CLINICAL VIGNETTE

Pulmonary Embolism in the Ambulatory Setting

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Introduction

Pulmonary embolism (PE) is a blood clot that interferes with blood flow in a pulmonary artery. In most cases the blood clot develops in the leg, as a deep vein thrombosis (DVT), which travels to the lung.[1] Without prompt diagnosis and treatment, PE can result in long term damage to the heart and lung and can even result in death. PEs are not common, about 23 cases per 100,000 persons/year. It is potentially life-threatening and accurate detection is important.[2] Autopsy study reported 12% of patients with evidence of a PE, with only 10% of patients having the PE detected prior to death.[3] Among patients referred for evaluation a suspected PE, only 15% of these patients were confirmed to have a PE.[2] In the ambulatory setting, the incidence of confirmed PEs is low among those suspected. Risk stratification approaches have been used to improve the yield of PE diagnoses. Identified risk factors are associated with PE, including underlying cancer, recent surgery, prolonged immobility, leg trauma, and diagnosis or family history of hypercoaguability. The WELLS score is based on risk factors and physical findings, to categorize a low, moderate or high probability of PE.[2] When combined with serum D-dimer measurement in ambulatory patients it stratifies risk in patients with suspected PE.[2] In ambulatory older (>age 60 years) adults, low risk WELLS score and normal D-dimer measurements were reported in several patients subsequently found to have a PE, representing about 3% of those evaluated.[4] We report a case of a patient seen in an ambulatory setting with minimal PE symptoms and risk factors, that was correctly identified as likely to have a PE using a combination of WELLS score and serum D-dimer measurement.

Case

Patient is a 61-year-old healthy male with no significant past medical history and a 3-day history of pleuritic chest pain, but no other symptoms. He was initially seen at an urgent care and was evaluated, which included an EKG and chest x-ray, which were both normal. He was told this his chest pain was most likely due to gastroesophageal reflux disease (GERD)-related pain and was prescribed a proton pump inhibitor (PPI). This treatment did not alleviate his symptoms of chest pain, which was so severe that it interfered with his sleep.

The patient came to primary care clinic for evaluation of his persistent chest pain. He denied recent travel, surgery, leg trauma, immobilization, history of deep vein thrombosis (DVT) or known history of hypercoaguability. He was on no medications.

His vital signs were normal; Pulse 68/min, Blood Pressure 108/60. Respiratory Rate 20. SpO_2 (oxygen saturation) 96% on room air. On physical exam, the patient was breathing comfortably, had normal cardiac exam, no prominent P2 sound on cardiac auscultation, pulmonary exam was normal, and no calf tenderness, calf swelling, or calf asymmetry.

It was recommended that the patient be evaluated in the emergency department, but he did not want to go, so an outpatient evaluation of PE risk stratification was pursued (Table 1). His WELLS score was 3 (no better diagnosis to explain pleuritic chest pain) putting him in the moderate risk category (>2 and <6), and a serum D DIMER was ordered (Table 1). Result of D- DIMER was 3.39 mg/L (normal is<0.5 FEU). Based on the moderate risk WELLS score and elevated D-DIMER, the patient was felt to be at a significant risk for a PE and was referred for inpatient hospitalization.

The patient's inpatient evaluation included the following studies and results: 1) Lower extremity DVT in peroneal and popliteal veins, 2) Computed Tomography Angiogram (CTA) showed large bilateral lower lobe pulmonary embolus and left lower lobe pulmonary infarct, 3) Echocardiogram demonstrated evidence for right heart strain, 4) Hypercoagulation work-up showed a slightly elevated Factor 8, but was otherwise normal, 5) Malignancy work up negative including CEA <0.2. PSA 3, LDH and Beta 2 globulin were normal.

The patient was diagnosed with DVTs and PE, and treated with Enoxaparin, 1mg/kg q 12, for 5 days and was discharged on Apixaban. He was subsequently evaluated by hematology and cardiology consultants. He was diagnosed with idiopathic pulmonary embolism, with no underlying contributing condition. Due to the high clot burden, it was recommended that he continue on long term Apixaban therapy.

