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CASE REPORT

Prolonged Profound Hypoxia and Cardiac Failure in a Young Woman Presenting to the Emergency Department

Unexpected Pulmonary Embolus, Catheter-Directed Thrombolysis, and Subsequent Multi-Organ Failure

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Abstract: Pulmonary emboli are rare occurrences in young patients, especially those who present precipitously to the emergency department. In a young unresponsive patient, recognition of thromboembolic etiology may be delayed due to atypical presenting physiology or competing diagnoses. In this report, the authors describe an initially confounding case of catastrophic bilateral pulmonary emboli in a young woman who presented to the emergency department having been found unconscious on the street. Despite severe and prolonged hypoxia as well as multi-organ failure, the patient achieved a near complete recovery.

Keywords: pulmonary embolus, contraceptive, interventional radiology, ST elevation myocardial infarction

Case Report

A 24-year-old woman suffered a witnessed collapse and loss of consciousness. The alerted emergency medical service personnel documented a Glasgow coma scale (GCS) of 6, a blood pressure (BP) of 165/102 mm Hg, a heart rate (HR) of 160 beats per minute, and an oxygen saturation of 75% on arrival to her location. The patient was reportedly in the vicinity of a "rave party," the source of another nearly simultaneous emergency department (ED) admission for acute alcohol and drug intoxication. In the field, she received intranasal Naloxone, oral and nasal airways were placed for hand mask ventilation and an external jugular peripheral intravenous catheter was inserted.

> "Pulmonary embolus classically presents with symptoms of dyspnea, pleuritic chest pain, cough, and exam findings of tachypnea, tachycardia, and crackles on lung auscultation."

On arrival to the city hospital trauma center, the primary survey in the ED revealed patent airways, bilateral breath sounds, an oxygen saturation of 75%, a BP of 153/110 mm Hg, a HR in the 150 beats per minute range, and reduced GCS of 3.The patient was immediately intubated without medications and end-tidal carbon dioxide ($ETco_2$) capnography revealed consistent wave forms measuring 18 to 20 mm Hg. [Of note, consistent $ETco_2$ wave forms are considered to be the best confirmation of correct endotracheal tube intubation and the normal range for $ETco_2$ values is approximately 35 to 45 mm Hg. Situations that decrease either arterial carbon dioxide or decrease lung perfusion (such as decreased cardiac output) can lower $ETco_2$].

DOI: 10.1177/1944451612455500. From the [1]Department of Anesthesia and Perioperative Care and [2]Department of Radiology and Biomedical Imaging, San Francisco General Hospital University of California, San Francisco, California. Conflict of Interest: The author(s) declare no potential conflicts of interest with respect to the authorship, research, and/or publication of this article. Address correspondence to: Arun Prakash, MD, PhD, Department of Anesthesia and Perioperative Care - University of California, San Francisco, 521 Parnassus Avenue, San Francisco; CA 94143; e-mail: prakasha@anesthesia.ucsf.edu.

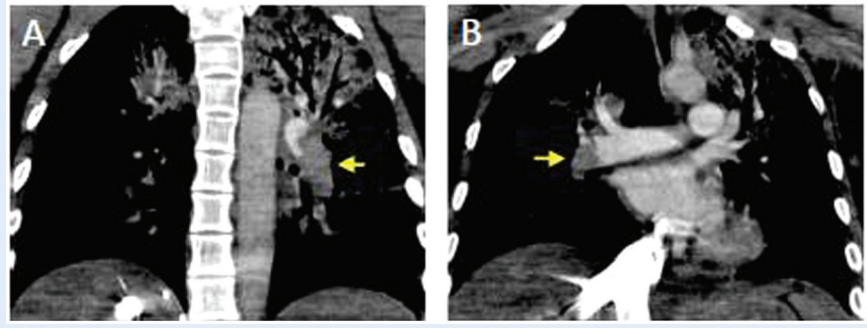

Figure 1. Initial computed tomography (CT) scans on arrival. Coronal CT scans of the chest with intravenous contrast demonstrate a large pulmonary embolus in the left and right main pulmonary arteries (arrows, A and B) occluding flow to all lung lobes except the right and left upper lobes (A).

A secondary survey did not reveal any external signs of trauma, a focused assessment with sonogram in trauma (FAST) exam was negative, and a chest radiograph confirmed endotracheal intubation but was otherwise unremarkable. Of note, cardiac interrogation during her FAST exam did not reveal any signs of pericardial fluid, overload, or abnormalities in contractility.

