ESC European Society of Cardiology

European Heart Journal - Case Reports (2024) **8**, ytae133
https://doi.org/10.1093/ehjcr/ytae133

CASE REPORT
Heart failure

Pulmonary embolism with paradoxical embolization to right coronary artery in the presence of a large patent foramen ovale: a case report

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Received 6 February 2023; revised 28 February 2024; accepted 13 March 2024; online publish-ahead-of-print 15 March 2024

Background Pulmonary embolism (PE) is the leading cause of in-hospital death and the third most frequent cause of cardiovascular death. The clinical presentation of PE is variable, and choosing the appropriate treatment for individual patients can be challenging.

Case summary A 64-year-old man presented to hospital with acute chest pain, shortness of breath, and pulmonary oedema. Electrocardiogram revealed ST-elevation myocardial infarction. D-dimer was 18.8 mg/L fibrinogen equivalent units (FEU) (normal <0.64), and troponin was 25 (normal 5–14 ng/L). After systemic thrombolysis, respiratory failure persisted, and the arterial blood gas showed PaO_2 of 6.0 kPa (normal 10.5–13.5 kPa), with 100% oxygen delivery via high-flow nasal cannula. A computed tomography diagnosed bilateral lobar PE, and coronary angiogram showed multiple thrombus in the right coronary artery. A bubble study with thoracic echocardiogram revealed a large right–left inter-atrial shunt. The patient denied treatment with extracorporeal membrane oxygenation and surgical thrombectomy. With no access to percutaneous catheter-directed thrombectomy, the patient received three separate thrombolysis treatments followed by a continued infusion for 22 h. After 6 weeks in hospital, the patient was discharged to rehab.

Discussion For a long time, PE has been largely seen as a medical disease. Intra-cardiac shunts such as patent foramen ovale can complicate thrombo-venous disease and introduce paradoxical shunts leading to arterial emboli and persistent hypoxaemia. Over recent years, modern percutaneous catheter-directed thrombectomy has been developed for both high-risk and intermediate to high-risk PEs. Thrombectomy might improve right ventricular function and haemodynamics, but there is lacking evidence from randomized trials on efficacy, safety, and long-term outcome.

Keywords Case report • Pulmonary embolism • Right ventricular infarct • Systemic thrombolysis • Patent foramen ovale • Right to left shunt • Catheter-directed thrombectomy

ESC curriculum 3.4 Coronary angiography • 7.1 Haemodynamic instability • 7.3 Critically ill cardiac patient • 9.5 Pulmonary thromboembolism • 6.7 Right heart dysfunction

Learning points

- Nuanced clinical presentation of an acute pulmonary embolism (PE) with concomitant patent foramen ovale.
- Case-based discussion of different treatment options for intermediate to high-risk PE.
- Continuous systemic thrombolysis has not been studied, and its use as a rescue therapy is uncertain.

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Handling Editor: Andrew Peter Vanezis
Peer-reviewers: Aiste Monika Jakstaite; Dmitry Duplyakov
Compliance Editor: Polyvios Demetriades

Introduction

Venous thromboembolism, clinically presented as deep vein thrombosis or pulmonary embolism (PE), is the third most frequent acute cardiovascular syndrome following myocardial infarction and stroke.[1] As the population ages and cancer becomes more prevalent, incidents of PE rise.[2] In acute PE, risk stratification based upon patient haemodynamics, the simplified PE severity index, and right ventricular (RV) dysfunction guide therapy. For high-risk PE, there is a Class I recommendation for systemic thrombolysis. Moreover, extracorporeal membrane oxygenation (ECMO) should be considered in combination with surgical embolectomy or catheter-directed treatment (CDT) in patients with refractory circulatory collapse or cardiac arrest. For intermediate to high-risk patients characterized by RV dysfunction and elevated circulating cardiac biomarkers, systemic thrombolysis is reserved as a rescue therapy in case of circulatory deterioration, where CDT denotes a Class IIa recommendation.[3] Full-dose systemic thrombolysis is a potentially life-saving treatment, but it also increases the risk of life-threatening bleeds; hence, percutaneous thrombectomy strategies are growing in number and currently under scientific and clinical investigation.[4,5] We here introduce a case of PE with paradoxical embolization to the right coronary artery (RCA) in the presence of a large patent foramen ovale (PFO) with persistent refractory hypoxaemia and hypertension.

