Case report

Saddle pulmonary embolus resulting in cardiovascular collapse requiring extracorporeal membrane oxygenation in a postoperative patient with endometrial cancer

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A B S T R A C T

Background: Venous thromboembolism after open gynecologic surgery is not uncommon, especially in the presence of other risk factors such as obesity, prolonged surgical time or gynecologic malignancy.
Case: We present the case of a 62 y.o. patient who underwent open hysterectomy and surgical staging for uterine serous carcinoma. She was readmitted with lower extremity edema. During her workup, she underwent cardiovascular arrest secondary to saddle pulmonary embolus requiring cardiopulmonary resuscitation and extracorporeal membrane oxygenation. After systemic and catheter directed thrombolysis, and a long hospitalization, she was discharged home in stable condition.
Conclusion: Saddle pulmonary embolus is a potentially catastrophic and fatal postoperative complication. This case demonstrates a successful implementation of directed thrombolysis, veno-arterial extracorporeal membrane oxygenation and multidisciplinary management in a case of postoperative saddle pulmonary embolus.
Précis: We report a case of an endometrial cancer patient who sustained a massive postoperative pulmonary embolus and was successfully resuscitated using extracorporeal membrane oxygenation.

1. Introduction

Postoperative pulmonary embolism is a rare but substantial cause of mortality and morbidity in patients undergoing surgery for gynecologic malignancy. Risk factors for thromboembolism after hysterectomy include body mass index (BMI) > 35 kg/m^2, laparotomy, prolonged surgical time and cancer as the indication for surgery. The thirty-day postoperative incidence of pulmonary embolism is 1.8% among all gynecologic malignancies and 1.4% in patients with endometrial cancer (Swenson et al., 2015). Substantially higher rates of venous thromboembolism are seen after open abdominal surgery for gynecologic malignancy; VTE is 66% more likely after open abdominal surgery than after laparoscopic surgery (Graul et al., 2017). To mitigate this risk, the 2016 American College of Chest Physicians' CHEST guidelines recommend that patients undergoing abdominal or pelvic surgery for cancer should receive extended duration (up to four weeks after discharge) thromboprophylaxis with low molecular weight heparin (Guyatt et al., 2012). However, the rate of postoperative thromboembolism among women with gynecologic malignancy despite these precautionary measures remains high.

1.1. Case

We present the case of a 62 year old African American gravida 0 who presented to the emergency department 23 days after a total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymphadenectomy for stage IIIC1 uterine serous carcinoma. Her chief complaint at presentation was three days of worsening right lower extremity edema and erythema. She reported compliance with daily prophylactic enoxaparin (40 mg subcutaneous once daily) from the time of hospital discharge after her index surgery. Her review of systems was negative for shortness of breath, chest pain, palpitations, and fever. The patient's medical history was remarkable for venous insufficiency, class III obesity, and psoriasis. Her gynecologic history included menopause 12 years prior with no other pertinent positive reports.
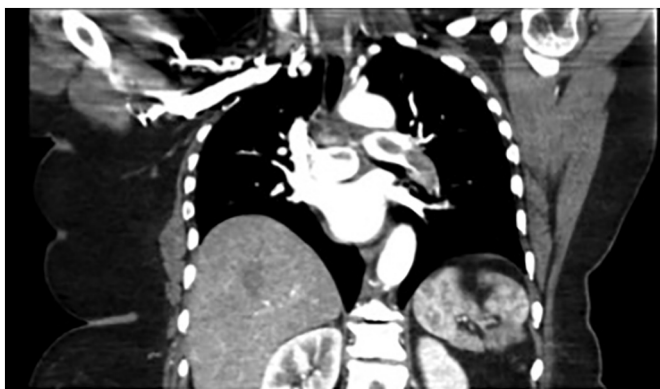
Fig. 1. Coronal image of a computed tomography angiogram demonstrating a large filling defect in the pulmonary artery consistent with saddle pulmonary embolus.

On initial evaluation, her heart rate was 80 beats per minute and oxygen saturation 100% on room air. Her other vital signs were unremarkable. Significant edema was noted to the level of her mid- thigh on the right side. A 4 × 5 cm area was noted on the patient's right calf that was non-tender but had calor and erythema. Laboratory evaluation showed no leukocytosis. Venous duplex ultrasound was negative for venous thromboembolism. She was admitted for presumed lower extremity lymphedema with superimposed cellulitis and started on intravenous antibiotics. Prophylactic dose enoxaparin was continued throughout her admission.