Over the next few minutes, the patient's BP and oxygen saturation readings became more difficult to obtain. Venous blood gas revealed a lactic acidosis (6.9/65/28/12.7/−21) with a lactate level of 13.7 and hematocrit of 49%. Although bounding neck pulsations were noted (in retrospect determined to be jugular venous pulsations), the cannulation of a peripheral artery was challenging in the setting of diminishing peripheral pulses. Cardiopulmonary resuscitation (CPR) was initiated soon thereafter for bradycardic pulseless electrical activity arrest.

Two separate rounds of CPR were performed and resuscitation efforts included intravenous (IV) administration of atropine, vasopressin, epinephrine, sodium bicarbonate, Naloxone, Tham (2-amino-2-(hydroxymethyl)-1,3-propanediol), administration of a Cyanokit and methylene blue. The differential diagnosis at this point included cyanide poisoning, meth-hemoglobinemia, methamphetamine overdose, and pulmonary embolus (PE). Following the 2 cycles of CPR, spontaneous peripheral pulses returned with sinus tachycardia. Vasopressin, epinephrine, and norepinephrine IV drips were continued for hemodynamic support with BPs maintained at approximately 90s/50s. FAST exam was repeated and remained negative. The repeated venous blood gas at that time (67 minutes after arrival to the ED) was 6.92/82/25/16.8/−15.7 with a hematocrit of 30%.

The patient was then transported to the radiology department for an emergent head, chest, abdomen, and pelvis computed tomography (CT) scan with IV contrast. CT angiography of the chest demonstrated large pulmonary emboli occluding the left and right main pulmonary arteries with only residual flow to the left and right upper lobes (Figure 1A and B). There was evidence of right heart strain on CT (right ventricular dilation and septal wall bowing), though a head CT did not reveal early evidence of hypoxic brain injury. Heparin (10 000 units IV) was given soon after and the patient taken to the medical intensive care unit (MICU) for continued resuscitation while the interventional radiology (IR) team was mobilized. During this time, systemic tissue plasminogen activator (tPA, 100 mg over 2 hours), inhaled Flolan (aerosolized epoprostenol), and a cooling protocol to reduce the potential for hypoxic brain injury were all initiated.

Within 3 hours of arrival to the ED, the patient was in the IR suite where left-sided pulmonary angiography demonstrated only segmental blood flow to the left upper lobe (Figure 2A). Partial disruption and distal embolization of the clot was achieved, however, residual clot remained and an infusion catheter was left in the main left pulmonary artery for localized tPA infusion (Figure 2B). Pulmonary angiography in the main right pulmonary artery demonstrated minimal flow to the right middle lobe and absent flow to the right lower lobe (Figure 2C). Mechanical thrombolysis was performed with subsequent markedly improved flow to the right middle and lower lobes (Figure 2D). With clot disruption and thrombolysis the patient's oxygenation and ventilation improved from 40% to 50% to 70% to 80% and arterial carbon dioxide decreased from 98 to 58 mm Hg (and $ETco_2$ increased). The patient's BP stabilized but she continued to require epinephrine, norepinephrine, and milrinone IV drips.

The patient then returned to the MICU for monitoring and further resuscitation. The patient's acid–base status, oxygenation, and ventilation all continued to greatly improve following IR intervention. However, she remained critically ill requiring multiple vasopressors, inhaled Flolan, and supportive care. She became profoundly coagulopathic, with worsening oozing of blood from multiple sites and she required rapid transfusion of multiple units of plasma with the activation of a massive transfusion protocol. Consequently, the cooling protocol, tPA, and

