[1] The incidence of post-operative pulmonary embolism is as high as 19 percent of cases and highest among cancer related surgery,[2] whereas major bleeding events following thrombolysis therapy is 12 percent.[2] Managing major bleeding in post thrombolysis patients who under cancer related surgery is very challenging and needs a multidisciplinary team approach.

In this case report, we describe the presentation, management, clinical dilemmas, and outcome of a cancer patient who developed massive pulmonary embolism during the post-operative period.

CASE PRESENTATION

A 51-year-old Malay female who was diagnosed with invasive left breast cancer stage T3N0M0 with ER/PR positive developed syncope on day 1 post an uneventful left mastectomy under general anaesthesia. She was hypotensive with a blood pressure of 80/60mm/Hg, tachycardia with heart rate of 120 beats per minute, and hypoxia with pulse oximetry of 90%. The patient regained consciousness spontaneously. She also complained of dyspnoea and severe chest pain.

Based on her electrocardiogram (ECG) and positive Troponin I, she was diagnosed of an anterior ST-elevation

myocardial infarct. Subsequently, dual antiplatelet and intravenous (IV) tenecteplace 8000IU (Metalyse®) was commenced in Cardiac Care Unit (CCU) setting.[10]

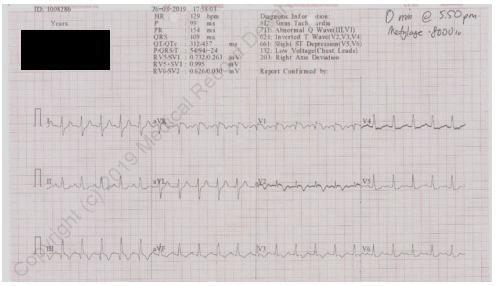

Figure 1: ECG post syncope. sinus tachycardia, S1, QIII, TIII, right axis deviation, negative T waves in lead 111, V1-V3, ST elevation in V1 & V2 and ST depression in lead II, AVL, V5 & V6.

She responded well to the thrombolysis therapy in terms of clinical improvement, normalisation of blood pressure and ECG resolution (refer to figure 1 and 2). Nevertheless, a transthoracic echocardiogram was performed which revealed dilated right ventricle although no regional wall motion abnormalities were detected. Her diagnosis was revised as massive pulmonary embolism.

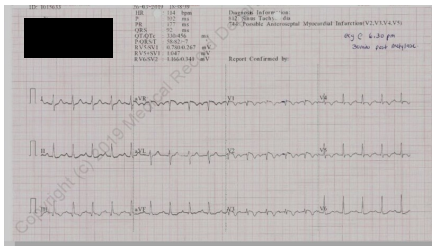

Figure 2: ECG showed sinus tachycardia, S1, QIII, TIII, right axis deviation, negative T waves in lead 111, V1-V5 and ST elevation in V1 and V2.

Unfortunately, she developed hypovolemic shock due to bleeding from surgical site after 4 hours of thrombolysis therapy. Her haemoglobin (Hb) dropped from 8.5 g/dL to 6.5 g/dL with of platelet 361 x 109/L. Her international-normalised ratio (INR) was 1.5, and activated partial prothrombin time (APTT) was 44 seconds. Despite receiving 2 consecutive units of packed cells transfusion, she remained in hypovolaemic shock and was on the verge of developing disseminated intravascular coagulopathy (DIC) at 8 hours post thrombolysis. Various surgical interventions were attempted to control the bleeding including suture ligation and clamping the surgical drainage site to create tamponade effect but all the attempts failed andas a result, patient developed significant haematoma at the chest wall.

Further deterioration of her condition led to intubation as well as commencement of vasopressor. A local compression bandage with continuous vacuum drain was applied at the surgical site. An urgent computed-tomography pulmonary angiogram revealed a right sided small pulmonary artery embolism that could have been a residue of a massive pulmonary embolism.

