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Jerrica N. Mueller  
*Washington Hospital St Louis /Barnes Jewish Hospital*

Bobby Mathew  
*Anne Arundel Medical Center*

Douglas D. Reh  
*Greater Baltimore Medical Center*

Joseph Fuscaldo  
*Greater Baltimore Medical Center, jfuscaldo@gbmc.org*

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Cases from a Community Hospital...JCHIMP Series #1: 55-Year-Old Male with Acute PE Who Developed Persistent Epistaxis

Jerrica N. Mueller a, Bobby Mathew b, Douglas D. Reh c, Joseph Fuscaldo c,*

a Washington University in Saint Louis, Barnes Jewish Hospital, USA  
b Anne Arundel Medical Center, USA  
c Greater Baltimore Medical Center, USA

Abstract

This is the first in a new series of case reports that will present real scenarios from our community hospital. The cases are chosen to highlight clinical dilemmas and offer review and perspective on what is currently known about the topic. We present the case of a 55-year-old Caucasian male who presented to the emergency department of our community hospital for worsening dyspnea. Evaluation in the Emergency department revealed a diagnosis of extensive pulmonary emboli in the pulmonary vasculature. The patient was admitted to the ICU. A clinical decision was made to initiate treatment with low-dose tissue plasminogen activator (tpa) followed by intravenous heparin infusion. Several hours later the patient developed significant epistaxis. A decision was made to stop the heparin infusion. Later that day, the patient had abrupt clinical deterioration with subsequent cardiac arrest and did not recover. We discuss the classification and treatment of acute pulmonary embolism, the management of epistaxis in an anticoagulated patient, and the clinical conundrum of balancing active bleeding in patient requiring anticoagulation.

Keywords: Pulmonary embolism, Low-dose tpa, Epistaxis, Anticoagulation, Risk of anticoagulation versus bleeding

This inaugural case highlights the challenges physicians face when weighing the benefits and risks of treatment with therapeutic anticoagulation when unexpected bleeding occurs.

The clinical teams’ relevant questions:

1. How should significant pulmonary embolisms be classified and treated?  
2. How should epistaxis be managed in a patient requiring systemic anticoagulation?  
3. When do risks outweighs benefits when anticoagulating a patient with active bleeding? Do clear guidelines exist?

1. Case summary

We report a case of a 55-year-old Caucasian male who presented to the emergency department of our community hospital for worsening dyspnea. His shortness of breath started three days prior and was associated with a pre-syncopal event, pleuritic-type chest pain, and a cough productive of blood-tinged sputum. His only pertinent past medical history was atrial fibrillation, for which he was taking propafenone 225 mg every 8 h; he was not on any systemic anticoagulation. He had no allergies to medications, no pertinent family history, and no personal history of smoking, alcohol, or drug use.

He denied any systemic symptoms such as fever and chills, recent travel, or sick contacts. Review of systems was positive for decrease in activity, decrease in appetite, and fatigue, but was otherwise negative. In the emergency department, his vital signs were significant for a heart rate of 166 beats per minute that was irregularly irregular, and a SpO2 of 88%. He was afebrile and had blood pressure of 127/74. His respiratory rate was 33

* Corresponding author at: Greater Baltimore Medical Center, Baltimore, MD, USA.  
E-mail address: jfuscaldo@gbmc.org (J. Fuscaldo).

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physical exam was also significant for diminished breath sounds in bilateral lower lung fields; the remainder of exam was normal. ECG shown below.

Supplemental oxygen of four liters via nasal cannula was initiated, a one-liter normal saline fluid bolus was given, and three doses of diltiazem 10 mg were administered intravenously. The patient was also treated with ceftriaxone and doxycycline for possible community acquired pneumonia.

