

Clinical quiz: What causes a rapidly fatal event within hours?

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Clinical scenario

A 53-year-old male complained of sudden exertional dyspnoea at midnight hour. There was cough productive of pink sputum. Past health was good except for congenital left lower limb swelling.

He was afebrile. B.P. 150/90 mmHg.
Pulse 145/min. Respiratory Rate 20/min.
SaO₂ 90% on room air.
JVP was not raised.

Chest examinations: There were crepitation heard over right chest.

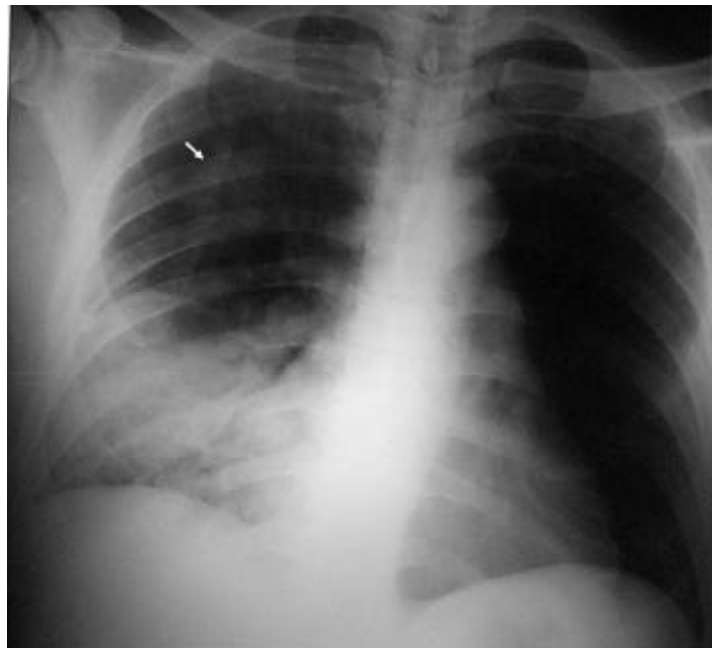


Figure 1.

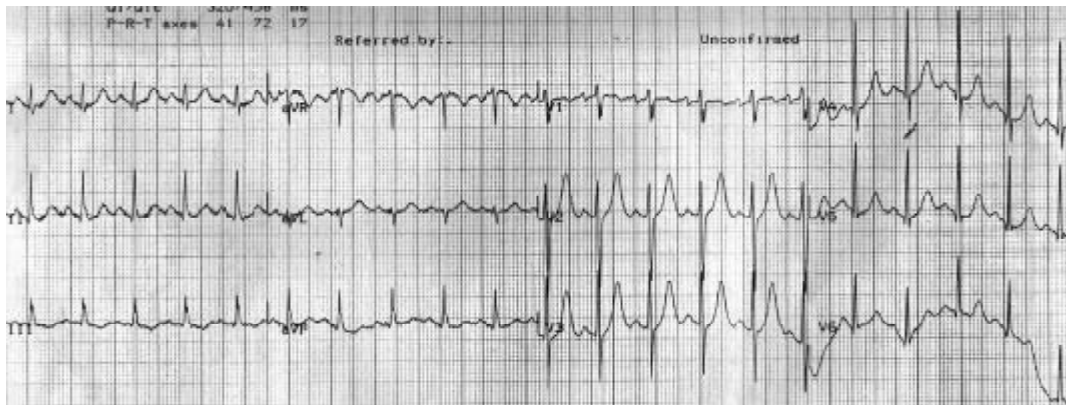


Figure 2.

Questions

1. Chest X-ray was performed and what are the radiographic signs present?
2. What are the likely radiological diagnosis?
3. ECG was performed and what are the findings?
The patient deteriorated and had cardiopulmonary arrest within 3 hours after admission and could not be revived despite resuscitation.
4. What is the most likely diagnosis?

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Answers

1. Frontal chest radiograph has the following findings:
 - a. Decreased right lung volume
 - b. Two large opacities: one in the right upper lobe and one in the right lower lobe
 - c. Right decreasing pulmonary artery appears enlarged
 - d. Cardiomegaly

Upper lobe opacity appears triangular in shape which represent wedge-shaped pleural-based infarct (Hampton's Hump).

2. Differential diagnosis
 - a. Pulmonary embolism
 - b. Chest infection
 - c. Primary lung tumour
 - d. Metastasis
 - e. Aspiration pneumonia
 - f. Adult respiratory distress syndrome (ARDS)
3. ECG shows sinus tachycardia, rate at 112 per minute. Normal axis. There was presence of S wave in I and T inversion in III
4. Massive pulmonary embolism

Discussion

Post-mortem findings showed pulmonary embolism in both lower branches of pulmonary arteries with bronchial haemorrhage and ischaemic necrosis corresponding to X-ray appearance. There was angiomatosis of left leg with engorged abnormal vascular channels which was filled with blood. The presence of tachypnoea and left leg angiomatosis are hints pointing to the diagnosis of pulmonary embolism. Nevertheless pulmonary embolism is difficult to diagnose and deteriorates rapidly. A high index of suspicion is crucial to early life-saving treatment.

