CASE REPORT

All contraindications to thrombolysis for life-threatening pulmonary embolus should be considered relative

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SUMMARY

Acute massive pulmonary embolism (PE) can be fatal; however, timely thrombolytic therapy can be life saving. Guidelines advocate the use of thrombolysis for massive PE in patients with an acceptable bleeding-risk profile. Nonetheless, estimating what constitutes an acceptable bleeding risk in those with life-threatening PE is a clinical challenge, and even contraindications considered 'absolute' may present lesser risk than leaving PE untreated. We discuss the case of a 77-year-old man who received thrombolysis for a massive PE 4 weeks following admission with a significant intracerebral bleed. There was rapid resolution of hypotension and hypoxia and he survived to be discharged home. This case is used to illustrate that no potential therapy should be discounted in patients faced with acute life-threatening PE. Decisions to thrombolyse patients with traditional contraindications—even those considered absolute—must be taken by clinicians able to weigh relative risks.

BACKGROUND

Acute pulmonary embolism (PE) is a potentially fatal complication of hospitalisation whose outcome varies substantially depending on the patient's condition.¹ Massive PE, defined as PE accompanied by persistent hypotension (systolic blood pressure <90 mm Hg) for longer than 15 min, pulselessness or profound bradycardia, is associated with a 90-day mortality rate of 52.4%.²

Thrombolysis in massive PE can be life saving.³ The advantages of thrombolysis are rapid stabilisation of cardiorespiratory function and reduction of right ventricular (RV) strain reducing the likelihood of RV damage and subsequent cardiogenic shock.⁴

Multiple consensus guidelines recommend thrombolysis in patients with massive PE with an acceptable bleeding profile.^{1 5 6} The risk of causing intracranial bleeding from thrombolysis is small but significant (1.9%) and may result in long-term disability if the patient survives.⁷ Given the potential for causing intracranial bleeding following thrombolysis, a recent haemorrhagic stroke has been cited as the most absolute contraindication to thrombolysis.⁸

Despite multiple guidelines, a clinician presented with a critical patient and incomplete diagnostic information can face challenging decisions. We report the case of successful thrombolysis for massive PE in a man with a recent intracerebral haemorrhage and the underlying clinical reasoning.

CASE PRESENTATION

A 77-year-old man was admitted with left hemiparesis and hemisensory loss. He had a history of hypertension and paroxysmal atrial fibrillation treated with aspirin, but was otherwise fit and previously independent. CT scanning of his brain on admission revealed a right thalamic haemorrhage (figure 1). He was admitted to an acute stroke unit for management and rehabilitation. His course was uneventful save for treatment for a suspected catheter-associated urinary tract infection.

One month into admission, his condition abruptly deteriorated. He became pale, agitated and reported severe thoracic back pain. He was found to be in shock (BP 65/40 mm Hg, HR 130 bpm, capillary refill time 4 s) and in respiratory distress (RR28 breaths/min, 64% SpO₂ on 2 L inspired O₂). He was afebrile. Clinical examination did not reveal any evidence of pulmonary oedema, consolidation or new heart murmurs, but jugular venous pressure was raised. Abdominal examination was unremarkable.

INVESTIGATIONS

A bedside ECG showed sinus tachycardia (133 bpm). White cell count and C reactive protein were not significantly elevated. Arterial blood gas analysis on 15 L/min inspired oxygen showed profound type 1 respiratory failure and metabolic acidosis (pH 7.29, pCO₂ 3.0 kPa, pO₂ 17 kPa, base

Figure 1 CT performed on admission showing right thalamic intraparenchymal haemorrhage.

To cite: Mercer RM, Bowen JST, Armstrong RJ. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-009724

excess -17, lactate 9.8). His calculated A-a O₂ gradient was 60.06 kPa. A chest radiograph was unremarkable.

CT of his chest with intravenous contrast demonstrated filling defects within the segmental pulmonary arterial branches of the left and right lower lobes, right middle and left upper lobes, and subsegmental branches of the right upper lobe consistent with multiple large volume pulmonary emboli (figures 2 and 3). There was no evidence of lung consolidation or other focus of infection.

DIFFERENTIAL DIAGNOSIS

The key differential diagnosis was PE, overwhelming sepsis or a combination of the two. However, the former was favoured due to the significant hypoxaemia along given the lack of clinical evidence of pneumonia.

TREATMENT

Initial fluid resuscitation corrected hypotension (to 106/80 mm Hg) and hypoxia (SpO₂ 96% on 15 L/min oxygen) but his tachycardia persisted. Intravenous morphine 5 mg was administered to treat back pain, dyspnoea and agitation.

While haemodynamic stability was maintained, frank discussions regarding the risks of thrombolysis in the event of further haemodynamic compromise were undertaken with the patient's family. It was agreed that in the event of further extreme haemodynamic compromise thrombolysis would be given, acknowledging the risks of extension of intracerebral bleed and death. Surgical or radiological embolectomy was not considered viable. The patient was involved in discussions although his acute agitation was felt to affect his capacity to agree to the treatment.