On her second day of hospitalization, she complained of chest tightness which resolved spontaneously. Laboratory evaluation, including troponin T and creatinine phosphokinase was negative and EKG was unchanged from prior study. However, the following day, a repeat troponin level was elevated to 0.17 ng/mL. A CT pulmonary angiogram was performed, which revealed a saddle pulmonary embolus with evidence of right heart strain (Fig. 1). Upon return to the unit from the radiology department, she collapsed to the floor, and became diaphoretic, dyspneic, and confused. She was tachycardic and hypotensive but responded well to fluid resuscitation. Low dose (50 mg) systemic alteplase was administered intravenously and she was taken to interventional radiology for urgent catheter-directed thrombolysis. However, prior to the start of the procedure, she suffered cardiac arrest and the procedure was aborted. Advanced cardiac life support resuscitation was performed for < 5 min before spontaneous return of cardiac function. She was severely hypotensive and was supported with norepinephrine and vasopressin continuous infusion. A heparin drip was started for anticoagulation. She was then intubated, placed on extracorporeal membrane oxygenation with femoral vascular access, and transferred to the cardiac care unit.

Ultimately, she underwent catheter directed thrombolysis 4 days after her initial event. She was then extubated and extracorporeal membrane oxygenation was discontinued on day 5 and her anticoagulation was transitioned to therapeutic enoxaparin. Her course in the critical care unit was complicated by supratherapeutic anti-factor Xa levels with pelvic hematoma requiring massive transfusion. She also developed acute kidney injury with urinary tract infection and multidrug resistant E. coli bacteremia. The pelvic collection was drained, she clinically improved and she was discharged with continued antibiotics and therapeutic anticoagulation on hospital day 42.

1.2. Comment

We describe a case of saddle pulmonary embolism in a patient with endometrial cancer on prophylactic dose enoxaparin. She was successfully rescued from massive thromboembolism and subsequent cardiac arrest using systemic thrombolytic therapy and veno-arterial extracorporeal membrane oxygenation as supportive, temporizing measures to allow for catheter directed thrombolysis.

Malignancy and recent surgery have been well described in the literature as risk factors for VTE. Current evidence supports primary and extended duration prophylaxis against VTE for cancer patients undergoing surgery [45]. Obesity is another independent risk factor for VTE but obesity can also influence the pharmacokinetics of thromboprophylactic agents and alter the dose effect. Numerous weight and BMI adjusted dosing regimens have been studied. However, these studies are difficult to perform due to need for long term follow up and large sample sizes and interpretation is limited by use of surrogate measures of anticoagulation(Streiff et al., 2015).

After her index surgery, our patient was treated with 40 mg of daily subcutaneous enoxaparin as well as sequential compression devices. She had numerous risk factors for VTE including BMI 36, recent surgery, malignancy and chronic venous stasis. She was discharged on the same pharmacoprophylaxis regimen and reported excellent compliance. During her readmission and prior to the reported complication, 40 mg of daily prophylactic dose enoxaparin as well as sequential compression devices were also continued. At our institution, this approach is routinely used and supported by evidence-based guidelines[34]. However, the optimal enoxaparin dosage regimen for obese patients remains unclear. In one prospective comparative study, Freeman et al. compared standard 40 mg daily enoxaparin to weight-based dosing in patients with extreme obesity (BMI > 40) and showed more frequent achievement of target anticoagulation level when dosed by weight (Freeman et al., 2012). Singh et al performed a retrospective study of 170 obese postoperative patients receiving 30–60 mg twice daily BMI-based enoxaparin prophylaxis. No VTEs were identified within the two year follow up period(Singh et al., 2012). Despite these findings, well-controlled studies are lacking. As a result, National Cancer Care Network guidelines do not support more frequent enoxaparin dosing for moderately obese patients or weight-based or BMI-based regimens (Streiff et al., 2015). Management should be based on individual patient factors. Current guidelines stratify pulmonary emboli into massive, submassive and low risk categories based on prognostic factors for mortality. Treatment is based on risk stratification. Massive pulmonary embolus is defined by sustained hypotension or requirement for pressor support and has a 25–65% mortality rate (Jaff et al., 2011). Massive pulmonary embolus has traditionally been managed with reperfusion therapy (systemic vs. percutaneous catheter-directed thrombolysis) or surgical embolectomy. Systemic thrombolysis is performed with a standard dose of 100 mg tissue plasminogen activator infused intravenously over 2–3 h. Patients with contraindications to systemic thrombolysis or who are too unstable to undergo lengthy thrombolytic infusion can be managed with low-dose or even no tissue plasminogen activator, followed by catheter directed thromobolysis. There is evidence that initial treatment of massive pulmonary embolus with low dose tissue plasminogen activator (50 mg) has similar efficacy to standard dose tissue plasminogen activator (100 mg) but less risk of major hemorrhage(Wang et al., 2010).

