CASE REPORT

Fulminant pulmonary embolism with fatal outcome in a patient with low clinical prediction scores

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SUMMARY

We present a case of a 72-year-old man with submassive acute pulmonary thromboembolism. Pulmonary embolism severity index Score and common clinical risk stratification recommended systemic anticoagulation and a clinical course without complications was expected. A primary reperfusion strategy was not indicated by the current guidelines. Under established anticoagulation, the patient was found in cardiac arrest immediately after mobilisation from the bed the next morning. Right heart catheterisation under ongoing resuscitation revealed a complete obstruction of the right pulmonary artery by a big thrombus. Catheter-directed intervention trying to bypass the thrombus with interventional guidewires failed. Ultimately, the patient died from acute right heart failure. The current case raises concern that the prediction scores available for pulmonary embolism may insufficiently predict short-term outcome in isolated patients.

BACKGROUND

Pulmonary embolism (PE) is a frequent disorder, often seen in emergency departments worldwide. Because of varying extent of pulmonary artery obstruction and consequently afterload failure of the right ventricle, its management is often challenging. Several well-validated risk scores are available to predict clinical outcome in these patients. We report this case to raise awareness among the medical community that these prediction scores may fail in isolated patients.

CASE PRESENTATION

A 72-year-old patient presented himself with chest pain radiating to his left arm and progressive dyspnoea over the past few weeks. He had a history of a deep vein thrombosis of the lower limb and controlled arterial hypertension. There were no other relevant comorbidities.

On physical examination, the patient presented himself in good general condition without signs of heart failure, a blood pressure of 156/101 mm Hg and a heart rate of 73 bpm. He was eupneic and the arterial oxygen saturation was 93%. Renal function was impaired with a serum creatinine of 115 µmol/L and an estimated glomerular filtration rate of 54 mL/min/1.73 m², high-sensitivity troponin T was slightly elevated at 29 ng/L and NT-proBNP significantly increased at 5463 ng/L. The ECG (figure 1A) showed newly diagnosed atrial flutter with an irregular heart rate of 93 bpm, as well as anterior and

inferior repolarisation disorders (T-wave inversion in II, III, aVF, V1–V4). CHA₂DS₂-VASc Score was of 4 points.

Transthoracic echocardiography showed normal left ventricular ejection function (LVEF 55%), a slightly impaired right ventricular function (Tricuspid annular plane systolic excursion (TAPSE) 18 mm), and increased pulmonary arterial pressure (sPAP 47 mm Hg). A bicycle stress test was performed and showed a relevant blood pressure drop from 138/74 mm Hg at rest to 118/76 mm Hg at 67% of the age-predicted maximal heart rate.

Based on these findings, relevant coronary disease was expected, probably with left main disease (based on the blood pressure drop in the stress test).

PE was a possible differential diagnosis (Wells Score of 4.5 points predicted a moderate risk with a 16.2% chance of PE). Anticoagulation was already indicated due to atrial flutter.

The newly documented atrial flutter was seen as associated with the underlying disease. There were no signs of neurological abnormalities.

INVESTIGATIONS

The coronary angiogram revealed a coronary two-vessel disease followed by ad hoc percutaneous coronary intervention with complete revascularisation. Right heart catheterisation, performed because of the slightly increased sPAP, revealed an elevated mean PAP (mPAP) of 38 mm Hg of precapillary and postcapillary origin. Pulmonary angiogram showed thromboembolic occlusion of the subsegmental pulmonary artery of the right lower lobe (figure 2A). Arterial blood gas analysis showed respiratory alkalosis, partly metabolically compensated (pH 7.49, pCO₂ 3.4 kPa, pO₂ 11.7 kPa, HCO₃ 19.5 mmol/L, base excess –3.8 mmol/L).

TREATMENT

The patient was then admitted to the coronary care unit (CCU) where dual antiplatelet therapy (DAPT) with aspirin and clopidogrel, as well as oral anticoagulation with apixaban was started.