Pulmonary embolism (PE) is acute occlusion of pulmonary artery by thrombosis. The emboli most commonly arise from pelvic venous system, followed by deep veins of calf. It is traditionally classified as acute massive PE with shock when

greater than 60% of vascular bed are affected. Acute non-massive PE can mimic other medical conditions. Haemodynamically it can evolve rapidly within an hour to massive PE.

PE is the third most common cause of death in the United States. Autopsy reports indicate the incidence of PE at 40% to 50%, with 5% to 15% of deaths in acute care hospitals due to PE!

Over 90% patients of PE occur in presence of clinical risk factors. Any venous stasis, vessel wall damage and hypercoagulopathy may predispose to thrombo-embolism.

Immobility, Plaster of Paris, prolonged bus or airline trips,¹ major trauma, recent surgery within 3 months are examples of risk factors for deep vein thrombosis. Thirty percent of general surgical patients over 40 years old undergoing major surgery develop deep vein thrombosis (DVT) postoperatively. Forty to sixty percent of patients having major joint replacement and no preventive measure develop DVT. The incidence of PE in unprotected patients having major joint replacement is between 5% and 15%. This is reduced to less than 4% with DVT prophylactic measures. Fatal PE incidence is in the order of 0.5% to 1% patients.

In the absence of cancer, trauma, recent surgery and immobilisation, inherited coagulation disorders and environmental factors may account for the development of DVT. In patients less than 40 years old, one may test for deficiency of anti-thrombin III, Protein C, Protein S, lupoid anticoagulant and anticardiolipin antibodies. Resistance to activated protein C is by far the most frequent coagulation disorder.²

Severe obesity, cigarette smoking, hypertension and high oestrogen oral contraceptive (OC) pills increase the risk of PE. Pathological obesity predisposes to venous stasis and DVT while cigarette smoking and hypertension probably cause direct damage to the endothelial lining of the venous wall, impairing the endogenous response to incipient thrombosis. Anabolic steroid use, hormonal therapy and hypercholesterolaemia may also increase the risk of PE.

The diagnosis of PE should be kept in mind in children with tachypnoea when risk factors for venous thromboembolism are present, to avoid delay in anticoagulant treatment and a fatal outcome.³ For women, PE is the most common medical cause of maternal mortality associated with live births.

Acute non-massive PE may mimic acute bronchitis, bronchiectasis, pneumothorax, pneumonia, pericarditis, lung tumour, hysteria and rib fracture. Dyspnoea (80%) and chest pain are the most reliable symptoms. Classical triad of tachypnoea, pleuritic chest pain and frank haemoptysis only occur in less than 20% of patients. Physical examination is often normal. It is found that 70% of patients with proven PE have DVT. However DVT is very often clinically silent. Hence diagnosis of PE requires a high index of suspicion.

Pathologically there is occlusion of small vasculature by minor emboli from pelvic venous system resulting in a pulmonary infarct. The clots begin as small deposits of platelets, fibrin and red blood cells which adhere to the valve cusps of veins. The lodged platelets degranulate and secrete histamine, catecholamine, serotonin and prostaglandins. Pulmonary hypertension may develop with repeated episodes. Unusual causes are fat emboli from multiple trauma, renal tumour emboli and amniotic fluid.

Clinically there may be tachycardia, pleural rub and mild pyrexia. ECG is normal in less than 10% PE patients. The most common ECG abnormality is sinus tachycardia and non-specific ST-T changes. CXR may be normal in first 24 hours and becomes wedge-shaped pleural-based infarct (Hampton's Hump), pleural effusion, elevated hemidiaphragm and plate atelectasis.

In acute massive PE, the emboli cause occlusion of more than 60% of vascular bed leading to shock. It may present suddenly with syncope and death. Subsequent CPR may disperse a central clot sufficiently to restore the pulmonary circulation. If insidious and progressive, it may then mimic other medical conditions such as acute myocardial infarct and pulmonary oedema. There is often a history of one or more minor emboli before the current

episode. Instead of pleuritic pain, it causes central chest pain. There may be dyspnoea with cyanosis, tachycardia, hypotension, distended neck veins and raised jugular venous pressure. Features of right ventricular strain may be present such as loud pulmonary component of the second heart sound, ECG showing right axis deviation, right atrial P waves, RBBB, right ventricular hypertrophy. Atrial fibrillation may also occur. S wave in lead I, Q wave in lead III, T wave in lead III is uncommon and non specific. CXR shows oligoemia with central emboli (Westermark sign), consolidation and hilar enlargement (Pulmonary artery dilatation). Arterial blood gas (ABG) shows low PaO₂ and low PaCO₂. Alveolar-arterial oxygen gradient is high.

