Massive pulmonary embolism treated with low-dose thrombolysis on the geriatric ward during the COVID-19 pandemic

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BACKGROUND
Since the start of the COVID-19 pandemic, our understanding of the multiorgan and systemic effects of COVID-19 has been continually evolving. Of particular note, multiple studies have shown an increased risk of thromboembolism with COVID-19. Furthermore, there are increased odds of mortality in patients with COVID-19 who present with thromboembolism.¹

Massive pulmonary embolism (PE), presenting with shock, persistent hypotension and/or signs of right heart strain, carries a significant mortality risk. Management of massive PE involves prompt diagnosis and anticoagulation, often with admission to the critical care unit for circulatory support.

Our case examines an elderly male patient who presented with a fall and tested positive for COVID-19. The patient subsequently developed a massive PE during admission, which was successfully treated with low-dose thrombolysis on the geriatric ward.

CASE PRESENTATION
A man in his 70s was brought by ambulance to the emergency department following a fall, on a background of alcohol consumption and 2 weeks of urinary incontinence. His medical history was significant for a stroke 3 years prior, moderate aphasia, gout, dyslipidaemia and hypertension.

The patient’s fall was ascribed to postural instability, and antibiotics were started for a concurrent urinary tract infection. His admission was complicated by a positive COVID-19 test, and he was treated for this with dexamethasone, prophylactic enoxaparin and supplemental oxygen. The patient subsequently suffered from a hypoactive delirium and decline in mobility that delayed his discharge.

While on the geriatric ward, the patient developed sudden onset dyspnoea, tachypnoea and hypoxaemia. His observations showed oxygen saturations (SpO₂) 85%–90% on 1 L O₂ via nasal cannulae, respiratory rate (RR) 24, blood pressure (BP) 83/54 and heart rate (HR) 121. On examination he was alert and responsive, Glasgow Coma Scale (GCS) was 14/15, airway patent, peripherally cool with a capillary refill time of 4 s, bilateral crepitations on his chest, normal heart sounds with no added sounds and his abdomen was soft and nontender. His blood glucose was 7.4.

INVESTIGATIONS
Blood tests showed a raised d-dimer, a raised troponin and a lactate of 7.4. An electrocardiogram (ECG) revealed a sinus tachycardia with a new right bundle branch block (RBBB) (figure 1).

A computed tomography pulmonary angiogram (CTPA) scan was performed which showed bilateral extensive pulmonary emboli with right ventricular strain and bilateral lower and upper lobe dependent subsegmental peripheral ground-glass opacification representing COVID-19 pneumonitis (figures 2 and 3).

A CT scan of the head was performed in order to rule out an intracranial event prethrombolysis. This was undertaken because the patient had an ongoing aphasia secondary to a previous stroke, and it was regarded as imperative to ensure that he had not had another stroke. The CT scan of the head showed no mass lesion or acute bleed. There was low attenuation in a periventricular fashion, in keeping with small vessel disease. Normal ventricular anatomy and posterior fossa were observed, and there were no vault abnormalities.

DIFFERENTIAL DIAGNOSIS AND TREATMENT
Intravenous fluids and treatment dose low-molecular-weight heparin were administered; however, the patient remained haemodynamically unstable. A differential diagnosis of PE and hospital-acquired pneumonia was considered, but a CTPA confirmed bilateral extensive PEs. The Pulmonary
Embolism Severity Index (PESI) Score gave a 10%–25% chance of 30-day mortality and a decision was made to thrombolys the patient on the ward. This procedure would ideally be performed in a higher dependency unit such as the ICU, but staffing and capacity constraints during the COVID-19 pandemic meant it had to be undertaken on the ward. The thrombolysis was performed in the presence of the ward consultant, a medical registrar, a core medical trainee, a foundation doctor and the critical care outreach team in order to provide the maximum amount of support possible.

The case was discussed with the thrombosis team who advised that half-dose thrombolysis be given to the patient, as he carried a significant bleeding risk given his advanced age and that he had previously been given a treatment dose of enoxaparin (140 mg) earlier in the day to no effect. A prethrombolysis CT scan of the head was performed, which was unremarkable, and a 10 mg bolus of alteplase was given, followed by 40 mg over the subsequent 1 hour.

Figure 1  ECG performed prior to thrombolysis, showing sinus tachycardia and a new right bundle branch block.

Figure 2  Transverse section of the CTPA scan image, which shows a large clot extending across the main pulmonary artery. The image slice is of poor quality as the patient was significantly breathless during the scan.

Figure 3  Coronal section of the CTPA scan image, which shows a large clot in the left pulmonary artery branch. The image slice is of poor quality as the patient was significantly breathless during the scan.
OUTCOME AND FOLLOW-UP
The immediate post-thrombolysis ECG showed sinus tachycardia with complete resolution of the RBBB (figure 4). Observations improved significantly and the post-procedure lactate was 1.7. A post-thrombolysis thoracic echocardiogram subsequently confirmed normal right ventricular structure and function with no signs of pulmonary hypertension.

The patient was discharged to his home 2 weeks later, with an anticoagulation clinic follow-up arranged for within 3 months. However, the patient’s functional status and mobility were significantly reduced on discharge following his prolonged hospital admission.