Haemodynamic monitoring on the CCU was acceptable with a blood pressure of 140/100 mm Hg, heart rate of 85 bpm, respiratory rate of 17/min and SO₂ 94% in ambient air. CT of the thorax on the following day confirmed the PE with extensive, bilateral, central to peripheral PEs (figure 3). These findings were progressed compared with the results of the pulmonary angiography from the day before. In a further

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Figure 1 ECG. (A) At time of presentation: newly diagnosed normocard atrial flutter. (B) Shortly before resuscitation: compared with the ECGs before, there is a new complete right bundle branch block.

assessment, the only additional change was a newly diagnosed right bundle branch block (RBBB) and a change of the heart axis in the ECG (figure 1B). The patient was still without any discomfort or signs of cardiopulmonary instability and the arterial blood gas examination was unchanged.

During a falling after independent mobilisation on the CCU, the patient developed circulatory arrest with pulseless electrical activity (PEA). Immediate cardiopulmonary resuscitation was started. During resuscitation, right heart catheterisation was performed, which showed an occlusive thrombus in the right pulmonary artery and was found impossible to mobilise by interventional techniques (figure 2B).

OUTCOME AND FOLLOW-UP

After 45 min of mechanical resuscitation, the patient developed a flatline in the ECG. Based on the recent finding in the pulmonary angiogram and the already prolonged and unsuccessful mechanical resuscitation, return of spontaneous circulation was very unlikely and the resuscitation efforts were stopped, on which the patient died.

DISCUSSION

PE is a common and potentially lethal cardiovascular condition with a wide range in necessity of treatment and in mortality. PE

Figure 2 Angiography of the right pulmonary arteria. (A) At time of presentation: (star, white arrow) small parietal thrombus. (B) At time of resuscitation: (black arrow) a big thrombus is completely obstructive in the right pulmonary artery.

Figure 3 CT. (A) Massive central pulmonary embolism on both sides. (B) Complete obstruction of the right pulmonary artery by a thrombus.

accounts for 5%–10% of in-hospital deaths in the western world and up to 10% of all patients with acute PE will die within 3 months after diagnosis.¹

In cases of sudden cardiac arrest, PE is found in 2.8%–4.8%.^{2,3} If presenting with initial PEA, PE is reported in 36% of the cases.⁴ In case of an additional cardiopulmonary arrest, the mortality of massive PE is reported as high as 65%.⁵

To distinguish high-risk PE from less serious conditions, the well-validated *pulmonary embolism severity index (PESI)* is used in emergency departments. With <85 points based on 11 clinical parameters, the 30-day mortality is <3.5% and an outpatient management could be considered. On the other hand, with >125 points, the 30-day mortality goes up to 24.5% and the patient should be monitored on an *intensive care unit (ICU)*.⁶

In the presence of shock or relevant hypotension, the patient is at high risk and primary reperfusion should be performed without any delay (Evidence Class I, Level C).⁷ If there are signs of right-ventricular dysfunction in CT or echocardiography and elevated cardiac biomarkers are found without signs of haemodynamic decompensation, it is an intermediate-high-risk situation. The best management then is still not sure, since several studies found controversial results. For example, the The Pulmonary Embolism Thrombolysis Study (PEITHO) Investigators found in patients with intermediate risk under systemic thrombolysis a decrease of haemodynamic collapse within 7 days, but all-cause mortality was not reduced because of a significant increase in bleedings.⁸ In a systematic review and meta-analysis, Marti *et al* found a reduction in PE-associated mortality in intermediate-risk patients when treated with thrombolytic therapy, but in studies including low-risk patient as well, mortality of PE was not significantly affected.⁹ Following the guidelines of the *European Society of Cardiology (ESC)*, thrombolytic therapy should be considered for patients with intermediate-high-risk PE and clinical signs of haemodynamic decompensation (Evidence Class IIa, Level B). Otherwise, anticoagulation should be started immediately and haemodynamic monitoring may be considered.⁷

Still unclear is the prognostic value of the findings in CT. Several studies found controversial results.^{10,11} One prospective,

multicentre study found the *CT obstruction index* to be associated with the PE-related but not with the overall mortality after 90 days. The ratio of the right and the left ventricular (RV/LV) diameter was neither associated with overall nor PE-related 90-day mortality.¹²

Systemic thrombolysis is the most frequently used strategy to achieve primary reperfusion. However, it is a potentially harmful treatment with an increased risk of major and non-major bleeding.^{8,9,13,14}

