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Case Report

Paradoxical Coronary Embolization After Massive Pulmonary Embolism Treated with Extracorporeal Membrane Oxygenation

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Introduction

High-risk pulmonary embolism (PE) is a relatively rare cause of intensive care unit (ICU) admission, with an overall in-hospital mortality rate of approximately 14%.[1] Treatment of high-risk PE includes reperfusion therapy (in the absence of contraindications) and hemodynamic support, depending on the severity of the situation. Mechanical circulatory support with venoarterial extracorporeal membrane oxygenation (VA-ECMO) may be considered if standard treatments are insufficient to ensure adequate O_2 delivery, or if cardiac arrest occurs.[1] Furthermore, coronary embolization is a rare but well-recognized cause of acute coronary occlusion, accounting for up to 3% of all acute coronary syndromes.[2] The occurrence of this phenomenon during PE through interatrial communication (termed "paradoxical coronary embolization") is extremely rare and its true incidence is unknown.

Case Report

A previously healthy 44-year-old man was admitted to the hospital after a major motorcycle accident. On presentation to prehospital emergency service, he had no neurological deficits, but he presented severe hemodynamic instability and major lower limb trauma. He was intubated on the scene and subsequently transferred to our hospital. Whole-body computed tomography scan revealed an isolated severe left leg trauma, including a compound fracture of the fibula and tibia and muscle contusion. The patient was promptly transferred to the operating room for lower extremity fixation and debridement. During these initial stages, he developed a severe hemorrhagic shock and required 2g of tranexamic acid (1g bolus and 1g infusions over 8 hours), 16 units of red blood cells, 3L of fresh frozen plasma, and 2 platelet pools. After surgery, he was admitted to the ICU. The subsequent clinical course was characterized by repeated surgical explorations, vacuum therapy, wound debridement, multidrug-resistant bacterial wound infection, and limb ischemia due to occlusion of the left leg arteries (anterior tibial artery, tibiofibular trunk, and common interosseous artery). Venous thromboembolism prophylaxis was started on the first postoperative day with continuous intravenous infusion of unfractionated heparin, monitored at least daily with a coagulation profile (international normalized ratio, activated partial thromboplastin time [aPTT], platelets,

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and renal function) aimed at normal values and an aPTT in the prophylactic range. The platelet count was always within range, and the aPTT was within range from the second day after surgery. After 12 days, he was successfully discharged from the ICU to the surgical ward. A few hours after discharge, he suddenly presented with severe dyspnea, tachycardia, and hyporesponsiveness. The electrocardiogram was negative (Fig 1A), but bedside transthoracic echocardiography revealed a dilated and hypokinetic right ventricle, raising the suspicion of massive PE.

Due to his clinical deterioration, the patient was rapidly transferred to the ICU, where he collapsed into asystolic cardiac arrest within minutes from arrival. After Advanced Cardiovascular Life Support was started, given the high suspicion of PE, intravenous thrombolysis (alteplase 50-mg bolus and 50-mg infusion) was administered, and VA-ECMO cannulation was initiated. The left common femoral artery and the right common femoral vein were cannulated percutaneously with a 15F arterial cannula and a 23F multistage venous cannula, and VA-ECMO was started 15 minutes after cardiac arrest with a blood flow of 4 L/min, gas flow of 5 L/min, and FiO_2 100%. After the initiation of VA-ECMO, a narrow QRS electrocardiogram reappeared on the monitor, and a transient hemodynamic improvement was achieved. A few minutes later, an arrhythmic storm with multiple episodes of ventricular fibrillation occurred. Between these arrhythmic episodes, the patient presented with a wide QRS electrocardiogram trace and anterior ST-segment elevation (Fig 1B).

The presence of rhythm instability associated with new-onset ST-segment elevation raised the suspicion of coronary occlusion. Based on the complex clinical scenario, a paradoxical left-sided embolization during high-risk PE was hypothesized.

Transesophageal echocardiography revealed the unexpected presence of hyperechoic material floating in the left ventricle (Fig 1C and Supplementary Video 1). The interatrial septum was examined with color Doppler, which revealed a possible interatrial communication (Fig 1D).