Summary figure

Timeline	Clinical event
Past medical history	Long-standing essential hypertension. Previous minor stroke with no present sequela. Varicose veins ligation and stripping
Hospital admission	Acute shortness of breath, hypertensive pulmonary oedema, and substernal chest pain
First hour	Profound hypoxaemia, inferior ST-elevation. High D-dimer and low troponin. Transfer to intensive care unit (ICU) for ventilatory support. Echocardiogram: acute right ventricular (RV) strain and positive McConnell sign. Systemic thrombolysis
Day 1	Refractory hypoxaemia and persistent hypertension. The need for 100% FiO_2 with high-flow nasal oxygenation. Rising troponin values and suspected RV infarction
Day 2	Transthoracic echocardiography with an inter-atrial shunt. Computed tomography with bilateral lobar pulmonary emboli. Coronary angiogram with right coronary artery thrombus
Day 3	Extracorporeal membrane oxygenation contact. Surgical thrombectomy and catheter-directed treatment discussion
Day 5	Second thrombolysis
Day 7	Third thrombolysis
Day 9	Continuous systemic thrombolysis
Day 12	Discharged from ICU to cardiac ward
Day 31	Hospital discharge to cardiac rehab facility

Case presentation

A 64-year-old man visited the emergency department with acute respiratory distress and hypertensive pulmonary oedema. He complained of substernal chest pain without radiation. Saturation was 50% in room air, and blood pressure was measured at 190/100 mmHg. A physical examination showed normal heart sound, no murmur, and lung auscultation with rhonchi. An electrocardiogram showed sinus tachycardia, inferior Q waves, and ST-elevation inferior-anteriorly with reciprocal changes in lateral leads (*Figures 1* and *2*). Transthoracic echocardiography revealed an acute RV strain and positive McConnell sign, and a rapid Covid-19 antigen test was negative. The arterial blood gas showed metabolic alkalosis, normal lactate, and a PaO_2 of 6.0 kPa (normal 10.5–13.5 kPa), with the administration of 0.9% of FiO2 (normal 0.21%). Blood tests revealed normal renal function and electrolytes, N-terminal prohormone of brain natriuretic peptide of 900 ng/L (normal <300 ng/L), D-dimer of 18.8 mg/L FEU (normal, adjusted for age <0.64 mg/L), and a high-sensitivity troponin of 25 ng/L (normal 5–14 ng/L).

The patient was transferred to the intensive care unit for non-invasive ventilation with bilevel positive airway pressure (BiPaP). He was also started on nitroglycerin infusion and given a loop diuretic. With laboratory findings and clinical signs of a PE, systemic thrombolysis was given followed by a heparin infusion. Serial troponins increased by the hour and peaked at 14 000 ng/L, 12 h after admission. With concern and suspicion of an acute RV, myocardial infarction heparin was bridged to tinzaparin with a full dose (175 anti-Xa units/kg) in addition to concomitant loading with clopidogrel and aspirin at 300 mg each. The patient was treated with both BiPaP and a high-flow nasal oxygen device and was judged to be on the verge of intubation. With 60 L of flow per minute at 100% oxygen, the PaO_2 remained low and fluctuated between 6 and 7 kPa. With the impression of acute PE, RV infarction, hypoxia, and conflicting hypertension in the absence of circulatory shock, radiology and acute coronary angiography were postponed.