Alternatively, a catheter-directed intervention may be considered if the anticipated risk of bleeding under a systemic thrombolysis is high.⁷ The role of catheter-based therapies still needs to be further evaluated. The The Ultrasound Accelerated Thrombolysis of Pulmonary Embolism Study (ULTIMA) Study showed decreased RV/LV ratio at 24 hours and after 90 days in ultrasound-assisted catheter-directed thrombolysis for acute intermediate risk PE compared with heparin alone, without any increase in bleeding complications.¹⁵ In a retrospective review, the catheter-directed treatment resulted in faster restoration of RV function and shorter ICU stay, however, at the cost of higher complication rates. In submassive PE, the midterm outcomes are similar compared with anticoagulation alone in this study.¹⁶ No randomised trials have compared systemic thrombolysis versus catheter-assisted primary reperfusion yet. The ESC and the American College of Chest Physicians (ACCP) Guidelines therefore favour systemic thrombolytic treatment over percutaneous catheter-directed treatment if the anticipated risk of bleeding under thrombolytic treatment is not elevated (Evidence Class IIb, Level B respective Grade 2C).^{7,17}

Surgical pulmonary embolectomy seems to be a reasonable option, if performed early in patients with acute massive PE without profound cardiogenic shock or cardiac arrest.¹⁸ Sareyyupoglu *et al* reported in a small study a 78% early and 67% long-term survival rate in these severely compromised patients.¹⁹ But the surgical procedure performed in this study included cardiopulmonary bypassing with aortic and bicaval cannulation, massage of the lung with bilateral pleurotomies and filters placed in the inferior vena cava, performed by a

well-trained, always available team. Therefore, surgical pulmonary embolectomy should be reserved for trained centres.

The descriptive case is an example for failure of the evidence-based forward-looking systems and standard treatment. As long as our patient had normal vital signs, his PESI score reached 82 points. Following the guidelines, he could have been managed as an outpatient with systemic anticoagulation alone.

After the first catheter-based intervention, anticoagulation was started and the patient was monitored in our CCU. Following current guidelines, no systemic thrombolysis was performed at this time.^{7 17}

There was an obvious progression between the findings seen in the first right heart catheter intervention (figure 2) and the findings in the CT imaging (figure 3) 12 hours later. In the meantime, there must have been additional embolisation of a second, larger thrombus, most likely from the leg, although the patient had 10 000 units of heparin during the first catheter intervention and apixaban was started.

After the CT showed the submassive central PE, a new RBBB (figure 1) was documented. The patient still declared no symptoms and the vital parameters were stable. The arterial blood gas analysis was unremarkable, with normal oxygenation and normal metabolism. Thereby it was unclear, if the elevated cardiac biomarker were related to the coronary artery disease with percutaneous intervention and stent implantation the day before. Based on these findings a conservative management with oral anticoagulation alone and monitoring of the vital parameters was favoured over the primary reperfusion strategy by an interdisciplinary team of physicians.

In the meantime, the patient mobilised himself, fell unwitnessed and was found in cardiac arrest. Because he hit his forehead when collapsing, systemic thrombolysis was associated with an elevated risk of intracranial bleeding and catheter-directed primary reperfusion under ongoing resuscitation was performed. The angiography showed a large, completely obstructive thrombus in the right pulmonary artery (figure 2B). Transthoracic echocardiography demonstrated a massive right heart forward failure with conclusive preload failure of the left ventricle. Bypassing the thrombus with a catheter and catheter fragmentation to restore pulmonary circulation was unsuccessful.

Learning points

- Severe pulmonary embolism is associated with a high mortality and demands immediate assessment and treatment.
- Haemodynamically unstable patients require primary reperfusion; in patients with intermediate high risk, reperfusion should be considered.
- If reperfusion is indicated, systemic lysis, catheter-associated or surgical reperfusion are possible.
- The significance of catheter-associated and surgical reperfusion remains unclear; international guidelines recommend systemic lysis if the anticipated risk of bleeding under thrombolytic treatment is not elevated.
- Clinical risk scores predicting low complication rates cannot exclude a tragic clinical course in isolated patients.

PESI Class II has a 30-day mortality of up to 3.5%. This report describes an especially impressive case of this statistically irrelevant circumstance.

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