# Treatment of massive right heart thrombi-in-transit and pulmonary embolism with low-dose ultra-slow tissue plasminogen activator in a patient with severe thrombocytopenia and cardiogenic shock

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## Introduction

Thromboembolic events have been reported in up to 8% of immune thrombocytopenic purpura patients (Takagi et al, 2015). Several studies have postulated the mechanisms underlying the paradoxical development of thrombosis in immune thrombocytopenic purpura, including elevated levels of platelet-derived micro particles (Jy et al, 1992).

This article reports a rare case of a patient with immune thrombocytopenic purpura presenting with right heart thrombi-in-transit and pulmonary embolism in extremis, managed successfully with low-dose ultra-slow infusion of tissue plasminogen activator.

## Case report

A 59-year-old man with known chronic obstructive pulmonary disease presented with a 2-week history of leg swelling and 1-week history of worsening breathlessness. His blood pressure on admission was 85/50 mmHg with a heart rate of 130 beats per minute. Clinical examination revealed significant peripheral oedema, gross ascites, bilateral lower limb bruising, widespread palpable purpura and notable left-sided calf swelling. A doppler ultrasound of the left lower limb confirmed a deep vein thrombosis. Electrocardiogram demonstrated sinus tachycardia with no ischaemic changes. His blood tests showed a white blood cell of $12 \times 10^9$/litre (normal range 4–$11 \times 10^9$/litre), haemoglobin 153 g/litre (normal range 130–180 g/litre), alanine transaminase 60 U/litre (normal range 7–55 U/litre) and platelet count $18 \times 10^9$/litre (normal range 150–$450 \times 10^9$/litre). Arterial blood gas on 6 litres of $O_2$ showed pH 7.30, pO2 5.7 Kpa, $pCO_2$ 7.8 Kpa, lactate 2.0 mmol/litre, $HCO_3$ 26 mEq/litre and $SaO_2$ 80%.

A transthoracic echocardiogram demonstrated a massive snake-like thrombi moving in and out of the right atrium and ventricle, and impaired right ventricular systolic functions. The left ventricular function was normal (ejection fraction 60%) (Figure 1a) (Video 1).

Thrombolysis was contraindicated in this patient because of his severe thrombocytopenia. Surgical embolectomy was considered, but the nearest surgical centre was over 3 hours away and there were no interventional facilities available on-site. Following a discussion with haematologists and starting 0.4 mcg/kg/min noradrenaline for cardiovascular support, low-dose ultra-slow tissue plasminogen activator infusion was selected as a potential life-saving intervention (25 mg infusion over 25 hours). A repeat transthoracic echocardiogram following this infusion showed a reduction in the thrombus burden, but clinically he remained in cardiogenic shock (Figure 1b) (Video 2).

A repeat low-dose ultra-slow infusion of tissue plasminogen activator (25 mg/25 hours) was given. This resulted in significant clinical improvement (blood pressure 110/70 mmHg, heart rate 90 beats per minute and oxygen saturation was 94% on 3 litres $O_2$). A repeat transthoracic echocardiogram demonstrated complete resolution of the thrombus (Figure 1c) (Video 3). At that point, the tissue plasminogen activator infusion was stopped and unfractionated heparin was continued for a week. A computed tomography pulmonary angiogram was performed once the patient was stable, which confirmed the presence of a bilateral pulmonary embolism and large left-sided pleural effusion (Figure 1d). The patient's platelet count slowly improved without any specific treatment, and once his platelet count had risen to over $70 \times 10^9$/litre (normal range 150–$450 \times 10^9$/litre), he was commenced on warfarin and subsequently safely discharged.

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## Case report (continued)

At 3 months, a follow-up transthoracic echocardiogram showed complete normalisation of right ventricular systolic function (Figure 2) (Video 4). Haematology consultation was sought, and further tests demonstrated normal viral serology, including hepatitis B virus, cytomegalovirus, human immunodeficiency virus and hepatitis C virus, Coombs negative, erythrocyte sedimentation rate 20 mm/hr (normal range 2–10 mm/hr), anti-nuclear antibody negative and Brucella negative. No atypical cells were observed in his admission peripheral smear screen, but two to three thrombocytes were seen in each region of the peripheral smear. Abdominal ultrasound demonstrated ascites but no hepatosplenomegaly. Consequently, following a thorough investigation, the patient was diagnosed with immune thrombocytopenic purpura as the aetiology of his severe thrombocytopenia. The pulmonary embolism was deemed to be 'pulmonary embolism with no risk', so anticoagulation was prolonged for 12 months.

