Case report

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

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ARTICLE INFO

Keywords:
- Pulmonary embolus
- Extracorporeal membrane oxygenation
- Thrombolysis
- Endometrial cancer

ABSTRACT

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/m², 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 IIIIC1 uterine serous carcinoma. Her chief complaint at presentation was three days of worsening right lower extremity edema and erythema. 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.

https://doi.org/10.1016/j.gore.2018.03.005

Received 25 November 2017; Received in revised form 13 March 2018; Accepted 14 March 2018

Available online 16 March 2018

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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 nor-epinephrine 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(Sreiff 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 compication, 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(44). 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 (Sreiff 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 thrombolysis. 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 thrombolysis 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 thrombolitics 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

Fig. 1. Coronal image of a computed tomography angiogram demonstrating a large filling defect in the pulmonary artery consistent with saddle pulmonary embolus.
gone radical hysterectomy for cervical cancer. In their report, the size
ECMO followed by surgical embolectomy in a patient who had under-
et al previously reported a case of acute massive PE managed with
saddle embolus. Venoarterial extracorporeal membrane oxygenation
tional radiology suite before catheter directed thrombolysis could be
alteplase while communicating with interventional radiology and while
the angiography suite was being prepared.

Venoarterial extracorporeal membrane oxygenation was utilized in
this case when our patient rapidly became unstable in the interven-
tional 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 under-
gone 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 oxygena-
tion 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 oxygena-
tion reported a 70.1% survival rate(Yusuff et al., 2015). Induction of
extracorporeal membrane oxygenation during cardiopulmonary re-
suscitation 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 extra-
corporeal 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 ep-
sodes although survival was not affected. Hemorrhage is a known
complication of extracorporeal membrane oxygenation and risk factors
in this patient population include thrombocytopenia, vasopressor re-

demand and clot burden. On bedside echocardiography, McConnell’s
sign and right ventricular dilatation and hypokinesis were seen, evi-
dence 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 embo-
lectomy. In this case, the patient was temporized with a low dose of
alteplase while communicating with interventional radiology and while
the angiography suite was being prepared.

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 pul-
monary embolism in a patient with endometrial cancer. Care of this
patient required coordination of multiple teams. Our experience sup-
ports 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 pub-
lication 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.

Acknowledgements

The authors have no acknowledgments to report.

References

Ching-Ho Hsieh, P., Wang, S.-S., Ko, W.-J., Han, Y.-Y., Cho, S.-H., 2001. Successful
Resuscitation of Acute Massive Pulmonary Embolism With Extracorporeal Membrane
Oxygenation and Open Embolectomy.

Corsi, F., et al., 2017. Life-threatening massive pulmonary embolism rescued by ve-
noarterial-extracorporeal membrane oxygenation. Crit. Care 21, 76.

Freeman, A., Horner, T., Pendleton, R.C., Rondina, M.T., 2012. Prospective comparison of
three enoxaparin dosing regimens to achieve target anti-factor Xa levels in hospital-
ized, medically ill patients with extreme obesity. Am. J. Hematol. 87, 740-743.

Graul, A., et al., 2017. Incidence of venous thromboembolism by type of gynecologic
malignancy and surgical modality in the National Surgical Quality Improvement
Program. Int. J. Gynecol. Cancer 27, 581-587.

Guyatt, G.H., et al., 2012. Executive summary. Chest 141, 75–475.

Jaff, M.R., et al., 2011. Management of massive and submassive pulmonary embolism,
iliofemoral deep vein thrombosis, and chronic thromboembolic pulmonary hy-
pertension: a scientific statement from the American Heart Association. Circulation
123, 1788-1830.

Sharifi, M., 2016. Systemic full dose, half dose, and catheter directed thrombolysis for
pulmonary embolism. When to use and how to choose? Curr. Treat. Options
Cardiovasc. Med. 18, 31.

Singh, K., et al., 2012. Evaluating the safety and efficacy of BMI-based preoperative ad-
ministration of low-molecular weight heparin in morbidly obese patients undergoing
roux-en-Y gastric bypass surgery. Obes. Surg. 22, 47–51.

Streiff, M.B., et al., 2015. Cancer-associated venous thromboembolic disease, version
1.2015. J. Natl. Compr. Cancer Netw. 13, 1079–1095.

Swenson, C.W., Berger, M.B., Kamarudin, N.S., Campbell, D.A., Morgan, D.M., 2015. Risk
factors for venous thromboembolism after hysterectomy. Obstet. Gynecol. 125,
1139-1144.

Wang, C., et al., 2010. Efficacy and safety of low dose recombinant tissue-type plasmi-
nogen activator for the treatment of acute pulmonary thromboembolism. Chest
137, 254–262.

Yusuff, H., Zochios, V., Vyulystee, A., 2015. Extracorporeal membrane oxygenation in
acute massive pulmonary embolism: a systematic review. Perfusion 30, 611-616.

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