The patient was then transferred to the cath lab for coronary angiography. The procedure revealed acute occlusion of the proximal left anterior descending artery and distal circumflex artery by thrombotic material (Fig 2), which was successfully thromboaspirated with immediate improvement in cardiac function (Supplementary Video 2). Whole-body contrast-enhanced CT was then performed to rule out other sites of paradoxical embolization. The body CT showed massive bilateral PE involving the main and lobar pulmonary arteries (Fig 3A) with no other sites of arterial embolism. Similarly, the brain CT was negative for acute intracranial arterial occlusion but showed severe and diffuse cytotoxic cerebral edema consistent with severe anoxic brain injury (Fig 3B). The patient was transferred back to the ICU, where he rapidly developed non-reactive mydriasis and profound hypotension despite VA-ECMO. Subsequent transesophageal echocardiography confirmed a patent foramen ovale (PFO). The patient developed progressive multiorgan failure and died 2 days later.

Discussion

Paradoxical coronary embolism during PE is a rare but potentially catastrophic event that is particularly difficult to

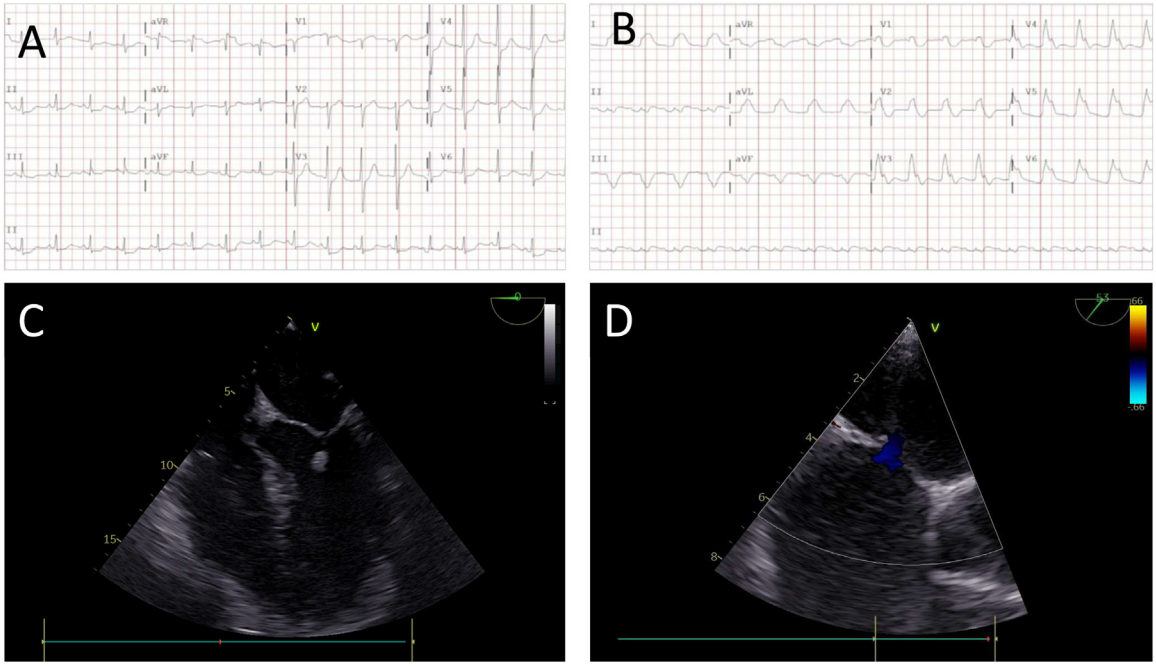

Fig 1. ECG and echocardiographic findings before and after ST-segment elevation. ECG recorded after the onset of symptoms was normal (A). After starting VA-ECMO, the patient had a normal ECG for a few minutes, then the QRS widened, anterior ST-segment elevation became apparent (B), and the patient experienced an arrhythmic storm. Transesophageal echocardiography revealed hyperechogenic material floating in the left ventricle (see mid-esophageal four-chamber view, C) while color Doppler unveiled a flow across interatrial septum (see mid-esophageal bicaval view, D).

