COMMON ERRORS IN INTERNAL MEDICINE

THE MISSED PULMONARY EMBOLISM

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Once this condition is suspected, diagnostic efforts must continue until it's confirmed or ruled out absolutely.

An internist working overseas at a relatively isolated, military medical treatment facility (MTF) is consulted by the on-call surgeon about an obese, 55-year-old woman, whose shortness of breath has progressed to hypoxemic respiratory failure within the two days following an elective, open, ventral, hernia repair. One day before the open repair, the surgeon had aborted an attempted laparoscopic repair upon encountering a larger than anticipated fascial defect and a series of intraoperative equipment malfunctions.

The MTF has no care capability on the level of an intermediate or intensive care unit (ICU). The internist attempts to transfer the patient to a facility for nuclear imaging and ICU admission, but is unable to do so because all the referral centers are full. The patient's chest X-ray suggests pulmonary edema. Her electrocardiogram shows sinus tachycardia with nonspecific ST and T segment changes and a prominent S wave in lead I. Since each of her two surgeries had, unexpectedly, lasted more than four hours, the internist assumes she received too much in the way of intravenous fluids, which could be contributing to her current predicament. He can't confirm this, however, because neither the operating surgeon nor the anesthesia records are currently available.

Bibasilar crackles and pitting edema of both legs support the assumption of fluid overload and congestive heart failure, which is further substantiated by the fact that only 40 mg of furosemide yields 800 mL of urine and marked clinical improvement. Since she received subcutaneous unfractionated heparin 5,000 IU twice daily and was treated with intermittent pneumatic compression (IPC) devices from the outset, pulmonary embolism (PE) goes from high to low on the internist's index of suspicion. He, therefore, abandons efforts to have her transferred to a facility with an ICU, in which PE could be ruled out definitively.

Over the next three days, the patient's condition continues to improve. On the fourth day, however, she collapses in the hallway as she begins to ambulate for the first time since surgery. Despite aggressive resuscitation attempts, she remains in asystole and dies. As the internist requests permission for an autopsy from the family, he learns that the patient took two nine-hour trips by airplane 10 days prior to her first surgery.

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The autopsy confirms that a massive PE was the cause of death. At the risk management meeting, a review of the nursing notes reveals that, on the day following her first surgery, the patient had refused to get out of bed in accordance with the surgeon's orders, but none of the physicians had acted on this.

CAN YOU IDENTIFY THE ERRORS?

The main error in the management of this case was failing to rule out PE completely once it was in the differential diagnosis. Because this patient's risk factors included obesity, age over 40, two major surgeries within a two-day interval, and (though unknown at the time) a recent transatlantic flight prior to surgery, PE should have remained high on the physician's index of suspicion—even though her physical examination and response to diuresis were consistent with fluid overload. No matter how a patient responds to various interventions, once PE is suspected, diagnostic efforts must continue until it's confirmed or ruled out absolutely.

Other errors included failure to insist that the patient ambulate as soon as possible following surgery and inadequate history taking (as an adequate history would have uncovered her recent travel). Perhaps low molecular weight heparin (LMWH) would have been a better choice for prophylaxis than unfractionated heparin, but this is debatable.

GETTING TO THE ROOT OF THE PROBLEM

A travel history is something easily neglected, especially in the perioperative setting in which clinicians tend to focus on the more traditional surgical risk factors, such as recent myocardial infarction, age over 70 years, or lung disease. How many of us honestly can say that we always ask about recent travel as part of our preoperative medical evaluations or during our perioperative consultations? Although usually inconsequential from a surgical standpoint, a recent history of prolonged travel increases the risk of deep vein thrombosis (DVT) and, secondarily, PE. It could be especially relevant, therefore, in an isolated facility, as this case demonstrates.

The classic triad of dyspnea, pleuritic pain, and hemoptysis is present in only 20% of patients with major PE.