On the second day with no significant improvement in oxygenation, a computed tomography (CT) was performed that revealed widespread bilateral lobar PE with the engagement of the lower lobes. Transthoracic echocardiography showed an increased RV:left ventricular (LV) ratio, a flattening of the inter-ventricular septum, a tricuspid annular plane systolic excursion of 9 mm, and a McConnell sign. An indirect systolic pulmonary arterial pressure of 35 mmHg and preserved LV function were also detected. A bubble study with agitated saline contrast showed an intra-cardiac shunt in line with the refractory hypoxaemia. A coronary angiography showed distal filling defect and multiple thrombi in the RCA, consistent with a paradoxical embolus in the presence of a potential right to left shunt (see Supplementary material online, *Videos S1–S4*). The left coronary artery and circumflex artery were patent, and aspiration thrombectomy and local intracoronary thrombolysis were given. Radiology of the chest, abdomen, and brain revealed no neoplasm. Pulmonary artery catheterization and a transoesophageal echocardiogram were not performed out of concern for arrhythmia and worsening hypoxia.

The ECMO team was consulted for an awake imposition and bridge to thoracic surgery. They did not believe that treatment with ECMO was likely to be of benefit at that juncture. Surgical thrombectomy could not be performed since the location of the embolus was not within surgical reach. At the time of the present case, there was no access to a novel percutaneous catheter thrombectomy device. Milrinone was continuously infused, and brief pauses in treatment caused rapid worsening of the hypoxaemia. On the fifth day after no clinical improvement, dual antiplatelet therapy was discontinued, and a secondary thrombolysis of 50 mg (100 mg over 2 h) was infused. With no clinical improvement, a joint decision was taken together with the experienced ECMO team and senior bleeding/coagulation specialists to try an 'off-label' approach with additional attempts at thrombolysis; a third round

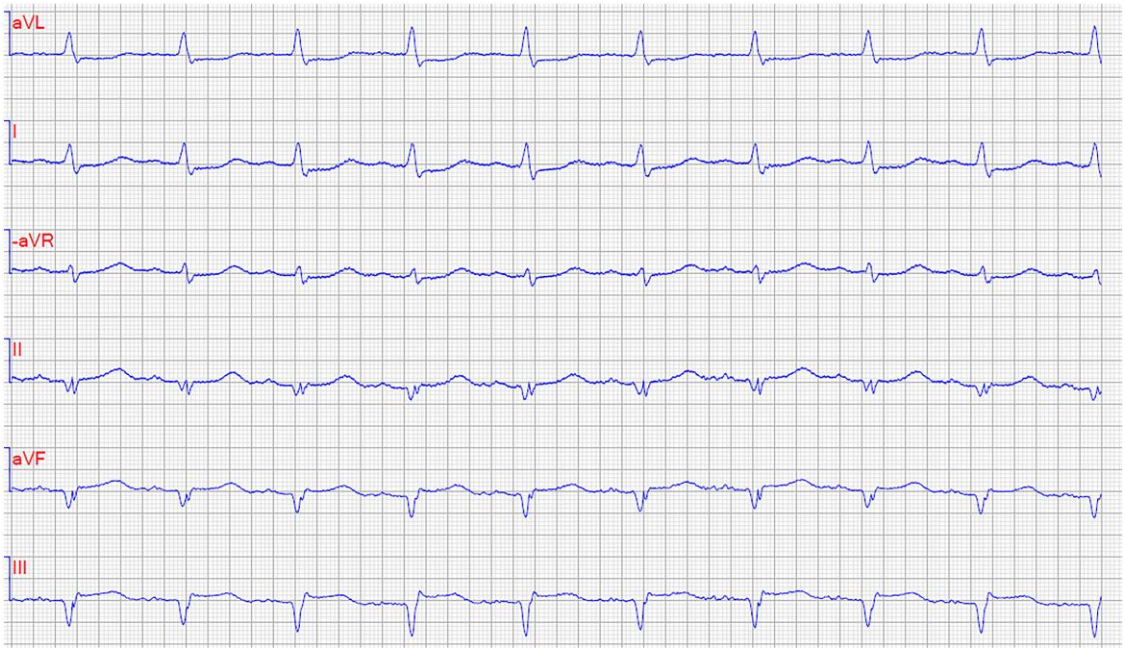

Figure 1 Admission ECG, limb leads: inferior Q waves and ST-elevation.