Treatment of submassive embolus (i.e without sustained hypotension but with evidence of right ventricular dysfunction or myocardial necrosis) with systemic thrombolytics is controversial. The current literature is mixed: some but not all trials show a benefit in long term outcomes but with increased risk of major bleeding. Several meta-analyses have been published but are plagued by differing definitions of submassive pulmonary embolus, surrogate outcomes, differing tissue plasminogen activator and anticoagulation protocols and other heterogeneity. Major professional bodies differ in their guidelines for use of thrombolytics in these circumstances. Systemic thrombolysis can be used in submassive pulmonary embolus based on clinical judgment in select patients with adverse prognosis, with careful assessment of bleeding risk(Jaff et al., 2011).

In this case, the patient initially presented with submassive pulmonary embolus with vital signs that responded to resuscitation. However, her saddle embolus was high risk in terms of anatomic clot

location and clot burden. On bedside echocardiography, McConnell's sign and right ventricular dilatation and hypokinesis were seen, evidence of right heart strain which is a poor prognosticator. In fact, some have even suggested early surgical embolectomy in patients without hemodynamic instability but with evidence of right ventricular strain since mortality is significantly increased. Considering these factors as well as latency from her surgery and her overall medical status, the decision was made to include systemic thrombolysis in her treatment. Other reports have described using stepwise escalation from systemic thrombolysis to catheter directed thrombolysis to surgical embolectomy. In this case, the patient was temporized with a low dose of alteplase while communicating with interventional radiology and while the angiograpghy suite was being prepared.

Venoarterial extracorporeal membrane oxygenation was utilized in this case when our patient rapidly became unstable in the interventional radiology suite before catheter directed thrombolysis could be performed and progressed to cardiovascular collapse and massive saddle embolus. Venoarterial extracorporeal membrane oxygenation rescue has an emerging role in the management of massive PE and has been described in various case reports and series (Ching-Ho Hsieh et al., 2001). The 2016 CHEST guidelines do not discuss this therapy. Hsieh et al previously reported a case of acute massive PE managed with ECMO followed by surgical embolectomy in a patient who had undergone radical hysterectomy for cervical cancer. In their report, the size and anatomic location were key factors that prompted open surgical embolectomy (Ching-Ho Hsieh et al., 2001). Our case demonstrates successful early intervention with extracorporeal membrane oxygenation used to directly relieve right ventricular strain from massive saddle embolus to stabilize a critical patient. t can be performed more rapidly than thrombolysis or thrombectomy and once stable, the patient can undergo further definitive procedures or be anticoagulated while awaiting autothrombolysis. A systematic review of 78 cases of massive pulmonary embolus managed with extracorporeal membrane oxygenation reported a 70.1% survival rate(Yusuff et al., 2015). Induction of extracorporeal membrane oxygenation during cardiopulmonary resuscitation was a poor prognostic factor and survival in this subgroup was 51%. They found no significant difference in mortality between surgical embolectomy, catheter embolectomy, and thrombolysis in conjunction with extracorporeal membrane oxygenation. More research is needed on the efficacy of these treatment modalities versus extracorporeal membrane oxygenation alone.

(Corsi et al., 2017) performed a retrospective observational study collecting data from a tertiary intensive care unit following short and long term outcomes. The 90-day overall survival rate in their cohort was 47%. Notably, 15 of the 17 patients suffered severe bleeding episodes although survival was not affected. Hemorrhage is a known complication of extracorporeal membrane oxygenation and risk factors in this patient population include thrombocytopenia, vasopressor requirement and cardiopulmonary resuscitation(Corsi et al., 2017). This was the case for our patient; following catheter directed thrombolysis and initiation of therapeutic anticoagulation for maintenance of extracorporeal membrane oxygenation, her anticoagulation became supra-therapeutic. She developed pelvic hematomas requiring significant transfusion of blood products. We suspect derangement of the physiologic clotting cascade in the setting of significant clot dissolution and reformation after catheter directed thrombolysis, subclinical clot formation known to occur with extracorporeal membrane oxygenation and concurrent anticoagulation. One author has suggested decreasing the dose of either thrombolytic or parenteral anticoagulation or both

when thrombolytic therapy is given, although further evidence is needed(Sharifi, 2016). In consultation with our hematology service, we were unable to identify any validated nomogram for titration of enoxaparin in the adult population.

In conclusion, this case demonstrates a successful application of low dose thrombolysis, venoarterial extracorporeal membrane oxygenation and catheter directed thrombolysis to manage a case of saddle pulmonary embolism in a patient with endometrial cancer. Care of this patient required coordination of multiple teams. Our experience supports a multidisciplinary approach with early collaboration between critical care medicine, interventional radiology, vascular surgery and the gynecologic oncologist. This therapy is safe and effective in the appropriately selected patient and can be a lifesaving intervention in this often fatal condition. Further research is needed to determine treatment protocol and long term outcomes of patients undergoing this therapy.

1.3. Consent

Written informed consent was obtained from the patients for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal, upon request.

Conflict of interest

The authors have no personal or financial affiliations to disclose.

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