WHAT WOULD YOU DO?

Bilateral Central Pulmonary Embolism and Recent History of Ischemic Stroke

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CASE PRESENTATION

A 55-year-old man with a history of hypertension and borderline hyperlipidemia had just completed a 1-mile walk and had returned home when he felt light-headed. He suddenly experiences acute onset of chest pain and shortness of breath. His wife calls 911, and upon emergency medical services arrival, he is diaphoretic and anxious with a heart rate (HR) of 110 bpm, blood pressure (BP) of 100/58 mm Hg, and respiratory rate (RR) of 28 breaths/min. His oxygen saturation is 90% on room air. He is started on intravenous (IV) fluids in the field and placed on supplemental oxygen, with oxygen saturation increasing to 98%.

Upon arrival to the emergency department at 10:00 AM, he is noticeably more comfortable. He is alert and oriented. BP is 112/68 mm Hg, HR is 90 bpm, RR is 22 breaths/min, and oxygen saturation is 96% on 4 L/min via nasal cannula.

Past medical history is significant for ischemic stroke, which occurred 4.5 weeks before this presentation. He did not have a large vessel occlusion and was treated conservatively. His MRI demonstrated a lacunar infarct in the basal ganglia. He does not have any significant neurologic deficit.

Medications include lisinopril 20 mg daily, atorvastatin 10 mg daily, and aspirin 81 mg daily. Notable initial labo-

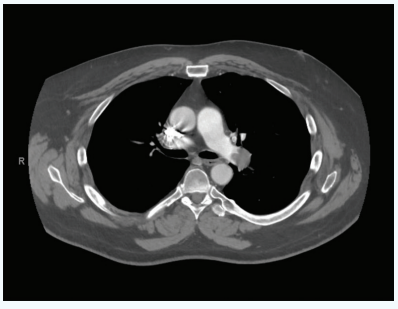

Figure 1

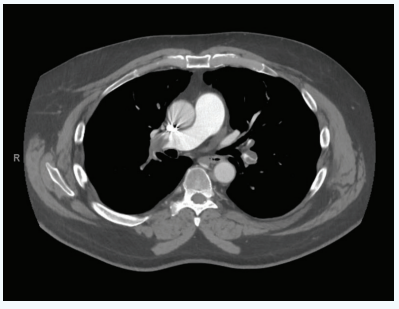

Figure 2

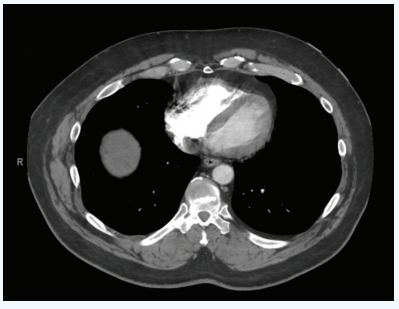

Figure 3

ratory results include a troponin I level of 0.22 ng/mL, brain natriuretic peptide (BNP) level of 350 pg/mL, and a lactic acid level of 3.1 µmol/L. CTAs of the chest show a bilateral central pulmonary embolism (PE) with a right ventricular-to-left ventricular (RV:LV) diameter ratio of 1.1 (Figures 1–3).

What additional workup would you do at this point?

Dr. Sista: This patient would certainly fit the criteria to be evaluated by our multidisciplinary pulmonary embolism response team (PERT). His case is complex—he has an intermediate-risk/submassive PE with an absolute contraindication (stroke) to thrombolytic drugs based on clinical trials. It is concerning that the patient's lactate level is elevated, as this finding implies that he was likely hypotensive at some point. His clot is central, which has a higher association with RV dysfunction and perhaps poorer 30-day outcomes.

Dr. Benenati: At this point, I think it would be ideal to have some multidisciplinary collaboration. If a PERT team were in place, a PERT consultation would be indicated. If this program were not operational, then consultation with pulmonary medicine would be the initial step. Based on the patient's history and exam, a venous duplex ultrasound may be considered if he had leg symptoms. Additionally, once he is stable, we would most likely do a walking test on the floor to see if his heart rate was stable with mild exercise. This information might determine which therapy he is offered.