A bedside point of care ultrasound (POCUS) demonstrated a 1:1 ratio of the right ventricle to the left ventricle, right ventricular basilar hypokinesis and apical hyperkinesis, also known as a positive McConnel sign. Given the high concern for PE, a CT

Laboratory evaluations were only significant for the following: Cr 2.1, glucose 221, lactic acid 3.0, troponin 0.96, pro-BNP 1.945, and a D dimer of greater than 20. Due to hypoxia, a PCR COVID was performed, which was negative. Initial diagnostic workup included an EKG, which demonstrated atrial fibrillation with rapid ventricular response. A chest x-ray did not reveal any acute cardiopulmonary process. CXR shown below.
angiography of the chest was performed, which revealed:

“There are extensive bilateral pulmonary emboli present within the distal portion of the central pulmonary arteries bilaterally, with a small amount of thrombus also present in the region of the bifurcation. There are emboli extending into the first and second order branches within the upper and lower lobes bilaterally …”

See CT image below:

The patient was admitted to the ICU for close observation and medical management of a pulmonary embolism. After discussion with the clinical team regarding the risks and benefits of systemic thrombolytics, the patient agreed to proceed with the recommended low-dose tissue plasminogen activator (TPA) 20 mg IV administered over 8 h. After completion of the TPA, a heparin infusion was initiated.

The patient’s oxygen requirement decreased. However, approximately 6 h after the initiation of the heparin drip, the patient was noted to have severe epistaxis. At that time, the decision was made to hold the heparin drip. Oxymetazoline nasal spray was administered, and nasal packing was applied. Despite these measures, the nasal bleeding
What is known about the classification and treatment of acute pulmonary embolism?

Bobby Mathew, MD

Venous thromboembolic disease (VTE) is among the leading causes of morbidity in the world and results in the hospitalization of >250,000 Americans annually (1). VTE can manifest as deep venous thromboses (DVT) or as an acute pulmonary embolism (PE). Treatment for DVT is typically limited to full dose anticoagulation with subcutaneous low-molecular-weight heparin (LMWH), intravenous unfractionated heparin infusion (UFH), a vitamin K antagonist with appropriate parenteral bridging, or any of several direct-acting oral anticoagulants (DOACs) (2). The management of acute PE, however, is dependent on the severity of disease and is a topic of much debate. There is a general consensus regarding patients with acute PE who have very low risk disease as well as those with very high-risk disease. It is in those patients who reside in the intermediate range of severity that there is far less certainty regarding the optimal treatment strategy. Here we will discuss the classification scheme for pulmonary embolism as well as the accepted treatment modalities and guideline recommended approach to early management.

Historically, PE has been classified into three broad categories: massive PE, sub-massive PE, and low-risk PE. Massive PE has been defined by the American Heart Association as acute PE with sustained hypotension (SBP <90 mmHg for over 15 min or requiring inotropic support) that is thought to not be from a cause other than PE, cardiac arrest, or severe bradycardia (pulse <40). Submassive PE is an acute PE that is absent overt signs of shock, but with clinical evidence of RV dysfunction in the form of RV dilation or dysfunction on echocardiography, RV dilation on CT, an elevated B-type natriuretic peptide, an elevated troponin, or EKG changes suggestive of RV strain. Low-risk PE is defined as disease that lacks any of these features (1). The American College of Chest Physicians (ACCP) has similar definitions when defining PE risk severity. The European Society of Cardiology (ESC) refers to massive PE as high-risk PE though it is also defined by the presence of hemodynamic instability. Sub-massive PE is identified as intermediate risk PE by the ESC (3). Short-term mortality is markedly different among these groups, ranging from ~1% at 30 days in the low-risk group to >50% in the group presenting with massive/high-risk PE (4).

The consensus recommendation for low-risk PE is full-dose anticoagulation with any of the pharmacologic agents previously described for the treatment of acute DVT. Absent progression of disease severity, the risks of more aggressive treatment appear to outweigh the potential benefits. For high-risk PE, there is again, little controversy regarding the optimal treatment algorithm. Absent contraindications for systemic thrombolytic therapy - initial reperfusion with systemic thrombolysis is the guideline recommendation.1-3 Marti et al. demonstrated in a meta-analysis of systemic thrombolysis that there was a reduction in all-cause mortality in the thrombolysis group when studies that included high-risk PE were used in the analysis.5 The rate of fatal bleeding and intracranial hemorrhage was significantly higher in the thrombolysis group, however (OR 3.18). Both the ACCP and ESC make a recommendation for short duration infusions (2 h) of thrombolytics in high-risk PE over longer infusions (24 h). Similarly, both state that full dose anticoagulation with UFH can be maintained while infusing TPA, though this practice is far less common in the United States.24