In the United States, more than 300,000 patients are diagnosed with PE annually, and it's estimated that another 600,000 patients with PE remain undiagnosed.[1] The annual death toll associated with this condition is approximately 50,000.[1]

The risk factors associated with DVT after elective thoracic or abdominal surgery are classified as follows:

- high risk—recent history of DVT or PE or extensive pelvic or abdominal surgery for malignancy;
- moderate risk—age over 40 and procedure longer than 30 minutes; or
- low risk—age under 40 with no other risk factors.[2]

Clinical manifestations of acute PE vary widely and range from subtle or nonspecific signs and symptoms to hypotension and sudden death. The classic triad of dyspnea, pleuritic pain, and hemoptysis is present in only 20% of patients with major PE.[3] Another common symptom is apprehension. Physical findings can include tachypnea, tachycardia, accentuation of the pulmonic component of the second heart sound, cough, and inspiratory rales.

Studies investigating congestive heart failure as a possible risk factor for thromboembolic events have had conflicting results. A retrospective examination of the database provided by the VA's Vasodilator-Heart Failure Trials (V-HeFT) I and II showed the incidence of all thromboembolic events to be 2.7 per 100 patient-years during 1,068 patient-years without warfarin in V-HeFT I and 2.1 per 100 patient-years during 1,188 patient-years in V-HeFT II—with no reduction in patients treated with warfarin.[4] This study concluded that the incidence of thromboembolism in class II or III congestive heart failure is not high and may not be reduced significantly with warfarin treatment.[4] Another study, however, concluded that left ventricular thrombus and thromboembolism are common in patients with dilated cardiomyopathy who aren't treated with an anticoagulant.[5] Echocardiography may be helpful in predicting which patients are at risk for thromboembolism.[5]

A small percentage of patients with clinically apparent PE die of massive embolism before the diagnosis is made, usually within the first hour.[1] Of patients who are diagnosed, those who receive heparin anticoagulation therapy and sur-

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vive two hours or more following PE diagnosis have a very good prognosis.[1] On the other hand, if anticoagulation therapy is not initiated at diagnosis, clinically significant embolization occurs in at least 30% of cases within the following six weeks.[1] For patients receiving adequate anticoagulation therapy, this figure falls to less than 5%, with most of these episodes occurring within the first several days of treatment.[1]

Among patients presenting with DVT, the rate of fatal PE occurring during anticoagulation therapy is 0.4%; following anticoagulation therapy, it's 0.3 per 100 patient-years.[6] The case fatality rate of recurrent DVT or PE during anticoagulation therapy is 8.8%; following anticoagulation therapy, it's 5.1%.[6]

When the clinical probability of an acute PE is moderate or greater, the absence of DVT doesn't rule out the possibility of PE. In such cases, further tests to rule out the presence of emboli are necessary. The majority of patients with PE have no leg symptoms at the time of diagnosis. In one major study, fewer than 30% of 117 patients with PE had symptoms or signs of lower extremity DVT.[7]

In acute PE, arterial blood gas studies usually reveal hypoxemia, hypocapnia, and respiratory alkalosis.[3] Nevertheless, approximately 18% of patients with submassive or massive embolism have a partial pressure of oxygen greater than 80 mm Hg, and up to 6% have a normal alveolar-arterial gradient for oxygen.[3]

GOOD NEWS IN DIAGNOSIS AND TREATMENT

Low dose, unfractionated heparin (LDUH) is an effective prophylactic agent that reduces the incidence of fatal postoperative PE.[8] Studies performed in the late 1970s and 1980s documented the efficacy of administering subcutaneous heparin 5,000 IU every 12 hours or 5,000 IU every eight hours, with the first dose given two hours preoperatively.[9,10] Initiating prophylaxis postoperatively also appears to be effective, though the practice hasn't been tested in randomized trials.[11]

Several clinical studies have shown LMWHs to be more effective than standard heparin in preventing venous thromboembolism (VTE) in surgical patients without increasing bleeding complications.[12] In patients undergoing orthopedic surgery, LMWHs administered once or twice daily for DVT prophylaxis were found to be significantly more effective than standard heparin administered two or three times daily; more effective than orally administered anticoagulants; and significantly more effective than dextran, aspirin, or adjusted-dose heparin in preventing proximal venous thrombosis.[12]

Later studies comparing LDUH with a low dose LMWH (enoxaparin 40 mg or the equivalent) in general surgery patients showed comparable efficacy with a moderate increase in the risk of bleeding associated with use of LMWH.[13] Use of LDUH is associated with a modestly higher incidence of bleeding compared with IPC devices.[14] Elastic (graduated compression) stockings or IPC may provide an additional protective effect when used with LDUH in patients at high risk.