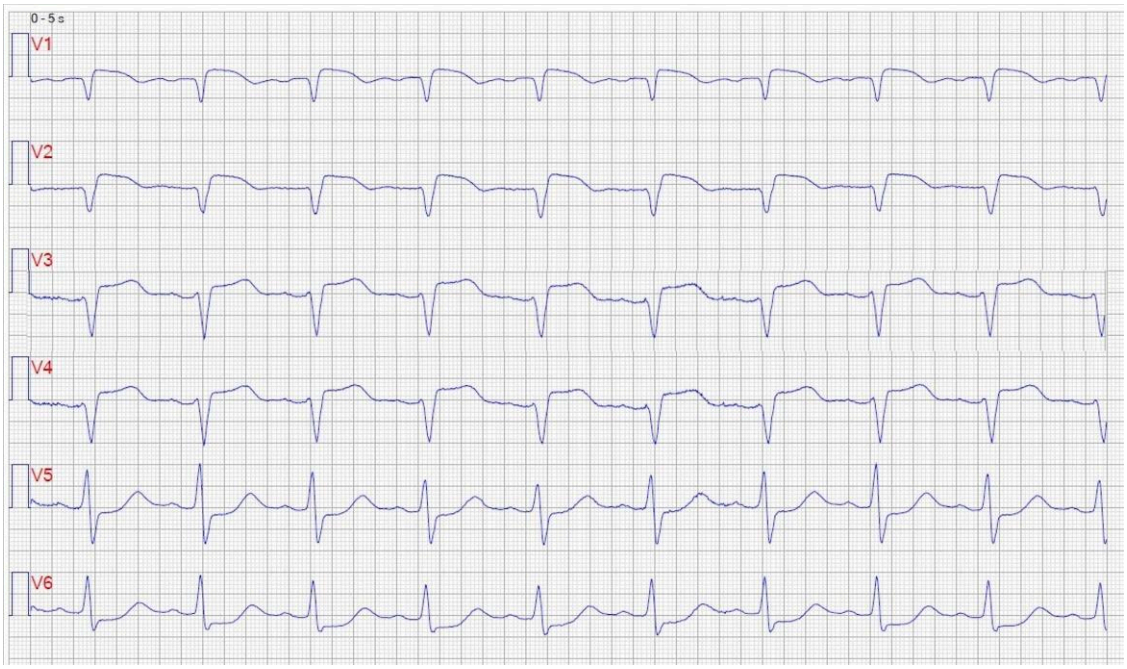

Figure 2 Admission ECG, precordial leads: anterior ST-elevations with reciprocal lateral ST-depression.

of 50 mg was also given. Each systemic lysis resulted in a brief period of increased PaO_2 but with a rapid return of pronounced hypoxaemia. Finally, a bolus of alteplase 50 mg was given over 2 h, followed by an infusion of 2 mg/kg for 24 h. During the continued treatment, the patient experienced transient dysarthria. An immediate CT of the head revealed no bleeding, and the infusion was resumed. After 22 h of systemic thrombolysis, the treatment was stopped due to emerging petechiae. After 12 days in the intensive care unit, all interventional and surgical options were exhausted. The patient slowly improved over time and was eventually discharged to a common cardiac ward with

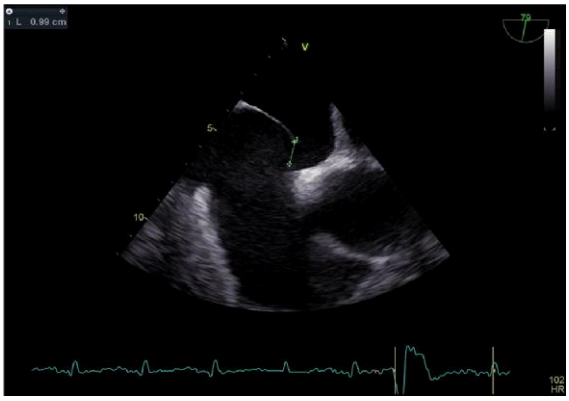

Figure 3 Transoesophageal echocardiography: multi-planar, two-dimensional, transoesophageal, bicaval view (79°) identifies a large patent foramen ovale (0.99 cm).