Percutaneous catheter directed treatments exist for the management of PE as well. These procedures typically involve the insertion of a catheter into the pulmonary arteries, which can then be used for direct mechanical fragmentation, thrombus aspiration, ultrasound-based fragmentation, or directed low dose thrombolysis. In an RCT comparing catheter directed thrombolysis vs UFH alone, Kucher et al. demonstrated a significant decrease in RV/LV diameter ratio at 24h in the catheter directed thrombolysis group without an increase in bleeding complications. Given the overall paucity of high quality data for catheter directed therapy, both the ACCP and ESC only recommend the use of a catheter directed treatment strategy in patients with high-risk PE and a contraindication to systemic thrombolysis, have failed thrombolysis, or are likely to die before systemic thrombolysis can have an effect. More specialized therapies including surgical embolectomy and ECMO are also available at tertiary care facilities for selected patients though the evidence regarding these strategies remains limited.
Intermediate-risk or sub-massive PE presents a more complicated question regarding the optimal early treatment strategy. These patients demonstrate clinical evidence of RV dysfunction or myocardial necrosis without sustained hypotension or obstructive shock. Mortality estimates for intermediate risk PE range from 1.8% to 15%. Several studies have attempted to answer the question as to whether systemic thrombolytics have a role in the management of intermediate-risk PE. The most notable among them is the PEITHO Trial by Meyer et al. The PEITHO investigators conducted an RCT comparing systemic TPA with UFH vs UFH alone. The trial demonstrated a statistically significant difference in the composite endpoint of death or hemodynamic decompensation (2.6% in the thrombolytics group vs 5.6% in the UFH alone group). Seven-day mortality, however, was not significantly different (1.2% vs 1.8%) but there was a statistically significant difference in the incidence of hemorrhagic stroke (2.0% in the thrombolysis group vs 0.2% in the UFH alone group).

In light of the significant heterogeneity among patients with intermediate-risk PE and in the face of an unclear benefit to early systemic thrombolysis, both the ACCP and ESC recommend against the routine use of TPA in all patients presenting without high-risk PE. Both groups make recommendation to pursue a reperfusion strategy in patients who demonstrate evidence of clinical worsening while on anticoagulation so long as there is no contraindication to systemic thrombolytic therapy. There is a growing body of literature that is attempting to identify those patients with intermediate-risk PE that are likely to face a higher risk of mortality and, therefore, may warrant consideration for early reperfusion. The quality of evidence for making this assessment based on any one clinical parameter is presently not robust, however.

What is known about managing acute epistaxis in a patient on systemic anticoagulation?

Douglas Reh, MD

Epistaxis is one of the most common otorhinolaryngologic emergencies. It is estimated that 60% of the general population will suffer from at least one episode and 6% will seek medical intervention for epistaxis at some point in their lives. The severity of this condition runs the spectrum from isolated, minor episodes handled in the emergency room or clinic setting to life-threatening instances of near exsanguination requiring definitive management. 90% of nosebleeds originate from the anterior plexus of vessels, Kiesselbach’s plexus, located on the caudal septal mucosa. 45% of patients hospitalized for epistaxis had some type of systemic illness. In a study of these patients, 33% had hypertension, 15% were on anti-coagulation and 0.9% had an underlying coagulopathy.

The traditional approach to managing epistaxis is to apply pressure with direct compression to the caudal septum and the vessels on Kiesselbach’s plexus where most nosebleeds occur. Direct visualization and cauterization of the bleeding area is ideal. However, in some cases that cannot be achieved. Nasal packing can be helpful when cauterization is not feasible as packs can apply diffuse pressure to the source of bleeding.