Dr. Jones: This is a challenging case and an excellent choice for panel discussion. Initial risk stratification of acute PE is critically important to help guide management decisions. At this point in the patient's presentation, there appears to be enough data to appropriately risk stratify. This patient is hemodynamically stable, but he has convincing evidence of acute RV dysfunction based on elevated biomarkers (troponin and BNP) and an abnormal CT-derived RV/LV ratio of > 0.9 with a large, bilateral, centrally located thrombus. The patient's presentation is consistent with acute submassive PE.

What location in your hospital would he be admitted to?

Dr. Benenati: Because he is stable, he would be admitted to a monitoring unit but probably not the intensive care unit (ICU).

Dr. Jones: Patients with a presentation consistent with acute submassive PE would be admitted to either a cardiac or general medicine telemetry unit.

Dr. Sista: Given these factors, I would urge admission to the ICU.

What is your recommended treatment and why?

Dr. Jones: The initial treatment for this patient would be anticoagulation with IV unfractionated heparin. With positive biomarkers and RV dysfunction demonstrated on CT scan, the patient, despite being hemodynamically stable, is at a much higher risk for cardiovascular complications compared to a similar patient with evidence of RV dysfunction and negative biomarkers. The standard of care at our institution is to work collaboratively among the specialties involved in acute PE care (eg, cardiology, cardiac surgery, interventional radiology, and pulmonary/critical care are all involved with acute PE cases and serve as the basis for collaborative and coordinated care). We typically consider advanced PE treatment options for submassive PE patients and primarily use ultrasound-assisted catheter-directed thrombolysis (CDT) (EkoSonic endovascular system, Ekos Corporation, a BTG International group company) at 1 mg/hr for 12 hours for a total of 24 mg tissue plasminogen activator (tPA) for bilateral PE cases. The rationale for this is primarily based on data from the SEATTLE II, ULTIMA, and OPTALYSE PE trials, which all demonstrated safe and effective rapid reversal of RV dysfunction in the hospitalized patient with very low rates of serious bleeding or intracranial hemorrhage. In addition, the Ekos system is currently the only US Food and Drug Administration–approved device to treat PE, which does factor into our considerations of advanced PE treatment options. However, for this patient, we would favor initial conservative strategy, especially given his recent history of an ischemic stroke was just over 4 weeks before presentation, which is an absolute contraindication for systemic IV fibrinolysis and would even require equipoise when considering Ekos-assisted CDT despite recent data from the OPTALYSE PE trial demonstrating effective RV dysfunction reversal with a very low dose of tPA. Furthermore, recent stroke was one of the exclusion criteria for the above-mentioned trials.

Dr. Sista: Although the patient has worrisome signs, at this time I would recommend anticoagulation alone. His trajectory at this point is going in the right direction.

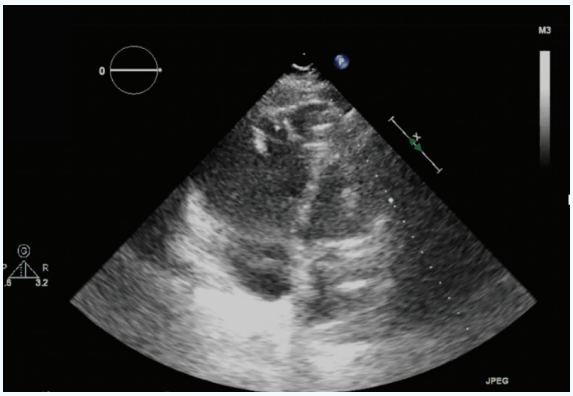

Figure 4. TTE showing RV dilatation and hypokinesis, flattening of the intraventricular septum, and an RV:LV ratio of 2.6.

Dr. Benenati: I was not certain if this was a massive PE initially because I didn't know his baseline BP. He did stabilize on his own, and his HR never exceeded 110 bpm. With his biomarkers elevated, I would think he either had a high-risk submassive PE or even potentially a massive PE. He would be fully anticoagulated, and we would consider catheter-directed therapy, especially if his HR was elevated on his walking test.