DISCUSSION
The association between COVID-19 and thromboembolism has been increasingly understood over the course of the pandemic. A retrospective observational study of 184 intensive care unit (ICU) patients with COVID-19 showed a 31% incidence of thrombosis.2 The pathophysiological link between the disease process and thrombotic complications is not fully understood, but it is believed to be due to dysregulated host immune response resulting in immunothrombosis,3 as well as endothelial disruption. Studies have shown that there is a significant risk of PE in particular as a complication of COVID-19,4 5 and this may in fact be the most frequent thrombotic complication of COVID-19.5

D-dimer, C-reactive protein (CRP), interleukin-2 receptor (IL-2R) and ferritin are noted to be significantly raised in severe cases of COVID-19, correlating with the severity of disease, as well as serum cytokine concentrations including interleukin-6 (IL-6), tumour necrosis factor-α (TNF-α) and interleukin-10 (IL-10).6 In addition, SARS-CoV-2 has a predilection for lung tissue, entering lung endothelial cells via the angiotensin converting enzyme-2 (ACE-2) receptor.7 Histological evidence from COVID-19 afflicted lungs shows increased ACE-2 receptor expression in endothelial cells, the presence of the SARS-CoV-2 virus within endothelial cells, perivascular inflammation and diffuse alveolar damage.6 These data combined are supportive of immune dysregulation and endothelial disruption being responsible for an increased thrombotic risk.

However, there is recognition however that COVID-19-associated coagulopathy (CAC) has features that distinguish it from sepsis-induced coagulopathy and disseminated intravascular coagulation, with CAC in particular exhibiting raised d-dimer and fibrinogen with little effect on prothrombin time and platelet count.9

The increased thrombotic risk associated with COVID-19 has led to changes in in venous thromboembolism (VTE) prophylaxis. The British Thoracic Society, as well as NICE and SIGN, recommends prophylactic dose low molecular weight heparin (LMWH) for standard risk patients and intermediate dose LMWH for higher risk patients (namely those requiring critical care beds).10 But the management guidelines of PE in the context of COVID-19 remain the same as for other cases. Therapeutic LMWH is recommended for non-massive PE, while thrombolysis should only be given in massive PE when confirmed via CTPA and/or echocardiography or on clinical suspicion if cardiac arrest is imminent.11

Post-thrombolysis complications can be severe, including haemorrhage and acute hypotension. Systemic thrombolysis for acute PE carries a 9.24% risk of major bleeding, with a higher risk (12.93%) in patients over the age of 65 years.12 Patients undergoing thrombolysis for stroke and severe venous thromboembolism require intensive monitoring during and post procedure. Guidelines frequently recommend patients be monitored in at least level 2 environments (high dependency unit, HDU), ideally in an ICU.

The COVID-19 pandemic has put unprecedented strain on healthcare systems both in the UK and worldwide. Huge controversy arose during the first and second waves over a lack of ventilators to match demand, an insufficient number of intensive care beds and an increased use of ‘do not attempt cardiopulmonary resuscitation’ (DNACPR) orders on older patients.
pressure on critical care services has in turn impacted patient care decisions and the treatment options available to them. The patient discussed in this case report had a previously agreed DNACPR order and was not regarded as suitable for intensive care management.

A treatment decision was made balancing the significant risk of adverse effects from thrombolysis outside of the HDU/ICU setting versus the likely poor outcome if the PE remained untreated. After consultation with the patient’s next of kin, consent was obtained for thrombolysis and subsequent monitoring to be performed on the ward. Low-dose thrombolysis was given to mitigate the significant bleeding risk given their advanced age and recent treatment with LMWH.

Use of low-dose thrombolysis has been explored previously in the ‘Moderate Pulmonary Embolism Treated With Thrombolysis’ (MOPETT) trial, which showed that low-dose tissue plasminogen activator (t-PA) is both safe and effective in treating moderate PE. A subsequent randomised control trial (RCT) has shown that the use of low-dose thrombolysis in submassive PE does not carry an increased bleeding risk when compared with LMWH. Despite this the role of thrombolysis remains uncertain in patient groups without haemodynamic compromise. A recent meta-analysis suggested that low-dose t-PA is superior to standard-dose t-PA in terms of bleeding risk, while maintaining similar efficacy. One RCT has found that low-dose t-PA may be as effective as standard-dose regimens in massive PE. Despite this the use of low-dose thrombolysis in treating massive PE is rare and not part of current treatment protocols. This report presents the case of a patient with massive PE who was successfully treated with low-dose thrombolysis. We suggest consideration should be given as to whether patients with a high bleeding risk may be given low-dose thrombolysis to treat massive PE, although further studies are required to fully assess the safety and efficacy compared with current treatments.

Massive PE is associated with significant mortality, and exact mortality estimates vary. A recent retrospective observational study estimated a 29.4% mortality for patients admitted to a London tertiary centre teaching hospital. According to European guidelines, mortality estimates for massive PE are 18%–65% overall and 20% if treated. Given the poor outcome associated with this disease process, the ability to deliver rapid and early treatment is crucial. In this case report, adaptation of existing treatment protocols by administering low-dose thrombolysis on a ward setting allowed for life-saving emergency treatment to be delivered to the patient, which they may not otherwise have had access to given the aforementioned burden of the COVID-19 pandemic has placed on the number of available intensive care beds and staff.

**Learning points**

- Pulmonary embolism (PE) should be considered a major differential diagnosis for patients with COVID-19 who rapidly deteriorate.
- Prompt assessment, diagnosis and treatment are key in treating life-threatening cases of pulmonary embolisms.
- During the second wave of COVID-19, there were significant limitations to high dependency unit/intensive care unit capacity. In such circumstances, adaptations should be made to treatment protocols depending on the risk versus benefit in individual cases.
- Low-dose thrombolysis may be a potential option in patients with massive PE who carry a significant bleeding risk.

**Contributors**

All authors conceived the idea for the case report together. TDS wrote the manuscript and all authors subsequently edited the manuscript. TDS and RY gained consent from the patient’s next of kin.

**Funding**

The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests**

None declared.

**Patient consent for publication**

Consent obtained from next of kin.

**Provenance and peer review**

Not commissioned; externally peer reviewed.

Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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