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GRAND ROUND
Cardiovascular imaging

A case report of an unprovoked neonatal pulmonary embolism: management strategies and cardiopulmonary complications

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Background Neonatal pulmonary embolism is a rare occurrence, especially when idiopathic, instead occurring in patients with identifiable risk factors including severe dehydration, presence or history of a central venous line, or identifiable genetic causes. Given the rarity of paediatric and neonatal pulmonary emboli, few guidelines exist to support the clinician in both the initial resuscitation and ongoing management of the critically ill patient with pulmonary emboli.

Case summary We present a 5-day-old female with unprovoked massive pulmonary embolism and associated haemodynamic compromise. She presented with central cyanosis and weak respiratory effort with hypoxaemia, persistent tachycardia, and hypotension despite initial fluid resuscitation, intubation, and administration of 100% FiO_2 with inhaled nitric oxide. She was ultimately diagnosed with a massive pulmonary embolism involving the right pulmonary artery by both echocardiography and computed chest tomography, initiated on inotropic support and systemic anticoagulation, after which she underwent mechanical thrombectomy. She was successfully extubated soon thereafter, with subsequent resolution of her emboli. No provoking factors were able to be identified for this patient.

Discussion This case highlights the cumulative burden of pulmonary obstruction and inter-ventricular interactions that lead to haemodynamic compromise in the event of massive pulmonary embolism, with resultant considerations of key management strategies. These include the risks of fluid resuscitation and introduction of positive pressure ventilation, as well as the need for early consideration of inotropic support and an institutional pathway for anticoagulation, ultimately proposing a multidisciplinary algorithm for the clinician to deploy when faced with impending cardiovascular collapse from massive pulmonary embolism.

Keywords Case report • Pulmonary embolism • Neonatal pulmonary embolism • Cardiopulmonary interactions

ESC curriculum 2.2 Echocardiography • 7.1 Haemodynamic instability • 9.4 Thromboembolic venous disease • 9.5 Pulmonary thromboembolism

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Learning points

- In the setting of massive pulmonary embolism, the cumulative burden of pulmonary obstruction and inter-ventricular interactions can potentiate right ventricular failure and cardiac collapse. This may be exacerbated by resuscitation efforts including excessive fluid administration and introduction of both sedation and positive pressure ventilation; thus careful consideration of risk–benefit is warranted for each of these measures.
- With suspicion for massive pulmonary embolism and right ventricular strain, early consideration should be given to use of inotropic support (epinephrine), pursuit of anticoagulation and/or mechanical thrombectomy by the multidisciplinary team, and anticipatory consideration of extracorporeal membranous oxygenation deployment in the event of cardiac arrest.

Introduction

Neonatal pulmonary embolism (PE) is a seldom-reported condition with non-specific manifestations like respiratory distress or cyanosis.[1] Diagnosis can be challenging, particularly in the absence of readily identifiable clinical risk factors, such as severe dehydration, known genetic predisposition, history of central venous access, or maternal gestational diabetes.[1] The rarity of this condition in paediatric patients with scant consensus management guidelines makes initial resuscitation and treatment challenging. In this case study, we present an instance of unprovoked massive pulmonary embolism in a 5-day-old female, with the aim of discussing key clinical management strategies.

Case

The patient was a 5-day-old, 3.5 kg full-term female born via uncomplicated, elective caesarean delivery. The pregnancy was generally unremarkable except by maternal metformin-controlled gestational diabetes. The infant presented to our emergency department for central cyanosis while feeding at home. She arrived in sinus tachycardia at a rate of 180–200 b.p.m., with initial oxygen saturation of 70% on room air that improved to 100% on 15 L flow delivered via non-rebreather face mask. She was noted to have weak respiratory effort, expiratory grunting, and episodic apnoea and was intubated prior to admission to the neonatal intensive care unit (ICU). Despite fluid resuscitation, she remained tachycardic and developed hypotension. Hypoxaemia persisted on maximal supplemental oxygen leading to initiation of inhaled nitric oxide (iNO) that improved her haemodynamic and gas exchange. Preliminary echocardiogram was concerning for anomalous pulmonary venous drainage with no visualization of flow in the right pulmonary artery (RPA) and right-to-left shunting across an atrial septal defect. With concern for congenital heart disease, the patient was transferred to the cardiac ICU where right heart strain on electrocardiography, an NT-proBNP of 63 943 pg/mL, and a mild troponin elevation were noted.