Discussion

Definition and nomenclature - Pulmonary embolism (PE) refers to the obstruction of the pulmonary artery or its branches by material which could be thrombus, air, fat or even tumor. PE is classified by the temporal presentation (acute, subacute or

chronic).[1,5] In an acute PE, patients typically develop acute symptoms immediately after the obstruction. Subacute PE patients present with symptoms several days to weeks after the initial event. Chronic PE patients slowly develop symptoms of pulmonary hypertension. A PE is further characterized by the presence or absence of hemodynamic instability. Hemodynamic instability results in hypotension which is defined as systolic Bp<90 or a drop in systolic BP >40 mmHg from baseline, for a period of 15 minutes or hypotension that requires vasopressors. Finally, the PE anatomic location is noted (saddle, lobar, segmental or sub segmental).

Epidemiology - The overall incidence of PE is higher in males (48 per 100,000) vs females (56 per 100,000). However, the incidence rises with increasing age especially in females as the incidence in women over 75 is >500 per 100,000. In the United States PE accounts for 100,000 deaths annually.[5]

Pathogenesis - The pathogenesis is similar to that of any thrombus which is the Virchow's triad (venous stasis, endothelial injury and hypercoagulable state).[6] Risk factors for PE are similar to those of DVT and can be classified as acquired or genetic. More than 50 genetic risk factors have been identified including factor V Leiden, prothrombin gene mutation. Acquired risk factors can be further classified as provoking (recent surgery, immobilization and hormone therapy) or non-provoking (obesity, heavy cigarette use). Most emboli are thought to arise from the lower extremity proximal veins (iliac, popliteal and femoral). Calf vein DVT's rarely causes Pulmonary Embolism.

Clinical Presentation and Diagnosis - Pulmonary embolism has a wide variety of presenting features which include pleuritic chest pain, cough, dyspnea, tachypnea and tachycardia.[1,5] With severe PE patients can present with shock, arrhythmia or even syncope. For patients who are hemodynamically unstable bedside echo or venous compression ultrasound may be used to obtain a presumptive diagnosis of PE to justify administering lifesaving therapies.

Treatment - For patients with acute PE initial therapy should focus on maintaining adequate oxygenation and stabilizing the patient and that could include anything from supplemental oxygenation to mechanical ventilation.[7] The mainstay of therapy is anticoagulation. Patients with life threatening PE may require additional therapy like thrombolysis, inferior vena cava (IVC) filters and embolectomy. Select populations, such as patients with malignancy, pregnancy, and heparin induced thrombocytopenia may require alternative therapeutic strategies. Parenteral anticoagulant therapy usually consists of weight adjusted low molecular weight heparin, fondaparinux or intravenous unfractionated heparin. In patients who are hemodynamically stable anticoagulation can now also be started with oral agents right away using one of the non-vitamin K antagonist oral anticoagulants (NOAC) like apixaban or rivaroxaban. This recommendation is based on phase 3 clinical trials that demonstrated superior safety and non-inferior efficacy of the oral agents. After the acute phase long term therapy is administered for a period of 3-6 months or 12 months depending on the underlying etiology. Patient goals and preferences are also critical in selecting a long-term agent for anticoagulation.

Conclusion

It is important to consider the diagnosis of PE in ambulatory patients that may present with a range of symptoms and findings. Many of these patients will have underlying risk factors for PE. Some, however, as the patient we report, have no risk factors or underlying condition detected, and present with only pleuritic chest pain. Risk stratification with a WELLS score and D-DIMER level successfully identified this patient and supports this approach to evaluation of a suspected PE in the ambulatory setting.

Table 1. Diagnostic Approach to Patient with Suspected PE[8]
For patients with suspected PE who are hemodynamically stable utilizing a pretest probability assessment (WELLS SCORE), D Dimer testing and definitive imaging, like pulmonary angiography and sometimes VQ scan is recommended.

WELLS SCORING

1) Physical findings like leg swelling (3 points)
2) No alternative diagnosis to better explain this (3 points)
3) Tachycardia with HR >100 (1.5 points)
4) Immobilization for 3 days or recent surgery (1.5 points)
5) Prior history of DVT/PE (1.5 points)
6) Hemoptysis (1 point)
7) Underlying malignancy (1 point)

Score of >6 High Probability, Score>2-<6 Moderate Probability, Score <2 Low Probability

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