As her bleeding risk outweighed the thrombotic risk at that moment, a total of 4 units fresh frozen plasma and 6 units of cryoprecipitate were transfused along with a total of 11 units of packed cells to correct the coagulopathy. A single dose of 500 IU of prothrombin complex concentrate, PCC (Octaplex®9) was given around 48 hours after thrombolysis. Eventually, the bleeding resolved with no further blood product support.

The patient was successfully extubated on day 5 and no further event of hypoxia occured. Only minimal haemoserous collection from the surgical drain was noted. The unfractioned heparin (UFH) infusion was commenced with a therapeutic target of APTT ratio between 1.5-2.0 for 48 hours with close monitoring. It was later switched to subcutaneous low-molecular-weight heparin (LMWH) since there was no recurrent bleeding complication. She made a remarkable recovery and was discharged home with rivaroxaban (Xarelto®) on day 9 post thrombolysis. In all her follow up clinic visits at 2 weeks, 4 weeks, and 8 weeks, no complications were noted. A repeated computed-tomography pulmonary angiogram was done before she commenced further cancer therapy which showed not evidence of thrombosis.

DISCUSSION

The clinical presentation and findings of both massive pulmonary embolism (PE) and acute myocardial infarct (AMI) are similar and could be indistinguishable, i.e. chest pain, acute dyspnoea, syncope, hypotension and sudden cardiorespiratory arrest.

Electrocardiogram could be helpful in diagnosing one from the other but it is neither sensitive nor specific especially in PE cases3. There are even reported cases where patients with ST elevation in ECG, and the

diagnoses were revised to pulmonary embolism after CTPA and this group of patients received tenecteplase.[4,5] Transthoracic echocardiogram (TTE) findings are valuable to guide in the diagnosis and management of PE. RV dilation, RV hypokinesia, presence of tricuspid regurgitation and elevated pulmonary artery pressure are the common findings. In our case, the clinical presentation (low cardiovascular risk, active cancer, recent major surgery), and RV dilation in TTE, made us revised the diagnosis of AMI to PE. It was further confirmed by CTPA finding.

The goal of treatment in massive PE is to rapidly reduce the RV afterload and prevent hemodynamic collapse and death. The approved and available fibrinolytic treatment for PE in our locality are IV streptokinase and IV altepase. However, the use of IV tenecteplase in this case successfully prevented the patient from further hemodynamic collapse due massive PE. Tenecteplase (Metalyse®) is a third-generation thrombolysis agent licensed for primary reperfusion in acute myocardial infarction but not for pulmonary embolism. Retrospectively looking at this case, tenecteplase was effective and lifesaving, and the bleeding complication was certainly compounded by the recent surgery. On the other hand, surgical thrombectomy in massive PE should only be reserved for those with absolute contraindication for thrombolysis and it also carries higher overall morbidity and mortality rate. Besides that, it also requires in-centre cardiopulmonary bypass capabilities

Bleeding is a well known complication in any thrombolysis therapy or anticoagulant. Nevertheless, management of bleeding patient with massive PE post thrombolysis with underlying active cancer is definitely very challenging. It requires meticulous evaluation between risks of clotting against bleeding. The ultimate aim of the management at that particular time is to control bleeding without increasing the risk of extension of thrombosis. In our case, the massive bleeding had continued beyond the plasma clearance of tenecteplase, and this has led to DIC. Reversal of thrombolytic effect options include blood products such as cryoprecipitates, FFP, and platelet, and PCC, recombinant activated factor VII (Novoseven®) as well as tranxenamic acid. The later options have relatively more prothrombotic preponderance.

The correction of anaemia and coagulopathy should achieve the parameter set in Table 1.

Table 1: Treat to target for massive transfusion protocol in SASMEC@IIUM

Lab parameters	target
Haemoglobin	> 8 g/dL
APTT ratio	< 1.5
PT ratio	< 1.5
Platelet count	> 50 x 10^9
Serum fibrinogen	> 150 mg/dL

The recommended dose of PCC is 25-30 IU/kg in dealing with bleeding secondary to thrombolytic agent. However, we used only a minimal dose of 500 IU (approximately 8-10 IU/kg) with consideration to minimize the thrombotic risk. PCC consists of human coagulation factor II, VII, IX, and X and are used in perioperative bleeding due to acquired deficiency of prothrombin complex coagulation factors such as Vitamin-K antagonist related coagulopathy or when rapid correction of the deficiency is needed. Although the incidence of pulmonary embolism is uncommon in PCC adverse effect profile, the propagation of existing PE or recurrence of PE was not mentioned and needs further evaluation.