Further review of the echocardiogram identified an occlusive right PA thrombus with normal pulmonary venous connections and lack of flow in the right-sided pulmonary veins (*Figure 1*) with severe right heart dilation and systolic dysfunction with estimated right ventricular (RV) pressures of 48 mmHg + right atrial pressure. The infant received a 50 units/kg heparin bolus followed by a maintenance infusion at 28 units/kg/h. Epinephrine was administered at 0.02 μg/kg/min to provide inotropic RV support (*Figure 2*). Subsequent chest computed tomography (CT) confirmed echo findings and identified an additional non-occlusive thrombus of the left lower PA and multiple, bilateral, small aorto-pulmonary collaterals (*Figure 1*). In consultation with interventional cardiology and haematology, the patient was referred to the cardiac catheterization laboratory, where the patient was found to have significant RV hypertension and complete occlusion of the RPA and near-complete occlusion of the left lower lobe PA. Catheter-directed thrombus debulking was performed via femoral venous access using a combination of a 6 French thrombectomy and aspiration catheter (Indigo® System, Penumbra, Alameda, CA) and balloon angioplasty (Emerge coronary balloon, Boston Scientific, Marlborough, MA). Post-procedural FiO_2 requirements declined rapidly, and a low-dose alteplase infusion was administered until repeat CT scan the following day provided reassurance against thrombus reformation. The patient was extubated on hospital day 4 and transitioned to enoxaparin for longer-term therapeutic anticoagulation (*Figure 2*). She remained hospitalized for 1 month for rehabilitation. CT angiography of the chest was repeated 2 weeks after initial presentation and showed no residual PE, and transthoracic echocardiogram 5 weeks after presentation showed normal RV pressure and function. A broad haematologic and genetic workup including whole genome exome sequencing did not identify any significant genetic contributors to the aetiology of her presentation. Acquired thrombophilia, such as antiphospholipid antibodies, was also negative, and on review, she had received vitamin K following birth. There was no significant family history of thrombosis.

Discussion

The incidence of pulmonary embolism in paediatrics, especially in neonates, is exceedingly rare. Studies report incidence ranging from 0.07 to 0.9 per 10 000 children ages 1 month–18 years.[2,3] Neonatal incidence is even less, with limited reports. One 30-year retrospective autopsy study found three infants (under 1 year of age) with massive pulmonary embolism,[4] while another single-centre study found an incidence of 0.7% in their neonatal ICU.[5] The top risk factors for paediatric PE identified include presence of a central venous line (CVL) (present in 33%–66% of paediatric and 89%–94% of neonatal thrombotic events), infection, or congenital heart disease, with increasing likelihood of PE as the number of risk factors increases,[6] whereas presence of a CVL, extreme dehydration, and maternal gestational diabetes pose the greatest risk in neonates.[5] Given the rare incidence of PE in infants, consensus guidelines are limited to the antithrombotic management without guidance on cardiac and critical care management.[7,8,9]

Extrapolating from the framework of adult guidelines for PE management, the goals of (i) cardiopulmonary support, (ii) anticoagulation, and (iii) reperfusion of the PA should remain the same for the neonatal population (*Figure 2*).[10] The cumulative burden of the pulmonary obstruction and adverse ventricular–ventricular interactions increase risk of cardiac arrest (*Figure 3*).[10,11] The balance between insufficient and excessive preload to a dysfunctional RV further contributes to this cycle. Sedation and intubation with introduction of positive pressure ventilation would both significantly diminish RV preload and could potentiate CV collapse; thus, intubation should be balanced against the degree of the patient's hypoxaemia and respiratory distress. In our case, the initial concern for anomalous pulmonary venous return is a contraindication for iNO, as it may exacerbate pulmonary oedema and diminish return to the RV.[12] However, extrapolating from adult studies looking at the role of iNO in PEs, iNO may improve both V:Q matching and pulmonary vascular reactivity, as demonstrated in this patient's course.[13]