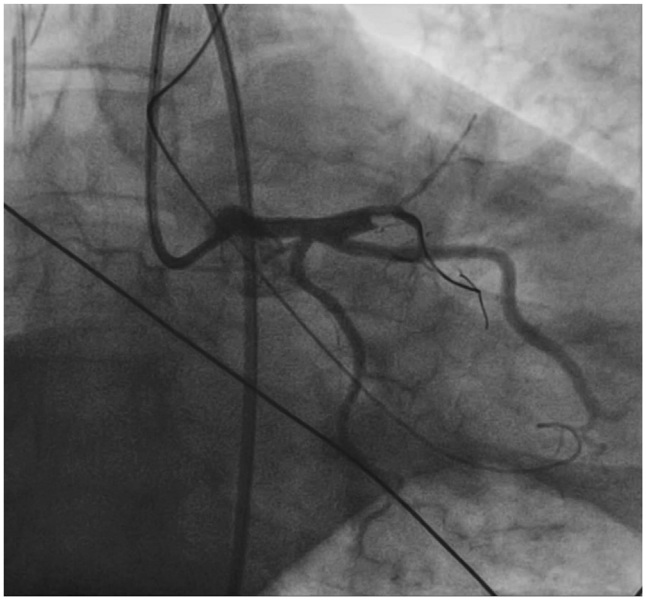

Fig 2. Coronary angiography findings. Coronary angiographic view showing filling defects in the proximal left anterior descending artery consistent with acute thrombotic occlusion.

recognize because most patients die immediately after massive PE without any resumption of cardiac activity.[3] We report a case of acute coronary occlusion leading to acute myocardial infarction after massive PE complicated by cardiac arrest and initiation of VA-ECMO. Coronary[4] or peripheral[5,6] embolization due to PE has been reported previously. To our knowledge, this is the first report of paradoxical coronary embolism in a patient with cardiac arrest who was resuscitated with VA-ECMO. This case highlights the complexity of managing a patient with massive PE, as such rare complications can only be recognized with a high index of suspicion.

Pathophysiologic Basis of PE

Four concomitant conditions are necessary for paradoxical coronary embolization to occur.[7] First, there must be an embolic source in the venous circulation or in the right heart. Second, there must be a right-to-left shunt, often represented by a PFO. PFO is a common condition, detectable in up to 25% of the healthy population,[8] and typically has a valve-like conformation that allows right-to-left shunting in the presence of high right atrial pressure. Third, a paradoxical embolus must enter a coronary ostium, which is relatively rare because coronary perfusion occurs mainly during diastole. Fourth, a reversal of the gradient between right and left heart pressures is required to open the valve mechanism of the PFO.

In the reported case, transient pulmonary hypertension due to massive PE may have opened a right-to-left interatrial shunt, allowing pulmonary emboli to move from right to left heart chambers and enter in the coronary arteries, causing acute myocardial infarction.

PFO as a Specific Risk Factor in Critically Ill Patients with PE

The clinical significance of the presence of a PFO in this scenario remains uncertain, but echocardiographic detection of a PFO has been found to be an independent predictor of poor outcome in patients at high risk for pulmonary embolism.[9] Because of the aforementioned relationship between PE, interatrial shunt, and paradoxical embolism, the presence of a PFO could be considered an additional risk factor in critically ill patients at risk for PE. Therefore, it is advisable to evaluate the presence of a PFO and a left-to-right shunt in a hemodynamically stable patient if a deep vein thrombosis is found, to achieve the anticoagulation target more aggressively and to be aware of the risk of systemic embolization. In the reported case, the patient received "standard" deep vein thrombosis