Bleeding in typical epistaxis usually occurs from a discrete mucosal vessel. However, epistaxis in anti-coagulated patients can be caused by diffuse mucosal bleeding from multiple sources. Controlling epistaxis in an anti-coagulated patient requires a different approach. Topical nasal decongestants such as oxymetazoline work by causing vasoconstriction. A retrospective study of 60 patients treated in the ER for epistaxis showed that 65% of those patients were successfully treated with oxymetazoline. These provide an excellent means of stopping nosebleeds. The placement of a nasal pack inherently causes mucosal trauma. Placing a nasal pack in an anti-coagulated patient, whose mucosal bleeding may be diffuse, may cause trauma that can increase bleeding. The use of dissolvable packing with pro-coagulant properties can control bleeding in atraumatic fashion and is preferred in these patients. Dissolvable packing or injectable pro-coagulant foams can be used to control epistaxis. These include products that use oxidized regenerated cellulose (Surgicel®, Johnson & Johnson, Inc.), collagen granules coated in thrombin (Floseal®, Baxter), and injectable carboxy methylcellulose (Sinu-foam®, Smith and Nephew).

Managing epistaxis in inpatients can be challenging, especially in patients with significant comorbidities such as poorly controlled hypertension or those who are anti-coagulated. The use of topical vasoconstrictors and dissolvable pro-coagulant materials is a good first option for controlling bleeding in these patients. The treating physician should have a low threshold for consulting an Otolaryngologist if these measures fail to control bleeding.
What is known about interrupting recommended anticoagulation in a patient with bleeding?

Jerrica Mueller, MD

This case presentation exemplifies the challenge in making clinical judgments regarding the need for systemic anticoagulation and the risk of related bleeding.

Reasonable physicians may disagree on the importance of maintaining anticoagulation and the degree of risk in specific cases. The complexity in clinical decision-making is related to each patient's unique set of risk factors for thrombosis and bleeding. Often patients are elderly and have significant co-morbidities such as hypertension.

Risk calculators may serve as useful tools to focus the risks of anticoagulation management. For example, in atrial fibrillation, the CHADS\textsubscript{2}VASC and HASBLED scores help to determine an individual's risk of stroke and the subsequent risk of bleeding with anticoagulation. Each risk score is stratified into low, moderate, and high risk, allowing clinician the ability to compare risk of thromboembolism with risk of bleeding through numerical scoring. However, there is little high-quality evidence on how to use these tools to guide our treatment in patient care.

Many patient care scenarios, including our case, are not addressed by existing tools. How should one proceed when a patient requiring anticoagulation develops an acute bleed? The site of bleeding is an important consideration. Two of the most feared complications of systemic anticoagulation are gastrointestinal bleeding and intracranial bleeding. Epistaxis, as in our case, is generally less morbid.

Annual bleeding rates of patients on oral anticoagulant therapy range from 2% to 5% for major bleeding, 0.5% to 1% for fatal bleeding, and 0.2% to 0.4% for intracranial bleeding. It is important to note that not all bleeds carry the same risk for harm. For example, intracranial hemorrhages (ICH) result in morbidity or mortality in up to 76% of cases while extracranial bleeding, including gastrointestinal bleeds, hematuria and epistaxis, lead to death or disability in only 3% of cases.

If a patient survives a major anticoagulant-related bleed, another dilemma surfaces: when is it safe to restart anticoagulation? Universal expert consensus standards are lacking. For one of the more lethal of bleeding scenarios, an anticoagulation-related intracranial hemorrhage, a three-step approach has been proposed to assist decision-making surrounding resumption of anticoagulation therapy. The first step evaluates the individual risk of thromboembolism and hemorrhage. The second step selects the optimal anticoagulant and appropriate timing to reinitiate therapy. Finally, reducing the risk of recurrent hemorrhage through improving modifiable risk factors.

While the three-step approach presented by Li and Lip was designed specifically to address anticoagulation in the context of an intracranial hemorrhage, there may be value in using a similar approach in other types of bleeds. In our patient with epistaxis, this type of model could provide a systematic approach to evaluating indications for anticoagulation and minimizing future bleed risk. With a goal of improving patient outcomes, the safest approach utilizes a multidisciplinary team to guide the complex decision-making. Depending on whether anticoagulation is ceased or resumed, these decisions often have a significant impact on morbidity and mortality.

Further study and analysis of multiple case scenarios and outcomes is suggested to help create and develop expanded anticoagulation models and guidelines in the future. One can imagine a Clot/Bleed Predication Index App on future clinicians’ smartphones.

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