Clinical aspects of pulmonary embolism

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1. Pulmonary Embolic Disease: An Overview

Venous thromboembolic disease, including deep venous thrombosis (DVT) and pulmonary embolism (PE), is an important medical condition. It is estimated that there are approximately 5 million cases of deep venous thrombosis annually in the US. At least 10% of these lead to PE, and approximately 10% of these result in death (50,000). PE is the sole or major cause of death in 10-15% of adults dying in the acute care wards of general hospitals. Therapy for thromboembolic disease exists in the form of anticoagulation medication. The majority of deaths arise not from failure of therapy, but rather from failure to diagnosis the disease or from prophylactic failure. Unfortunately the diagnosis of PE can be challenging.

Approximately 90% of PEs that achieve clinical attention arise in the deep venous system of the legs, with the remainder arising in the deep venous system of the upper extremities, or rarely within the right heart or the pulmonary arteries. Thrombi limited to the calf veins rarely embolize, whereas those that extend or originate more proximally (popliteal, iliofemoral veins) may embolize in up to 50%. The initiating event is typically platelet aggregation at venous valves due to turbulence, or at sites of intimal injury. This results in release of mediators which initiate the coagulation cascade, and development of a red fibrin thrombus. Fibrinolysis is subsequently initiated, resulting in breakdown of the clot, which can occur at varying rates and to various degrees. At any point in the process some or all of the thrombus may detach and travel to the lungs as an embolism, although the risk is greatest early on. Most emboli lodge in branches of the pulmonary arteries, a few straddle the bifurcation, and a very few lodge in the right heart. Major physiologic consequences include compromise of respiratory function, and cardiac complications due to elevated pulmonary arterial pressures. The patient's ability to cope with these processes is significantly compromised by the presence of pre-existing cardiopulmonary disease. In patients with impaired cardiopulmonary function, severe pulmonary arterial hypertension can result from pulmonary embolic disease involving a relatively small portion of the pulmonary vascular bed.

As mentioned, the diagnosis of PE can be challenging. Patient presentation falls into one of three syndromes: isolated dyspnea, pleuritic pain or hemoptysis, and circulatory collapse. The most common presenting symptom is dyspnea, and the most common sign is tachycardia. However, the clinical presentation is not specific and cannot be relied upon to make the diagnosis of PE. Rather it merely raises the suspicion, leading to diagnostic testing, including imaging.

2. The Chest Radiograph in Pulmonary Embolic Disease

The chest radiograph is a quick, readily available, inexpensive, low radiation means of evaluating the lungs, and is usually the first imaging modality obtained in patients presenting with possible PE. However, the findings on chest radiograph are neither sensitive nor specific for PE, and the primary benefits of the chest radiograph are to exclude alternate diagnoses such as pneumonia or pulmonary edema, and to aid in the interpretation of a V/Q scan. Still, as a radiograph will inevitably be available, it is worth reviewing the findings in the setting of PE.

As the chest radiograph is neither sensitive nor specific for PE, further imaging will be required. This typically involves the nuclear medicine ventilation/perfusion (V/Q) scan, or increasing computed tomography pulmonary angiography (CTPA). Evaluation utilizing these imaging modalities may be supplemented with compression ultrasound of the lower extremities to assess for DVT. Interventional pulmonary angiography is often taken to be the reference standard, but is not used in routine cases as it is invasive, involves some risk (especially in patients with right sided heart failure), suffers from accessibility issues, and is still an imperfect reference standard, with potential errors in interpretation. Nevertheless, it may be invoked when the diagnosis remains otherwise in doubt.
3. The V/Q Scan: Background and Technical Issues

Unlike angiography and CTPA, the nuclear medicine perfusion (Q) scan evaluates the sequella of a PE (decreased perfusion to the lung), rather than the direct presence of an embolism. However, decreased perfusion can also be seen in the setting of primary ventilatory abnormalities, such as pneumonia, atelectasis, and tumour, as the lung responds to such ventilatory conditions by decreasing blood flow to the effected portions of the lungs, to avoid perfusing non-ventilated lung. Thus it is necessary to also perform a ventilation (V) scan for correlation with the perfusion scan. It follows that primary ventilatory conditions will yield a decrease in both ventilation and perfusion (a “matched” defect), whereas a pulmonary embolism will result in a defect only on the perfusion portion of the study (an “unmatched” defect). This is the primary premise of the V/Q scan. These basic principles may not always be maintained. For example, occasionally a pulmonary embolism will result in secondary decreased ventilation due to focal edema, atelectasis, infiltrates, or even infarction, resulting in a matched defect. The interpretation of V/Q scans will be discussed later in this symposium.

The perfusion scan is usually performed using $^{99m}$Tc macroaggregated albumin (MAA). MAA particles are of varying size, with most in the 20-40u range, and with the vast majority in the 10-90u range. Pulmonary capillaries are typically 7-10u in diameter, while terminal arterioles are approximately 35u. Thus following injection in the venous system, MAA particles pass through the right side of the heart and lodge in the pulmonary precapillary arterioles. Typically 200,000-500,000 particles are injected, in a dose of 2-4mCi. As there are approximately 300 million pulmonary arterioles, roughly 1/1000 become occluded through injection of MAA. In spite of this, the number of particles should be reduced for safety reasons in the setting of pulmonary arterial hypertension, right-to-left shunt, single lung, and pediatric cases. Injection is performed in the supine position to yield a more even distribution throughout the lungs.

A number of different radiopharmaceuticals have been used for the ventilation scan. All are administered by having the patient breathe the agent through a mask. Common agents include $^{99m}$Tc aerosol agents such as aerosolized $^{99m}$Tc-DTPA, and gaseous agents such $^{133}$Xe. $^{99m}$Tc Technegas is a relatively newer ventilation agent, with physiologic characteristics intermediate between those of an aerosol and a true gas.

Imaging typically consists of multiple planar views of the lungs, and increasingly SPECT imaging. However, when $^{133}$Xe is used for ventilation, the rapid washout from the lungs allows imaging from only a single projection.

Further Reading