Pulmonary Embolism:
Cause and Effect

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Table 1
Patient investigation

William's vitals:
Normotensive: 147/43 mmHg
Temperature: 36°C
Tachypneic: 24 breaths per minute
Acyanotic
Severely hypoxic, 80% oxygen saturation at room air
Respiratory alkalosis on blood gases
Electrocardiogram: sinus tacycardia with Q waves in lead III

Jeffrey's vitals:
Normotensive: 112/70 mmHg
Afebrile
Tachycardic: 113 beats per minute
Normal oxygen saturation of 98% at room air

William's case

William, 70, has benign prostatic hyperplasia and diet-controlled diabetes. He presents to the emergency department with complaints of left-sided pleuritic chest pain and feeling feverish for a few days. He developed acute shortness of breath one hour before presentation. He has had no historical or familial risks for hypercoagulation. Chest X-ray was unremarkable (Figure 1). Patient was started on unfractionated intravenous heparin and an immediate VQ scan showed large perfusion defect on the right side (Figure 2).

About Jeffrey

Jeffrey, 42 and healthy, underwent left hip surgery for Legg-Calve Perthes disease, but presented on the seventeenth day postoperatively, with progressive left leg and calf swelling, and occasional left-sided plueritic chest pain. His physical examination was otherwise significant for swelling of the left leg below the knee (Figure 3), with left-sided Homans' sign being positive. Femoral deep vein thrombosis (DVT) was diagnosed with duplex ultrasound. A spiral computed tomography (CT) scan of his chest revealed right pulmonary embolism (Figure 4).

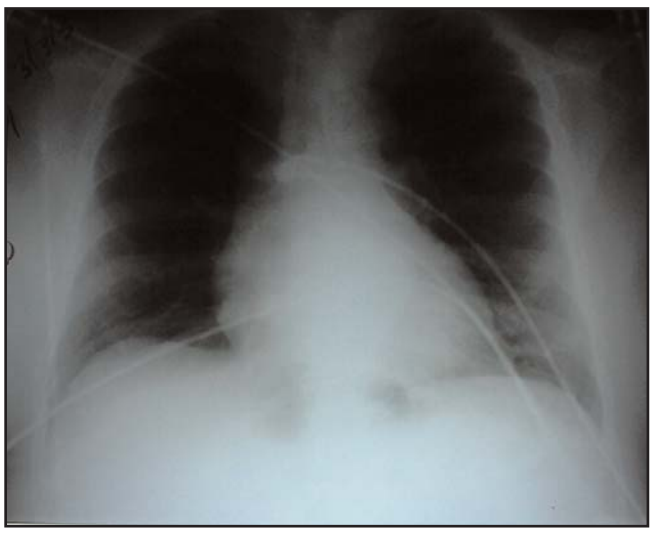

Figure 1. William's chest X-ray.

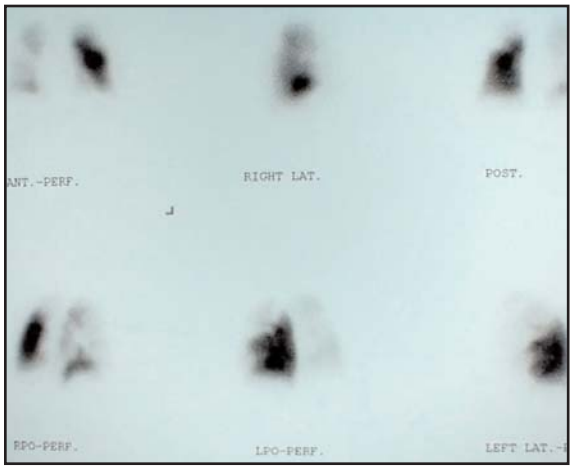

Figure 2. Massive right-sided perfusion defect on William's VQ scan.

About pulmonary embolism

Pulmonary embolism (PE) ranges from incidental, clinically unimportant thromboembolism to massive embolism with sudden death. Hypercoagulability leads to the formation of thrombus in the leg veins, with proximal extension as the clot propagates. As thrombi form in the deep veins of the legs or pelvis, they may dislodge and embolize to the pulmonary arteries. Pulmonary arterial obstruction results in elevated pulmonary vascular resistance, increased alveolar dead space, V/Q (ventilation-perfusion) mismatch, and impaired gas exchange. Reflex bronchoconstriction augments airway resistance, and lung edema decreases pulmonary compliance.[1,2]

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DVT is the usual cause of PE. Risk factors for thromboembolism can be explained by Virchow's triad—local trauma to the vessel wall, hypercoagulability, and stasis as causes of venous thromboembolism. Recognized risk factors may be acquired or hereditary. Acquired disorders include surgery (especially orthopedic), trauma, pregnancy, oral contraceptive pills, malignancy, immobilization, hyperviscosity (polycythemia vera, multiple myeloma), hyperhomocysteinemia, and lupus anticoagulant syndrome, amongst many others. Inherited factors are deficiency of proteins C and S, antithrombin III, and factor V leiden mutation.[1,3,4-7]

Clinical presentation varies from shortness of breath, pleuritic chest pain, cough, hemoptysis, hypoxia, sinus tachycardia, fever, pleural effusion, hypotension, and death. Right-sided heart failure is the usual cause of death from PE, and right ventricular dysfunction is a crucially important warning of a possible adverse outcome. Physical examination may reveal distention of the neck veins, an accentuated pulmonic heart sound, or a tricuspid regurgitation murmur. The electrocardiogram may show right ventricular strain with an S1Q3T3 pattern (prominence of the S wave in lead I and a Q wave and T-wave inversion in lead III), right bundle-branch block, or T-wave inversion in leads V_1 through V_4. However, the most objective, uniform, and quantifiable measure is the echocardiogram, which can be used to estimate pulmonary-artery systolic pressure and can show right ventricular dilatation and hypokinesis.[8]

Figure 3. Swelling of left leg below the knee (Jeffrey).