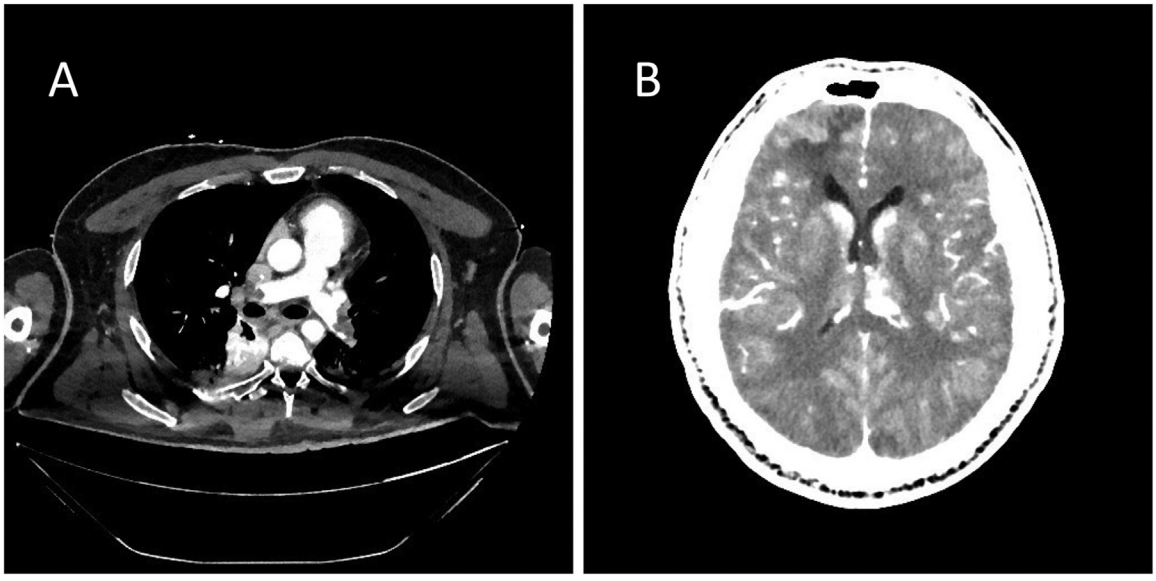

Fig 3. Computed tomography findings. Axial contrast-enhanced computed tomography of the chest showed a bilateral pulmonary embolism involving the main pulmonary arteries (A). Brain computed tomography was characterized by diffuse cerebral edema with cortical swelling and disappearance of cerebral sulci (B).

prophylaxis without mechanical compression because of the leg injury. Unfractionated heparin was chosen because of its short half-life and the possibility of reversal, as the patient was considered to be at high risk for bleeding due to repeated surgical revisions. This circumstance may have contributed to the reduced efficacy of the thromboprophylaxis regimen.

VA-ECMO on Stage: Benefits and Risks During Massive Pulmonary Embolization

The application of VA-ECMO, which achieved the return of spontaneous circulation, uncovered a rare complication, evidenced by electrical instability and ST-segment elevation. It is worth noting that without VA-ECMO, the patient would not have regained cardiac activity, and such a complication would have gone unnoticed.

VA-ECMO for massive PE is widely used, although without definitive evidence.[1]

Initiation of femoral-femoral VA-ECMO can interact with this physiologic scenario in various and mostly unpredictable ways.

First, as venous drainage from the right atrium or inferior vena cava reduces right ventricular preload, this tends to reduce central venous pressure, right ventricular stroke volume, and pulmonary pressure. The magnitude of this effect depends on the complex interplay between blood volume status and pulmonary resistances and requires left ventricular function (which may itself be compromised by pressure overload from VA-ECMO). PE represents an additional factor in this complex scenario. Therefore, within this simplified physiologic framework, we can speculate that the initiation of VA-ECMO may reduce right atrial pressure and the pressure gradient across the interatrial septum.

On the other hand, ECMO may also increase the risk of thrombosis and (paradoxical) embolization through different mechanisms.

First, the venous cannula may inadvertently dislodge venous thrombi during cannulation. We cannot exclude such a circumstance in the reported case, although it is worth noting that pulmonary embolism had already occurred at the time of ECMO cannulation. In addition, a thrombus may embolize directly from the arterial cannula into the arterial circulation, especially in the case of prolonged cannula clamping and inadequate anticoagulation. This seems unlikely given the emergency cannulation and coadministration of alteplase.

Cardiac Arrest Due to Pulmonary Embolism: VA-ECMO, Thrombolysis, or Both?

Current guidelines recommend systemic thrombolysis in patients with high-risk PE,[10] although there is some concern about the efficacy of this intervention in the setting of more severe clinical presentations, such as cardiogenic shock and cardiac arrest.[11] In addition, the choice of management strategy in this particular population is based on very limited evidence and lacks definitive consensus[10]

Mechanical circulatory support, in particular VA-ECMO, has been proposed and used as a bridge therapy to face hemodynamic collapse and to allow functional recovery of the right ventricle after adequate reperfusion therapy, either drug or catheter-based. In this setting, VA-ECMO can be used alone or in combination with one or more different reperfusion strategies. In summary, four different combinations can be hypothesized: ECMO plus appropriate anticoagulation, ECMO plus systemic thrombolysis, ECMO plus catheter-directed reperfusion therapy, and ECMO plus surgical embolectomy. Although ECMO alone or ECMO in association with systemic thrombolysis are the strategies most frequently reported in case series,[12] randomized clinical trials comparing specific strategies are lacking. For this reason, currently available guidelines suggest the use of ECMO in high-risk pulmonary embolism with a low class of recommendation.[10]

A recent large retrospective study from Germany analyzed the effect of ECMO combined with different reperfusion strategies in more than 2,000 patients with pulmonary embolism treated with ECMO. In patients with cardiac arrest, the use of ECMO (alone or combined with thrombolysis or catheter-based reperfusion) was independently associated with lower in-hospital mortality compared with thrombolysis alone. This benefit of ECMO alone or as part of a multi-interventional strategy was not observed in patients with high-risk pulmonary embolism but without cardiac arrest.[13]

This finding appears to have a solid biological basis: when the thrombolytic is administered intravenously to a patient undergoing cardiopulmonary resuscitation, the drug does not reach the thrombus in the pulmonary circulation (or does so to a lesser extent) and, therefore, cannot exert its effect.