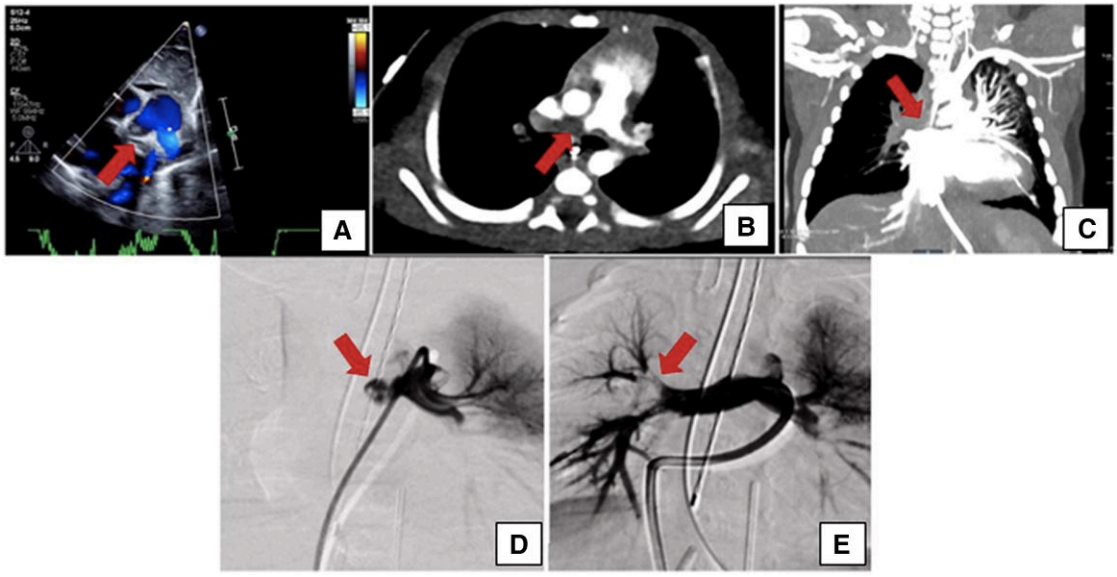

Figure 1 Diagnostic imaging. (*A*) Initial filling defect through the right pulmonary artery seen on echocardiography (indicated by arrow). (*B* and *C*) First computed tomography scan demonstrating filling defect through the right pulmonary artery on axial (left) and coronal planes (right) as indicated by arrows. (*D* and *E*) Contrast filling defect through the right pulmonary artery (indicated by arrows) seen by digital subtraction angiography in catheterization lab before (*D*) and improved after (*E*) mechanical thrombectomy and balloon angioplasty.