Serum elevations of D-dimer are nonspecific (*e.g.,* increased by aging, inflammation, cancer), an abnormal result has a low positive predictive value. Venous ultrasonography is highly accurate in symptomatic outpatients with suspected DVT, but normal results do not rule out PE.

Pulmonary angiography is the gold standard for diagnosis, but it is technically demanding to perform, may be difficult to interpret, and is costly. It is contraindicated in patients with renal impairment and may not be feasible in the sickest patients.[9] Lung perfusion scanning remains the most useful screening test to rule out clinically important acute PE. Normal results are almost never associated with recurrent PE, even if anticoagulants are withheld. In the prospective investigation of PE diagnosis, the use of a scanning pattern thought to indicate a high probability of PE identified only 41% of affected patients.[10] Lower-limb venous compression ultrasonography shows DVT in 30% to 50% of patients with proven PE. Helical CT of the pulmonary arteries is rapidly gaining acceptance as a diagnostic test for suspected PE. Helical CT is a relatively noninvasive procedure that can be used to diagnose PE by directly imaging the intravascular clot. Numerous validation studies have evaluated the accuracy of helical CT. Overall sensitivi-

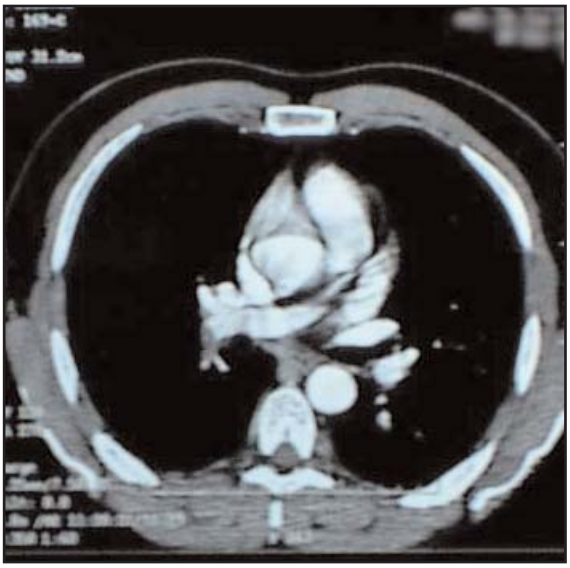

Figure 4. Jeffrey's chest CT scan.

ties range from 64% to 100% and specificities range from 89% to 100%. It has become evident that helical CT cannot identify all patients with PE because it may miss clots confined to the subsegmental pulmonary artery branches.[12] Echocardiography is not recommended as a routine imaging test to diagnose suspected PE. However, it is useful for identifying patients with PE who may have a poor prognosis. It can be used for rapid and accurate risk assessment. Moderate or severe right ventricular hypokinesis, persistent pulmonary hypertension, a patent foramen ovale, and free-floating right-heart thrombus are echocardiographic markers that identify patients at risk for death or recurrent thromboembolism.[13]

What to do?

Once venous thromboembolism is diagnosed, unfractionated heparin should be given for four to seven days and warfarin therapy should be initiated in conjunction preferentially 48 to 72 hours after inititation of heparin treatment. Thrombolytic therapy is justifiable for patients with acute massive PE and hemodynamic instability or cardiogenic shock.[14] In patients with acute venous thromboembolism and active bleeding or a high potential for bleeding, those who are noncompliant, and those with a history of heparin-induced thrombocytopenia, inferior vena cava filter may be considered. Treatment with hirudin and its analogues may be used when heparin therapy cannot be tolerated.

The optimal duration of anticoagulation after PE remains uncertain. A treatment period of three to six months is usually enough. Lifelong anticoagulation should be considered in patients with recurrent PE if the risk of major bleeding is low. For patients with deficiencies of antithrombin III, protein C, or protein S, several years rather than lifelong anticoagulation may suffice. Whether patients with factor V Leiden and PE should receive prolonged courses of anticoagulation remains sharply debated.[2,15] Long-term low intensity anticoagulation with international normalized ratio (INR) kept between 1.5 and 2.0 may be preferable to short-term anticoagulation.

What about William?

William was started on unfractionated intravenous heparin and warfarin. His work up had been negative for cancer (previous prostate biopsy one year ago, upper and lower endoscopy after admission). He was discharged 10 days after admission on coumadin, but presented again after 11 days with another

episode of moderate hypoxia and dyspnea due to suboptimal anticoagulation. He had normal ejection (66%) fraction on echo but it showed mild pulmonary hypertension. Venous ultrasound showed bilateral popliteal vein thrombosis. He had moderate left-sided pleural effusion which resolved upon subsequent follow up spontaneously. Investigations revealed that he had a heterozygous factor V leiden mutation. He was discharged on lifelong coumadin therapy.

What about Jeffrey?

After treatment with intravenous heparin and warfarin, Jeffrey was discharged uneventfully on the tenth day after admission. He was advised to be on warfarin for six months. His studies for familial hypercoagulable states were negative. CME

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