CASE CONTINUED

The patient is evaluated by our multidisciplinary PERT with consultations obtained from pulmonary/critical care, cardiology, and interventional radiology. The treatment team decides to admit the patient to the hospital's telemetry floor. He is started on anticoagulation therapy with low-molecular-weight heparin. He undergoes a venous duplex ultrasound of the lower extremities, which reveals a left popliteal, gastrocnemius, and peroneal vein deep vein thrombosis.

At 5 PM, he starts to complain of increased shortness of breath. The patient's BP is now 95/52 mm Hg, HR is 112 bpm, and RR is 24 breaths/min. His oxygen requirement increases, his oxygen saturation is 90%, and he is switched to a nonrebreather mask. A bedside transthoracic echocardiogram (TTE) is immediately performed and demonstrates RV dilatation and hypokinesis and flattening of the intraventricular septum with an RV:LV ratio of 2.6 (Figure 4). There was no thrombus within the right atrium or right ventricle.

What would you do at this point and why?

Dr. Sista: This patient is now clinically deteriorating, and this development is highly concerning. Submassive PEs had a rate of clinical deterioration of approximately 5% in the PEITHO trial. Some sort of treatment escalation is probably justified. Even though his BP is technically > 90 mm Hg, I would treat this as a massive PE with RV failure and mobilize cardiothoracic surgery, the interventional team, and cardiac anesthesia. Systemic thrombolytics would likely be looked upon unfavorably, but catheter-directed therapy or surgical embolectomy, both with extracorporeal membrane oxygenation (ECMO) at the ready, should be discussed. Catheter-directed therapy could encompass mechanical techniques such as aspiration or maceration, as well as low-dose thrombolytics if the patient fails to respond. Surgical embolectomy in the right hands can be life saving.

Dr. Benenati: We would call the pulmonologist and the cardiothoracic surgery team. He would be moved to the ICU immediately.

Dr. Jones: These are some of the most challenging cases. There is a "tipping point" in patients who initially present with submassive PE when the RV dysfunction worsens from either further thromboembolism or ongoing RV ischemia. This patient's clinical condition is deteriorating, and he is now demonstrating signs of massive PE. If left untreated, mortality from massive PE approaches 50%. IV fibrinolysis is a class I indication for massive PE;

however, the recent stroke in this patient represents an absolute contraindication for this therapy. As previously mentioned, coordinated and collaborated PE care among specialties is critical when offering advanced PE treatment options. We have a low threshold at our institution to initiate ECMO on patients with massive PE. In this case, given the existing large clot burden at presentation and now evidence of continued thromboembolism and severe RV dilatation and dysfunction on bedside echocardiogram, this patient would likely benefit from rapid initiation of venoarterial ECMO. Fortunately, at this time in the patient's presentation, adequate staff would be around to initiate ECMO rapidly. Furthermore, with contemporary coated ECMO tubing, the activated clotting time range is much lower than traditional cardiopulmonary bypass used for open heart cases. The activated clotting time range with coated ECMO tubing is typically from 200 to 250 seconds.

What is your recommended treatment and timing for such treatment in your institution?

Dr. Sista: This patient needs to have "all hands on deck" immediately, and a consensus decision needs to be achieved between the intensivist, interventionalist, and cardiothoracic surgeon. If the patient becomes more unstable, systemic thrombolysis also should be considered given the time it takes to mobilize a surgical or interventional team.

Dr. Jones: After placing a patient on ECMO, further adjunctive therapies can now be considered. In this patient, given the large clot burden on CT scan, adequate clot burden may not be accomplished with catheter-based fragmentation or aspiration, especially without any locally delivered thrombolytic. Surgical embolectomy would be a reasonable option, but again, the large amounts of IV heparin required for cardiopulmonary bypass may increase the risk of intracranial hemorrhage in this patient with a recent ischemic stroke. Ekos-assisted CDT locally delivered to the clot, using an OPTALYSE PE protocol as low as 8 mg tPA to 24 mg tPA for 2 to 6 hours based on the patient's clinical course, would also be a reasonable option and may achieve sufficient reversal of RV dysfunction, especially given the acute nature of the patient's presentation and thrombus formation, which generally correlates with more effective thrombolysis. Once stabilized and recovered, further workup for possible thrombophilia or secondary causes would be pursued.