Prompt decision on commencement on anticoagulation is crucial because the patient remains to be at high risk of VTE in spite of the recent bleeding. Anticoagulant was started after 48 hours upon resolvement of bleeding. UFH infusion was preferred at the initial phase due to its shorter half-life and reversibility. Our initial choice of anticoagulant was LMWH injection, but it was changed to the direct oral anticoagulant as it is now established to be the preferred option in cancer associated thrombosis (CAT). Duration of the anticoagulant in this case was at least 6 months and could be extended further to as long as the cancer is active or the presence of persistent risk of thrombosis.[7]

Surgical intervention to control the bleeding has limited value as the bleeding was coming from small vessels which could not be ligated. The main approach were

compression bandage and continuous vacuum dressing applied over the surgical site. The role of vacuum dressing was to prevent worsening of heamatoma that can potentially cause further breathing difficulty.

In conclusion, this case portrayed the complexity of managing a post-operative patient with cancer who developed massive pulmonary embolism and subsequently significant bleeding complication from the thrombolytic therapy. In this case, tenectaplase was eventually given as a primary reperfusion strategy for the massive pulmonary embolism, although it has only been studied in intermediate risk group in pulmonary embolism as a rescue reperfusion in PEITHO trial. It was a life-saving intervention but its complication was expected due to the recent mastectomy. The main principle in managing the complications is to have a fine balance between bleeding and thrombosis tendencies.

ACKNOWLEDGEMENT

Dato Dr. Abdul Hadi Bin Jaafar (Senior Cardiologist), Department of Anaesthesiology SASMEC@IIUM, Department of Surgery, SASMEC@IIUM.

REFERENCES

1. Gauruv Bose, Esteban Gandara, Marc Carrier, Petra Erkens, Marc Rodger, Philip Wells; Outcomes of Pulmonary Embolism In Surgical Patients: A Retrospective Cohort Study. Blood 2010; 116 (21): 3180.
2. Cohen AT, Agnelli G, Anderson FA, et al. Venous T hromboembolism (VTE) in Europe. The number of VTE events and associated morbidity and mortality. Thromb Haemost 2007;98:756-64
3. Ullman E, Brady WJ, Perron AD, Chan T, Mattu A. Electrocardiographic manifestations of pulmonary embolism. Am J Emerg Med. 2001;19(6):514–9.
4. Livaditis IG, Paraschos M, Dimopoulos K. Massive pulmonary embolism with ST elevation in leads V1-V3 and successful thrombolysis with tenecteplase. Heart. 2004;90(7):e41.
5. Zelfani S, Manai H, Laabidi S, Wahabi A, Akeri S, Daghfous M. Pulmonary embolism mimicking acute myocardial infarction: a case report and review of literature. Pan Afr Med J. 2019; 33:275. Published 2019 Jul 30.
6. Massive Transfusion Protocol https://litfl.com/ massive-transfusion-protocol/ (last accessed on 10 August 2020)
7. Farge D, Bounameaux H, Brenner B et, al. International clinical practice guidelines including guidance for direct oral anticoagulants in the treatment and prophylaxis of venous thromboembolism in patients with cancer. Lancet Oncol 2016;17:e452-e466.
8. 8.Martin, Colleen et al. "Systemic Thrombolysis for Pulmonary Embolism: A Review." P & T: a peer-reviewed journal for formulary management vol. 41,12 (2016): 770-775.
9. https://www.medicines.org.uk/emc/product/6566/ smpc- OCTAPLEX (last accessed on 10 August 2020)
10. https://www.drugs.com/uk/metalyse.html (last accessed on 10 August 2020)