Five hours later he deteriorated and developed refractory shock (BP 65/42 mm Hg). He was moved to the coronary care unit where thrombolysis was administered with 10 mg alteplase intravenous bolus followed by 90 mg alteplase intravenous infusion over 2 h and intravenous heparin infusion.

OUTCOME AND FOLLOW-UP

Within 12 h of thrombolysis, his hypoxia and hypotension had improved (SpO₂ 98% on 2 L/minute oxygen by nasal cannulae,

Figure 3 CT pulmonary angiogram showing filling defects within segmental pulmonary arterial branches of the left and right lower lobes (circled), right middle and upper lobes and subsegmental branches of the right upper lobe.

BP 81/50 mm Hg). Clinical examination did not identify any new neurological deficit. A repeat CT did not show any new intracerebral haemorrhage; indeed some resorption of the previous haemorrhage was demonstrated (figure 4).

Intravenous heparin was continued for 24 h after which he was converted to low molecular weight heparin (LMWH) (175 units/kg). One week later, an inferior vena cava filter was inserted and the LMWH dose reduced to the standard prophylactic dose of 3500 units.

The patient was discharged home 1 month later with care visits four times daily. Although he was wheelchair-dependent he was able to enjoy completing the daily crossword and able to follow his favourite sport of hurling. Prior to his discharge he was asked if the decision to thrombolysed, despite the risk of intracerebral haemorrhage, had been appropriate. He was tearful and agreed emphatically that it was.

Figure 2 CT pulmonary angiogram showing filling defects within segmental pulmonary arterial branches of the left and right lower lobes (circled), right middle and upper lobes and subsegmental branches of the right upper lobe.

Figure 4 CT performed one day postthrombolysis showing no further haemorrhage with partial resorption of previous haemorrhage.

Three months later the patient died at home. The death was not considered suspicious and was not investigated by the coroner.

DISCUSSION

To our knowledge, this is the first case reported of a patient successfully thrombolysed for massive PE following a recent significant intracranial haemorrhage in the absence of cardiac arrest. Koroneos *et al*⁹ reported a successful outcome in the context of a pulseless electrical activity cardiopulmonary arrest in a patient with previous intracerebral haemorrhage.

There are additional reported cases of successful thrombolysis for PE despite contraindications including intracranial neoplasms, arteriovenous malformation and postcaesarean section.^{10–12} Nonetheless, in the presence of few case reports and no controlled studies, the absolute risk of thrombolysis for massive PE following an intracerebral haemorrhage is not known. Postulated contraindications to thrombolysis in PE are predominantly extrapolated from experience with acute myocardial infarction where the use of thrombolysis has a different risk:benefit profile to that of life-threatening PE.

This case highlights a fundamental challenge facing clinicians: that of determining the relative risk involved. These challenges are compounded when dealing with elderly patients: making therapeutic decisions despite diagnostic uncertainty and concurrent acute pathology; limitations to resources, expertise and guiding evidence; interpreting quality of life in the context of pre-existing morbidity and substantial care needs with unclear prognosis; disentangling patient wishes despite acutely impaired capacity; managing family expectations frayed by prolonged admission and acute deterioration; maintaining honest and empathetic communication despite clinical uncertainty.

We report this case with a favourable outcome while accepting that other clinicians placed in a similar position may not have chosen to administer thrombolytic therapy. (An audience of geriatricians polled following the presentation of this case at a regional British Geriatrics Society meeting yielded an approximately equal split of those who would or would not have administered thrombolytic therapy.) Advocating the rewriting of traditional contraindications to thrombolysis in PE would seem a facile conclusion to a complex case with no clear correct treatment. Rather, individualised decision-making, incorporating patient and family perspectives tempered by nuanced clinical interpretation seeking the best interests of the patient is likely to be the most appropriate approach in similar complex cases. This case serves to reiterate statements by the British Thoracic Society: “Contraindications to thrombolysis that are considered absolute *eg* in myocardial infarction might become relative in a patient with immediately life-threatening high-risk PE.”⁶

Learning points

- ▶ Thrombolysis for massive pulmonary embolism (PE) after recent haemorrhagic stroke can be life saving and may not cause haemorrhagic extension.
- ▶ Thrombolysis for massive PE in patients with a known contraindication should be considered on a case-by-case basis, while relative risks should also be carefully assessed.
- ▶ The risk of neurological disability should be clearly explained to any patient undergoing thrombolysis with intracranial pathology.

Contributors All authors listed above were involved in the identification and management of the reported case. RMM and JSTB were responsible for initial drafting and literature search. RJA was responsible for final editing and refinement. JSTB is the guarantor of this case report.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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