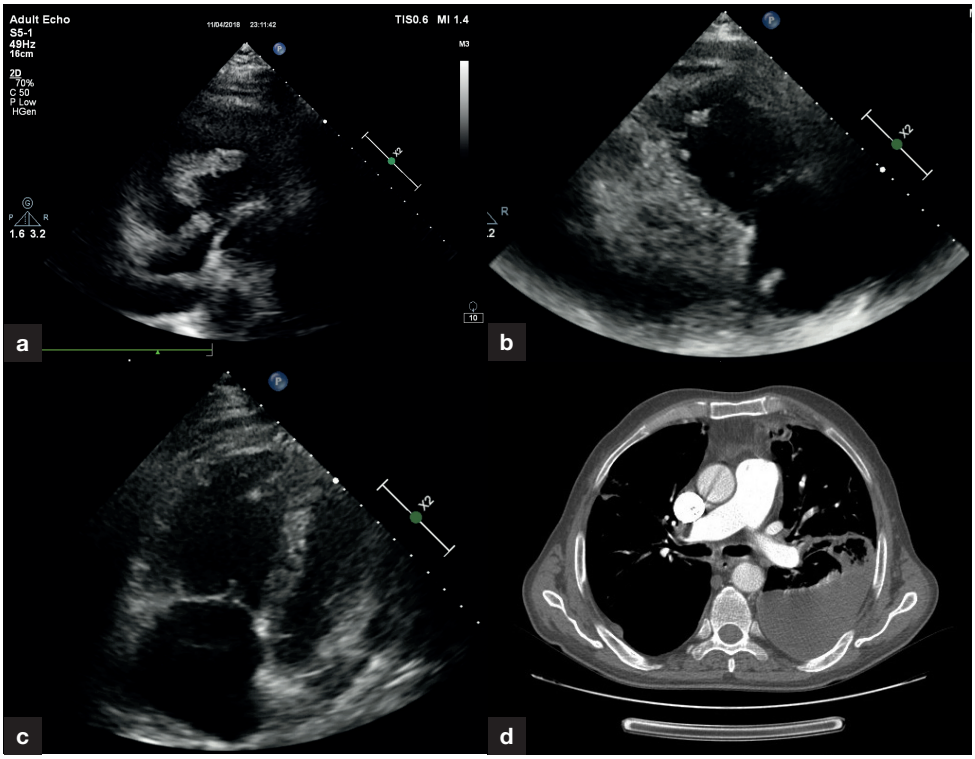


**Figure 1.** Transthoracic echocardiogram on admission showing (a) thrombus-in-transit in the right atrium and ventricle; (b) residual thrombus in the right atrium following the initial 25 mg tissue plasminogen activator over 25 hours; (c) complete resolution of thrombus in the right heart following administration of 50 mg tissue plasminogen activator over 50 hours; (d) computed tomography pulmonary angiogram confirming pulmonary embolism.

**[HMED_10.12968.hmed.2021.0196_Video 1]**

**Video 1.** Transthoracic echocardiogram on admission, thrombi-in-transit in the right atrium and ventricle

**[HMED_10.12968.hmed.2021.0196_Video 2]**

**Video 2.** Follow-up transthoracic echocardiogram, residual thrombus in the right atrium following the initial 25mg tissue plasminogen activator over 25 hours