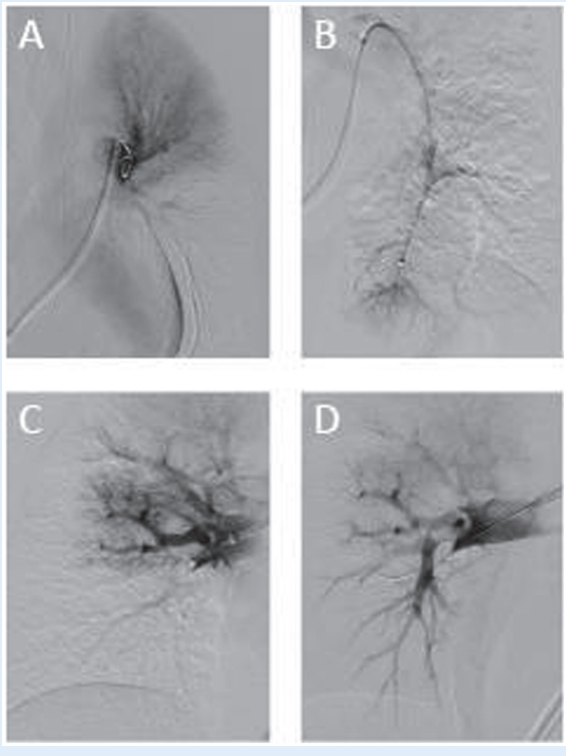

Figure 2. Fluoroscopic images during interventional radiology procedure. (A) Left main pulmonary artery catheter angiography demonstrating flow only to the left upper lobe. No flow is visualized to the left lower lobe. (B) Infusion catheter with side holes from the main left pulmonary artery to branches of the left lower lobe for local tissue plasminogen activator (tPA) infusion. (C) Right main pulmonary artery angiography revealing flow to the upper lobe. Minimal flow was appreciable in the middle lobe and no flow was seen to the lower lobe because of occlusive thrombus. (D) Following mechanical disruption of thrombus with pigtail catheters and an angioplasty balloon, improved perfusion of the right lower lobe was evident.

heparin infusions were all discontinued. ARDSNet protocol was initiated for lung protection and continuous veno-venous hemofiltration initiated for renal failure.

By hospital day 2, the patient's arterial blood gas analysis revealed normal pH and an improved Pao_2:Fio_2 ratio of 107. Since her coagulopathy had resolved, IV heparin was restarted. On hospital day 3, the patient began experiencing cardiac arrhythmias, including an episode of ventricular tachycardia which converted into rapid atrial fibrillation. An amiodarone drip was initiated and transthoracic echocardiography (TTE) demonstrated a severely dilated right ventricle with positive McConnell's sign, septal bowing, and a hypovolemic left ventricle. Electrocardiogram showed ST segment elevations in anterior leads V1, V2, and V3, and troponins were elevated with a peak of 58. The cardiothoracic surgery service was immediately consulted to initiate extra corporeal membrane oxygenation (ECMO) and the patient was transferred to a sister institution—a tertiary care university academic medical center-for venous–arterial cannulation and extracorporeal life support.

The patient remained on ECMO support for 6 days. TTE soon after her transfer revealed right ventricular akinesia with apical sparing—a positive McConnell's sign (supplementary movie S1). While on ECMO, vasopressor requirements decreased, electrocardiogram normalized, troponins trended down, and repeat TTE revealed improvement in right ventricular dilation and function (supplementary movie S2). ECMO was discontinued on hospital day 8 and a tracheostomy was performed. Vasopressor support was progressively weaned until hospital day 12. Inhaled nitric oxide likewise was weaned with the patient requiring minimal ventilator support by day 12. She no longer required continuous veno-venous hemofiltration at this stage but remained anuric and continued to receive intermittent hemodialysis. On hospital day 14, cardiac function by TTE had essentially normalized and she was transferred to a skilled nursing facility closer to her home.

Remarkably, the patient's neurologic status, as early as hospital day 2, appeared to be preserved with the movement of all 4 extremities and by day 4, she was following basic commands. At the time of the patient's transfer, she was awake, interactive, and able to converse albeit slowly. She continued to work with physical and occupational therapy and was able to draw shapes on paper. Approximately 4 months after the event, the patient is living at home with her family, exercising regularly, and has resumed her college courses (Figure 3, included with permission of patient and her family).

Risk factors for PE discovered during a thorough hematologic evaluation included the use of a contraceptive device and a positive lupus anticoagulant test. Repeat testing is planned for the near future to evaluate baseline coagulation parameter values as well. Our patient remains on therapeutic anticoagulation (Coumadin).

Discussion

Approximately 94 000 new cases of PE occur every year, and the case fatality rate at 3 months is estimated to be about 15%.[1] Massive PE is defined as pulmonary thrombus associated with hemodynamic instability (systolic BP <90 mm Hg or a drop of 40 mm Hg from the baseline systolic BP), tissue hypoperfusion (hypoxia, lactic acidosis, acute mental status change, oliguria), or the need for cardiopulmonary resuscitation. The incidence of massive PE is 4% to 22% based on different data sources with the reported inpatient mortality ranging from 15% to 25%.[2] Mortality increases to as high as 50% to 75% with concomitant cardiac arrest requiring CPR.

Pulmonary thromboembolic disease typically occurs in an older patient population with multiple comorbidities. Data from

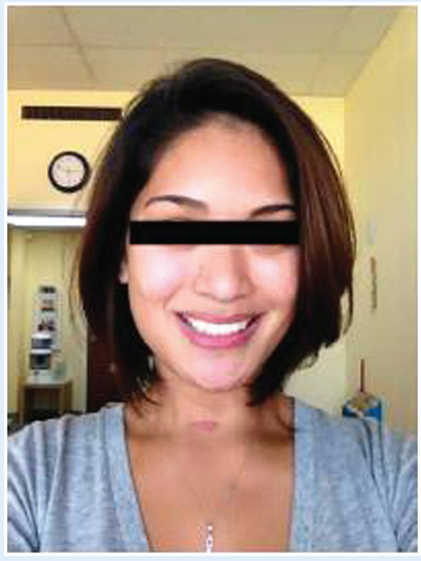

Figure 3. Image of patient after discharge from hospital (approximately 4 months later). Image obtained with permission of patient and patient's family.