Dr. Benenati: We would initiate catheter-directed therapy immediately. If the patient was unstable, we might consider systemic lysis, but if we could get him into the lab, then we would initiate catheter-directed therapy. Several scenarios in the lab might play out:

- If he was stable, we could initiate a thrombolytic infusion.
- If he was unstable in the lab or if his clinical situation was worsening, we would first do a mechanical embolectomy, probably with an Indigo device (Penumbra, Inc.). If he stabilized but had residual clot, we would continue with thrombolysis. If sufficient clot was removed, he might then be converted back to anticoagulation.
- If he was deteriorating rapidly, the early consultation with cardiothoracic surgery might lead to surgical embolectomy, especially because of his young age.

SUMMARY

When the patient experienced clinical decompensation, the multidisciplinary PERT team was immediately contacted, all of whom were physically in the hospital. In addition, cardiothoracic surgery was also consulted. Following the bedside TTE, the patient was transferred to the ICU. Although his unsupported systolic BP was > 90 mm Hg, classifying him as a submassive/intermediate high-risk PE, he was tachycardic and hypoxic, and his clinical presentation was bordering on a massive PE. In concordance with all the panelists, the team collectively agreed that treatment escalation was indeed indicated. Because he was just over 4 weeks out from his ischemic stroke, systemic thrombolysis was felt to be contraindicated. Consideration was given to surgical embolectomy and catheter-based intervention. The decision was to perform catheter-directed thrombembolectomy as an initial approach with CDT to be reserved depending on the result achieved with solely mechanical techniques.

Due to his borderline-stable condition, we were supported by a cardiac anesthesiologist. He was brought to the interventional radiology lab immediately and underwent pulmonary artery catheterization via right femoral vein access. At the time, his systemic BP was 94/50 mm Hg and HR was 114 bpm. His pulmonary artery pressure (PAP) was 54/26 mm Hg. He was maintained on a 100% nonrebreather mask with oxygen saturation increasing to 94%. Suction thromboembolectomy was performed with an Indigo CAT8 catheter, Separator 8 (Penumbra, Inc.), and aspiration system within both the right and left pulmonary arteries.

Although the clot was removed, a significant amount of obstruction was still present. In addition, the PAP was still elevated and measured 50/24 mm Hg, and systemic BP was 98/56 mm Hg. His oxygen saturation was still between 92% and 94%. He subsequently underwent placement of two 12-cm infusion-length EkoSonic catheters with recombinant tPA infusion at 1 mg/hr through each catheter.

He was then transferred back to the ICU for continued thrombolytic infusion and monitoring. At 90 minutes into his infusion, his breathing was noticeably less labored. His oxygen saturation was 99%, BP was 120/76 mm Hg, and HR was 86 bpm. In view of his relatively rapid clinical improvement, our desire to avoid a prolonged thrombolytic infusion, and based on our positive experience with short-duration infusion, the recombinant tPA was discontinued at 4 hours. Therapeutic anticoagulation was continued following the procedure. He continued to show progressive improvement through the night, and a repeat TTE in the morning demonstrated an RV:LV ratio of 1. He was ultimately discharged home on day 3 on oral anticoagulation with rivaroxaban. The patient has been followed longitudinally and has completely recovered from this event.

As demonstrated by this case presentation, a multidisciplinary approach in both evaluating and treating complex patients with acute submassive and massive PE is critical to delivering safe and potentially life-saving care. Patients such as this are typically excluded from randomized trials but not from our real-world practices. As eloquently stated by the panelists, there were certainly a variety of approaches that could have been taken with this patient using either catheter-based or surgical techniques once he clinically decompensated. The rapid deployment of coordinated care and the depth of resources both in and out of the lab contributed to his successful recovery. Evolution of catheter-based technology and results from PE trials to date have completely changed the way in which acute PE is treated in 2017. Future trials will hopefully assist us in refining algorithms in this dynamic patient population. ■

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