D-dimer testing, combined with clinical probability assessment (Table),[15] has been proposed as the first step in the diagnostic workup of patients with suspected PE. D-

Table. Clinical model for predicting the probability of acute venous thromboembolic disease[15]

Clinical parameter	Score*
Active cancer	1
Paralysis, paresis, or recent immobilization or casting of lower extremity	1
Major surgery within past four weeks or recently bedridden for more than three days	1
Localized tenderness along distribution of deep venous system	1
Swelling of entire leg	1
Calf swelling by 0.3 cm compared to asymptomatic leg	1
Pitting edema (greater in symptomatic leg)	1
Collateral superficial veins apparent	1
Likelihood of alternative diagnosis equal to or greater than that of acute venous thromboembolic disease	–2

*If total score is greater than or equal to 3, the probability of pulmonary embolism is high; if 1 or 2, moderate; if less than or equal to 0, low.

Spiral computed tomographic angiography…can be used as a primary diagnostic test in suspected PE.

dimer levels can be altered, however, by rheumatoid factors and surgical procedures, making this type of testing less useful in the perioperative population.[16] Other factors that may affect degradation products are heat stroke, infection, cancer, incompatible blood transfusion, prolonged coma, and any condition associated with disseminated intravascular coagulapathy.[16] In fact, in patients who have cancer, the negative predictive value of the D-dimer test is significantly lower than in patients without cancer.[17] In patients without these potentially confounding factors, however, the combination of a low clinical probability and a normal D-dimer concentration appears to be a safe and reliable method by which to exclude PE.[18]

Within the past several years, spiral computed tomographic angiography (SCTA) of the pulmonary arteries has emerged as a noninvasive means of evaluating patients with suspected PE. Single detector SCTA has a sensitivity of approximately 85% to 90% and a specificity of 88% to 95%.[19] SCTA can be used as a primary diagnostic test in suspected PE[20,21] and as a second-line imaging method for patients in whom ventilation/perfusion scintigraphy results are inconclusive.[19]

In the future, two advances will enhance further the role of SCTA in evaluating suspected PE: (1) multislice computed tomographic scanning of the pulmonary arteries with multiplanar reformation and (2) scanning pulmonary arteries and lower extremity veins in a single session.[19]

Having better bioavailability than unfractionated heparin, LMWHs have moved the treatment of uncomplicated DVT—and, for select patients, VTE—to the outpatient setting. LMWHs do not require monitoring of the partial thromboplastin time like unfractionated heparin does and they can be administered subcutaneously. LMWHs have resulted in shorter hospitalizations and fewer incidents of major bleeding complications.[22]

Thrombolysis is an accepted first-line treatment for inpatients with massive PE who present with hypotension or shock.[23] In most patients with hemodynamically stable, submassive PE, however, its role is controversial.[24,25]

The incidence of fatal PE is about 7% in patient registries, whereas it is 1% to 2% in randomized trials.[26] In general, thrombolysis for submassive PE has not been adopted widely due to a lack of compelling evidence of superior efficacy over heparin and concerns about a fourfold higher risk of major bleeding.[24] In the largest trial to date comparing thrombolysis with heparin, heparin plus alteplase reduced the combined endpoint of in-hospital death and clinical deterioration requiring escalating treatment more than did heparin alone.[27] For all-cause mortality, the groups did not differ.[27]

If, in the case presented here, acute venous thromboembolic disease had remained high on the internist's index of suspicion, as it should have, he would have had to weigh the risks of suspected PE against the benefits of full anticoagulation until a ventilation perfusion scan, a pulmonary angiogram, or an SCTA could be obtained. Placement of an intravenous umbrella could have been used as an alternative to full anticoagulation or as a next step if the patient were to have further thromboembolic events after initiation of full anticoagulation. ●

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