the International Cooperative Pulmonary Embolism Registry demonstrate that less than 10% of all PEs reported occurred in patients younger than 40 years.[3] Instead, more than 65% of PEs were reported in patients older than 60 years and those patients often had medical histories of thromboses, recent surgeries, greater than 5 days of bed rest, or concurrent malignant processes. In contrast, when PE occurs in younger patients, the disease tends to affect women more often than men, and this observation may relate to differential exposure to risk factors such as pregnancy, postpartum state, and the use of oral contraceptives.[4]

Virchow's triad has been used to categorize the risk factors for thromboembolic disease for more than 150 years. Risks include venous stasis, endothelial dysfunction/injury, and hypercoagulable states.* Oral contraceptives have been shown to increase serum levels of prothrombin, factors VII, VIII, and X, and fibrinogen while decreasing levels of anticoagulant factor V.[5] The risk of venous thromboembolism is 6-8 times higher in women taking oral contraceptives versus age-matched controls. A concomitant thrombophilia such as that from a genetic factor V Leiden mutation or an acquired lupus anticoagulant can increase the risk 10-fold.[6]

*Virchow RLK. Thrombose und Embolie. Gefässentzündung und septische Infektion. *Gesammelte Abhandlungen zur wissenschaftlichen Medicin.* Frankfurt am Main: Von Meidinger & Sohn; 1856:219-732. Translation in Matzdorff AC, Bell WR. *Thrombosis and Embolie (1846-1856).* Canton, MA: Science History Publications; 1998. ISBN 0-88135-113-X.

Pulmonary embolus classically presents with symptoms of dyspnea, pleuritic chest pain, cough, and exam findings of tachypnea, tachycardia, and crackles on lung auscultation. Clinical signs can be used to calculate a Wells pretest probability to determine the appropriate diagnostic tool to confirm or rule out the diagnosis in a non-urgent setting.[7] However, massive PE can present with acute *cor pulmonale* and pulse-less electrical activity arrest requiring rapid assessment and CT with pulmonary angiography can achieve a sensitivity of 84% to 94% and a specificity of 94% to 100%, and a positive predictive value of 96%.[8] The use of CT for definitive diagnosis of PE in a hemodynamically unstable patient is limited by the practicality of transport during ongoing resuscitation efforts. Portable modalities include the use of echocardiography; TTE demonstration of right ventricular dysfunction, right ventricular dilatation, and significant tricuspid regurgitation with a high pretext probability for PE can achieve a positive predictive value of 98%.[9] Transesophageal echocardiography provides enhanced thrombus visualization and has a sensitivity and specificity of 92% and 100%, respectively.[10] The McConnell sign-akinesia of the right ventricle with apical sparing (seen in this patient, supplementary movie S1)-improves specificity (to 94% to 100%) for the diagnosis of acute massive PE.[11] In the operating room or in the ICU, in the setting of an intubated patient, PE can present with acute onset hypotension, sudden decrease in the $ETco_2$ and alteration in the capnography tracing.

The treatment of massive PE almost always includes systemic thrombolysis unless there are absolute contraindications (major trauma, surgery or head trauma within 3 weeks, hemorrhagic stroke, ischemic stroke within 6 months, central nervous system neoplasm, gastrointestinal bleeding, and active bleeding). Systemic thrombolysis in systematic reviews resulted in improved clinical outcomes when compared with heparin alone.[12] However, in the presence of contraindications or if systemic thrombolysis fails, catheter directed therapies can be efficacious as well. These include any combination of fragmentation and local thrombolytics or embolectomy until an improvement of hemodynamics is achieved. A recent meta-analysis reported success rates in the 70% to 80% range if intervention happened within the first 36 hours.[13] Additionally, surgical embolectomy, especially in the presence of large clots, may be an option depending on institutional resources. Limitations include the requirement of cardiopulmonary bypass and the time required to mobilize a surgical team.

Overall, this case highlights a number of interesting issues. First, it emphasizes the importance of establishing a broad differential diagnosis when evaluating patients in the ED with contextually and age-confusing presentations of a common but potentially life-threatening clinical entity. Second, it reinforces the capacity for recovery and physiologic reserve associated with youth and good physical conditioning. As seen in this case, organ systems in younger patients can recover even when exposed to prolonged and extreme stressors. Finally, this case highlights the specific attributes of the care that can be provided in centers specialized in both trauma emergency care as well as tertiary critical care that commonly make up integral portions of a university hospital system.

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