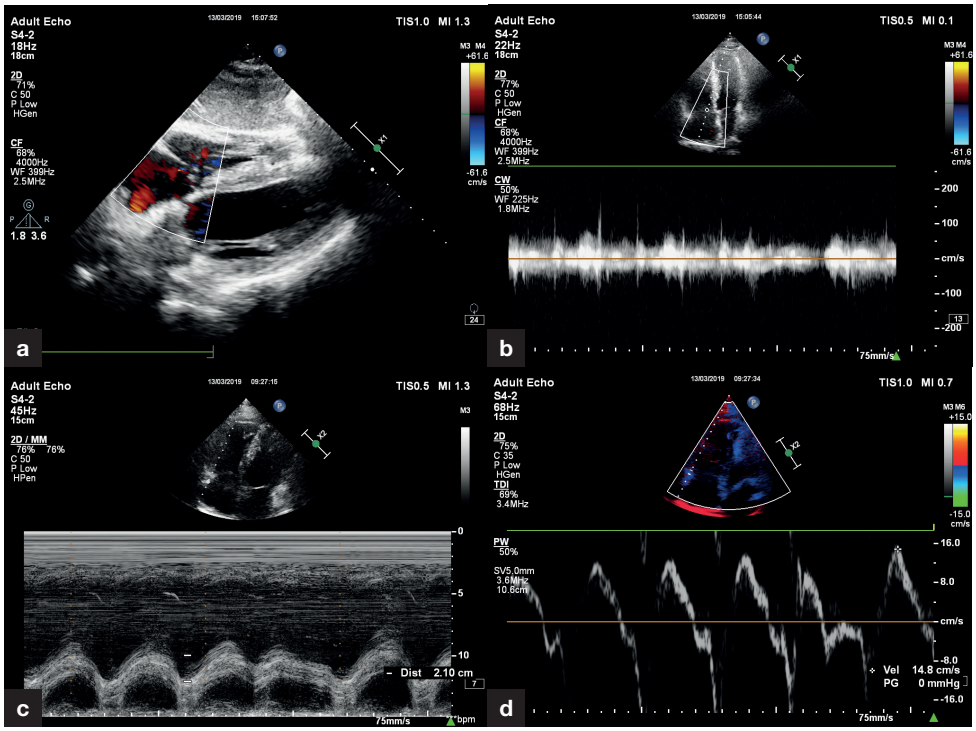


**Figure 2.** Follow-up transthoracic echocardiogram after 3 months. a. Subcostal view showing non-dilated right heart chambers with no significant tricuspid regurgitation. b. Normal pulmonary artery systolic pressure (20 mmHg). c. Normal right ventricular function assessed by tricuspid annular plane systolic excursion, (2.1 cm). d. Normal right ventricular systolic tricuspid annular velocity (14 cm/s).

**[HMED_10.12968.hmed.2021.0196_ Video 3]**

**[HMED_10.12968. hmed.2021.0196_Video 4]**

**Video 3.** Follow-up transthoracic echocardiogram, complete resolution of thrombus in the right heart following the administration of tissue plasminogen activator 50 mg over 50 hours.

**Video 4.** Follow-up transthoracic echocardiogram after 3 months, showing non-dilated right heart chambers with no significant tricuspid regurgitation

## Discussion

Immune thrombocytopenic purpura comprises a heterogeneous group of disorders characterised by autoimmune platelet destruction and is often associated with a higher risk of thrombosis, with the main treatment being with steroids (Cines et al, 2009; Sarpatwari et al, 2010). A case has been reported of a patient with immune thrombocytopenic purpura and a normal platelet count developing cardiac thrombus and pulmonary embolism, that was successfully treated with warfarin. However, this patient had several risk factors for thrombosis, including the use of eltrombopag (Andic et al, 2013).

This case highlights the successful use of ultra-slow low-dose tissue plasminogen activator in a patient with right-heart thrombus in-transit and pulmonary embolism, with severe thrombocytopenia and immune thrombocytopenic purpura. Similar management strategies have been used in patients with prosthetic valve thrombosis (Ozkan et al, 2018). Systemic thrombolysis is an alternative treatment which promotes thrombus lysis and improves

## Learning points

- Cardiac imaging is important in assessing thrombus burden and guiding diagnosis.
- The optimal management of thrombus-in-transit is emergency surgical embolectomy. However, low-dose ultra-slow tissue plasminogen activator can be a safe and viable option in patients with severe thrombocytopenia if surgery is not possible.

pulmonary reperfusion. In the current case, platelet transfusion was not given because of the absence of any active signs or symptoms of bleeding. As the patient presented in cardiogenic shock, ionotropic support was urgently initiated to stabilise the patient. A joint decision with haematology was made to not give platelets and to start an infusion of low-dose ultra-slow tissue plasminogen activator. Moreover, on admission and after thrombus resolution, thorough haematological investigations confirmed immune thrombocytopenic purpura. However, as the patient's platelet count improved spontaneously, there was no need for steroid therapy to treat immune thrombocytopenic purpura.

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