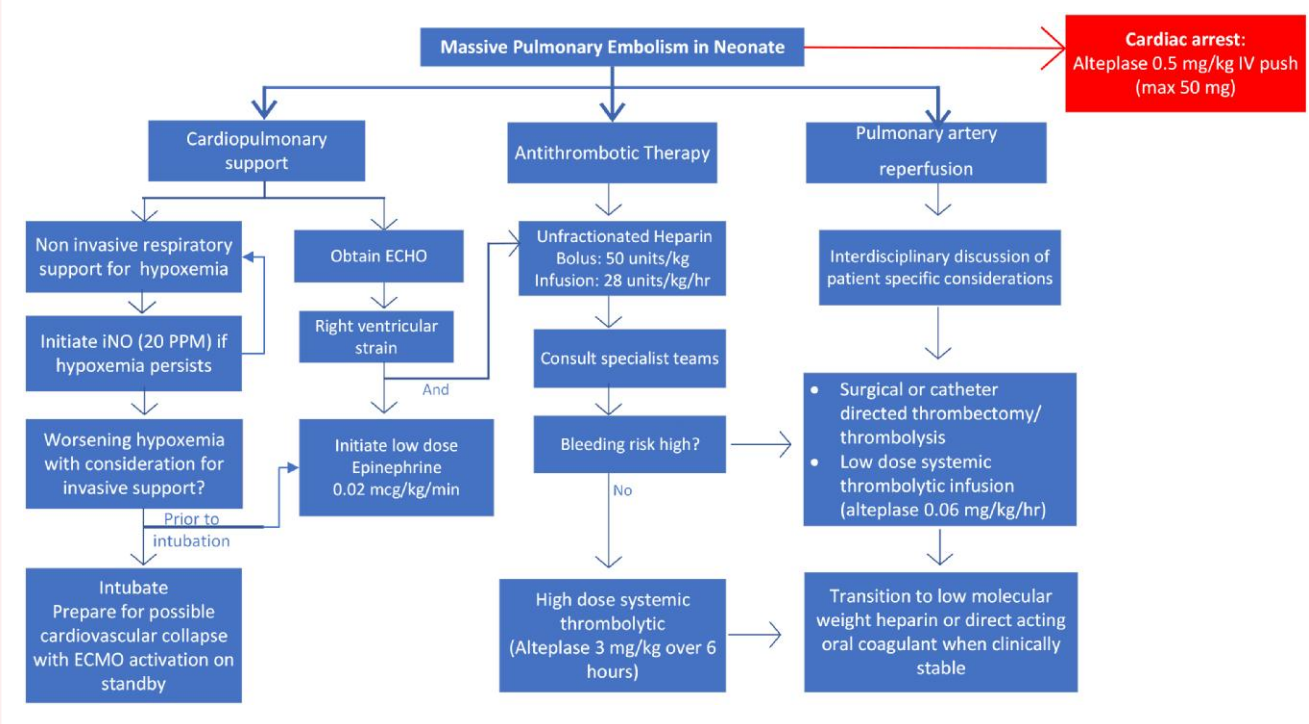

Figure 2 Proposed treatment pathway. ECHO, echocardiograph; ECMO, extracorporeal membranous oxygenation; iNO, inhaled nitric oxide.