The use of VA-ECMO after or in combination with thrombolysis raises concerns about the increased risk of bleeding. In a recently published large case series of patients with high-risk pulmonary embolism treated with ECMO, the authors found that patients treated with thrombolysis before ECMO initiation had a significantly higher risk of bleeding than those treated with ECMO alone, with no difference in survival.[14] It is worth noting that in patients who received thrombolysis, bleeding at vascular access sites accounted for only a small proportion of hemorrhagic events, while the majority were due to injuries related to cardiopulmonary resuscitation.

Conclusions

This clinical case demonstrates the potentially deleterious effects of paradoxical coronary embolization, complicating an already critical scenario of massive PE. The importance of this complication, albeit rare, also lies in the difficult differential diagnosis between PE and coronary occlusion, which have overlapping clinical features (tachycardia, dyspnea, neurological deterioration, cardiac arrest). Our report further highlights the vulnerability of patients with PFO and the care required in the management of critical patients at increased risk for thromboembolic events, although the best thromboprophylactic strategy in these patients remains uncertain.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Matteo Sola: Writing – review & editing, Writing – original draft, Investigation, Conceptualization. **Matteo Pozzi:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Conceptualization. **Simone Tresoldi:** Writing – review & editing, Investigation, Conceptualization. **Marco Giani:** Writing – review & editing, Methodology, Investigation. **Valeria Bellin:** Writing – review & editing, Investigation. **Roberto Rona:** Writing – review & editing, Supervision. **Pietro Vandoni:** Writing – review & editing, Supervision. **Gianluigi Redaelli:** Writing – review & editing, Supervision. **Giuseppe Foti:** Writing – review & editing, Supervision, Conceptualization.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1053/j.jvca.2024.08.027.

References

1 Helms J, Carrier M, Klok FA. High-risk pulmonary embolism in the intensive care unit. Intensive Care Med 2023;49:579–82.

2 Raphael CE, Heit JA, Reeder GS, et al. Coronary embolus. JACC Cardiovasc Interv 2018;11:172–80.

3 Windecker S, Stortecky S, Meier B. Paradoxical embolism. J Am Coll Cardiol 2014;64:403–15.

4 Chen W, Yu Z, Li S, et al. Concomitant acute myocardial infarction and acute pulmonary embolism caused by paradoxical embolism: a case report. BMC Cardiovasc Disord 2021;21:313.

5 Ko C-H, Forrest P, D'Souza R, et al. Successful use of extracorporeal membrane oxygenation in a patient with combined pulmonary and systemic embolisation. Perfusion 2013;28:138–40.

6 Grapatsas K, Leivaditis V, Zarogoulidis P, et al. Successful treatment of postoperative massive pulmonary embolism with paradoxal arterial embolism through extracorporeal life support and thrombolysis. Respir Med Case Rep 2018;23:1–3.

7 Johnson BI. Paradoxical Embolism. J Clin Pathol 1951;4:316–32.

8 Hagen PT, Scholz DG, Edwards WD. Incidence and size of patent foramen ovale during the first 10 decades of life: an autopsy study of 965 normal hearts. Mayo Clin Proc 1984;59:17–20.

9 Konstantinides S, Geibel A, Kasper W, et al. Patent foramen ovale is an important predictor of adverse outcome in patients with major pulmonary embolism. Circulation 1998;97:1946–51.

10 Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J 2020;41:543–603.

11 Keller K, Hobohm L, Ebner M, et al. Trends in thrombolytic treatment and outcomes of acute pulmonary embolism in Germany. Eur Heart J 2020;41:522–9.

12 Chopard R, Morillo R, Meneveau N, et al. Integration of extracorporeal membrane oxygenation into the management of high-risk pulmonary embolism: an overview of current evidence. Hämostaseologie 2024.

13 Hobohm L, Sagoschen I, Habertheuer A, et al. Clinical use and outcome of extracorporeal membrane oxygenation in patients with pulmonary embolism. Resuscitation 2022;170:285–92.

14 Prasad NK, Boyajian G, Tran D, et al. Veno-arterial extracorporeal membrane oxygenation for pulmonary embolism after systemic thrombolysis. Semin Thorac Cardiovasc Surg 2022;34:549–57.