6 L of supplement oxygen on nasal cannula. Ventilation improved steadily, and a transoesophageal echocardiography could be performed, verifying a large PFO (9.9 mm; *Figure 3*). The condition improved to the point where he was ambulatory and discharged to a cardiac rehab facility after 6 weeks in hospital.

Discussion

To the best of our knowledge, this is a rare case triad of an acute PE, a large PFO together with a right to left inter-atrial shunt with a subsequent embolic myocardial infarction to RCA, presenting refractory hypoxaemia and paradoxical persistent hypertension.

Most patients with acute PE die from a haemodynamic death due to RV failure[3] and circulatory collapse. Usually, in a patient with PFO, potential shunting is left to right due to the normal pressure differences between the RV and LV. However, in some instances, flow may be reversed and cause hypoxaemia. In our case, we believe the LV received enough shunt volume because of increased RV pressure, caused by high pulmonary arterial pressure secondary to the large PEs. With preserved LV volume, cardiac output was maintained, and together with untreated hypertension and high catecholamines, this state enabled continuous hypertension.

Our case presented several clinical challenges and limitations. Any physical movement by the patient caused profound desaturations that took several minutes to recover from. The severe hypoxia in combination with RV failure put both intubation and coronary angiography on hold during the first 24 h due to a fear of a hypoxic cardiac arrest. Extracorporeal membrane oxygenation was discussed early on, but the patient denied awake imposition and a bridge to surgical thrombectomy since the location of embolus was estimated as out of surgical reach. At the time, there was no access to catheter thrombectomy devices. Surgery is often seen as salvage therapy. A retrospective review by Goldberg et al.[6] showed safety and improvement in RV function with the surgical management of intermediate to high-risk PE. However, volume is low, and large variations exist between countries. The continuous infusion of thrombolytics was chosen based on multi-modality expertise as a rescue therapy when all other options had failed.

For a long time, PE has largely been seen as a medical disease. Systemic thrombolysis is the only treatment with mortality benefit with the downside being major bleeding and intra-cranial haemorrhaging.[7] Many PE patients are also excluded due to neoplasm or by relative contraindication. Continuous systemic thrombolysis as performed in our case has not been studied.

For high-risk and intermediate to high-risk PEs with haemodynamic deterioration, CDT holds a Class IIa recommendation.[3] Removal of the thrombus enables reduction of RV stress and improves haemodynamics,[8] with one caveat being the lack of randomized trails. CDT knowledge is based on registries, and single-arm and retrospective studies[9] examining primarily surrogate endpoints, RV to LV ratio, pulmonary artery pressure, and improved haemodynamics, as in the FLARE study.[10] At the time of the case, CDT was not available in our institution, but the FlowTriever system has since been implemented. We believe that an early percutaneous thrombectomy could have improved our patient's status and likely prevented the use of repeated systemic thrombolysis, if it had been at our disposal.

Lead author biography

Erik Boberg is currently a resident in anaesthesia and intensive care and a PhD student at the Center for Resuscitation and Science Karolinska Institute, Södersjukhuset, Stockholm, Sweden.

Supplementary material

Supplementary material is available at *European Heart Journal—Case Reports* online.

Acknowledgements

None.

Consent: The written informed consent for publication was obtained from the patient and conforms with COPE guidelines.

Conflict of interest: None declared.

Funding: None declared.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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