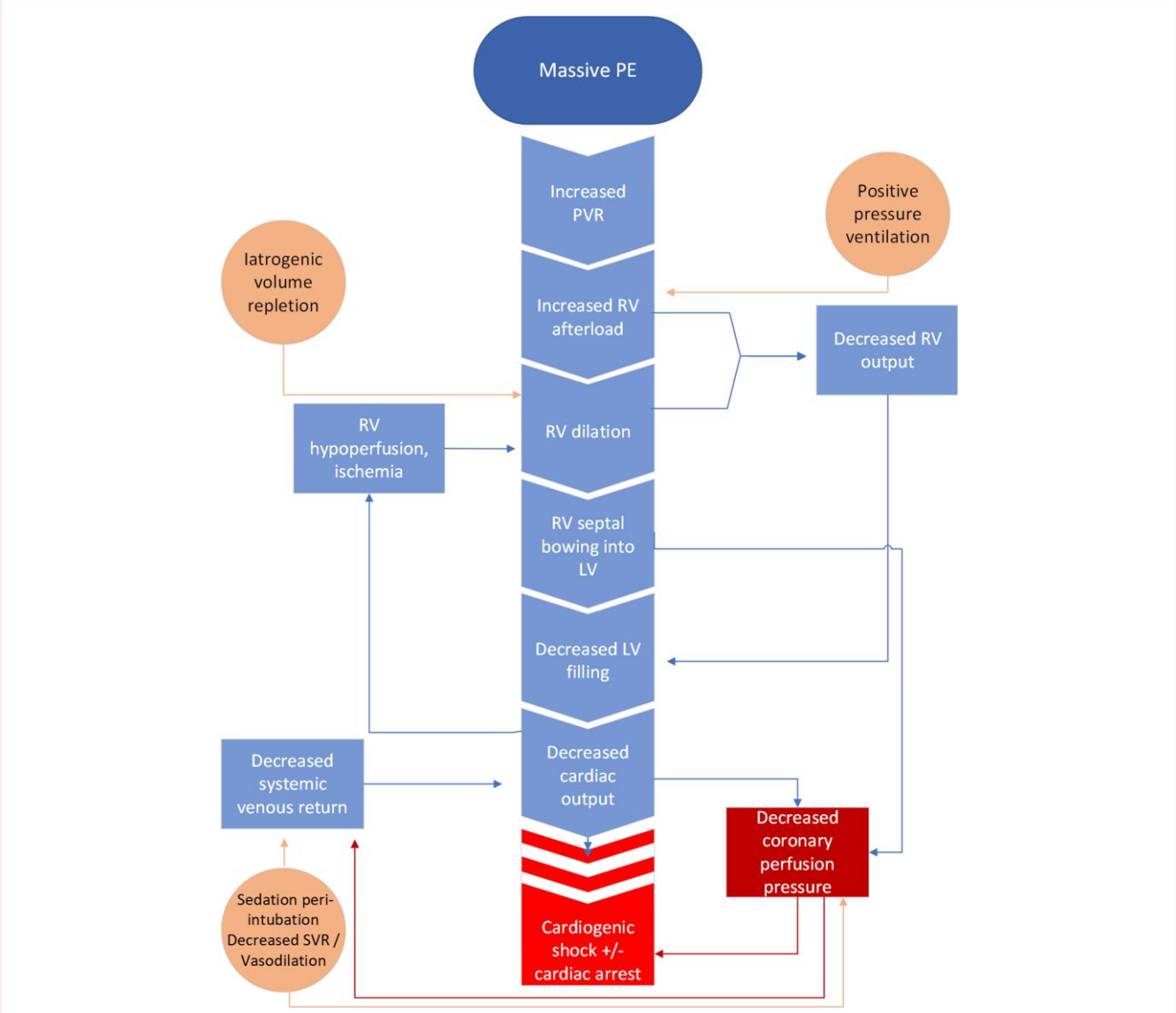

Figure 3 Pathophysiology of clinical decompensation from pulmonary embolus. RV, right ventricle; LV, left ventricle; SVR, systemic vascular resistance; PVR, pulmonary vascular resistance. Circular elements represent iatrogenic contributors to pathophysiology. Note: As both right ventricular pressure and left ventricular pressure increase, right ventricular pressure exceeds left ventricular pressure leading to bowing of the septum into the left ventricle and impaired left ventricular filling.

Lastly, given the high risk for rapid haemodynamic collapse from a mechanical thrombotic occlusion that would require time for either intervention (thrombectomy) or pharmacologic therapy (anti-thrombotics), even suspicion of the underlying diagnosis should prompt pre-emptive, anticipatory contingency planning. Specifically, initiation of low-dose inotropic support even with normal haemodynamics should be considered. Additionally, while each institution may have guidelines for antithrombotic therapy in the setting of a cardiac arrest, the realities of ordering, preparing, and obtaining the drug for emergent availability at bedside should be accounted for, especially if the patient has already developed unstable haemodynamics such as hypotension. This is especially true in the paediatric setting, where pulmonary emboli are a rare occurrence and thus the protocol for management and deployment of salvage therapies may not be vetted. Moreover, early and aggressive deployment of extracorporeal membranous oxygenation (ECMO) should be considered well in advance as routine resuscitation for cardiac arrest would be unlikely to bypass the underlying cause of arrest. This should include thoughtful consideration of central vascular access placement prior to decompensation with the goal of maintaining patency and access to right neck vessels in the event of surgical exploration for ECMO cannulation. This has been reflected in adult literature as well and readily extrapolates to paediatric consideration for this pathology.[10,14]

Summarily, while paediatric and neonatal guidelines for the management of acute pulmonary embolism are scant, extrapolating from international adult recommendations and understanding the underlying cardiopulmonary consequences of this management lead to the

approach proposed here. With emphasis on early inotropic support, judicious use of iNO and positive pressure ventilation, pre-emptive consideration of emergent interventional and pharmacologic therapies in the setting of cardiovascular collapse, and the practical delays one may encounter in deploying such therapies, as well as early and aggressive consideration of ECMO, these guidelines provide a practical reference for the clinical management of paediatric PE.

Lead author biography

Aashana Dhruva Cowan received her MD from Georgetown University School of Medicine, after which she completed her paediatric residency at UPMC Children's Hospital of Pittsburgh. She is currently completing her paediatric intensive care fellowship at the Washington University School of Medicine/St. Louis Children's Hospital where she remains interested in acute resuscitation and the clinical application of cardiopulmonary dynamics.

Supplementary material

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

Consent: Informed consent for use of protected patient information to present this case has been obtained from patient's legal guardian in compliance with COPE guidelines.

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Data availability

The data underlying this article are available in the article and in its online supplementary material.

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