Acute right heart failure is a principal cause of circulatory collapse and death in patients with massive PE. Helical CT identifies acute RV dilatation in addition to arriving at the primary diagnosis of massive PE.⁴

Diagnosis of PE requires a high index of suspicion. It may have many differential diagnoses such as viral pleurisy, pneumonia, minor trauma, pneumothorax, pericarditis, musculoskeletal pain and pulmonary oedema. Clinical risk factors are sought and one should look for tachypnoea, tachycardia, right heart failure, DVT and phlebitis. ECG and chest radiograph are essential to rule out other medical conditions. Early non-massive PE may have normal ECG, Chest radiograph and arterial blood gas. Further investigations may include Ventilation-Perfusion Scan (V/Q Scan), spiral or helical CT, Transoesophageal Echocardiogram (TEE), MRI, serum markers such as D-dimers. Pulmonary angiography however, remains the gold standard. Associated DVT may be investigated by Duplex Ultrasound, Impedance pletysmography and Venography. *Chest radiograph findings are often negative in most PE even in acute massive PE. This is because findings depends largely on when the chest radiograph is performed.*

Pulmonary angiography is highly specific but invasive and causes bleeding if followed immediately by thrombolytics as compared to V/Q Scan. It is suggested that angiography be reserved for diagnosing PE in those patients who have contraindications to the administration of

thrombolytics. It allows the site and extent of thrombosis to be visualised.

V/Q Scan is reserved for the highly suspected PE candidates planning to receive thrombolytic therapy. The perfusion scan is performed first by injecting intravenously 99-Tc labelled macroaggregated albumin with a gamma camera obtaining multiple views of the lungs. A normal perfusion scan rules out PE. An abnormal perfusion scan is followed by a ventilation scan. Xenon is imaged in the lungs during breath-holding and washout phases. The extent or severity of V/Q mismatch is then categorised as Low Probability, Intermediate Probability and High Probability of PE. Analysis is often aided by evidence of clinical risk factors and presence of DVT.

The pulmonary arteries can be visualised with spiral CT after injection of iodinated contrast material. Sensitivity for the detection of segmentary or more proximal thrombi is nearly 100% with a specificity estimated at 96%. These figures are much lower for subsegmentary emboli, varying from 63% to 83% for sensitivity and from 85% to 100% for specificity. The requirement for treatment in these minor forms, however remains a topic of debate. Due to its noninvasive character and the diagnostic performance, spiral CT is well adapted for cases of suspected massive embolism. However in the case of minimal embolism, spiral CT cannot eliminate the diagnosis before the results of other explorations are known.⁵

Contrast-enhanced magnetic resonance angiography (MRA) of the pulmonary vasculature has a sensitivity of 85% and specificity of 95% for PE.⁶ *However, the fact that patients with PE are often tachycardic and MRI are particularly susceptible to movement artifact, MRI are currently not the imaging modality of choice for PE.*

Studies measuring the fibrin degradation product D-Dimer using enzyme-linked immunosorbent assays (ELISA) in PE suggest that it is possible to exclude PE when the D-Dimer level is below a certain cut-off value. New rapid latex assay methods have been tried with sensitivity and negative predictive value of over 90%.^{7,8}

When managing a patient with suspected PE in an emergency setting, we must be aware of the possibility of sudden arrhythmia and cardiogenic shock. High flow oxygen and analgesic should be given. The presence of raised jugular venous pressure should not lead one to use diuretics and venodilators. A high venous pressure is required in PE to maintain adequate pulmonary perfusion. Inotropes and colloid may be used. The use of heparin in acute non-massive PE should be discussed with the receiving specialty and 5000-10000 IU is administered intravenously as a bolus dose, followed by maintenance infusion. Subsequent management may include thrombolytics and embolectomy. Thrombolytics must not be given together with heparin to avoid bleeding complications. Recurrent PE may require lower limb venous ligation or passage of umbrella filter so as to interrupt inferior vena caval emboli. Prophylactic measures are required after the acute treatment. Complete resolution of major PE treated with heparin alone can often take more than 3 weeks. Thrombolytic agents effectively resolve pulmonary artery thrombi within a few hours.⁹ Immediate thrombolytic therapy prior to institution of heparin is indicated in patients with acute massive PE and those with respiratory or circulatory failure, or evidence of moderate to severe right ventricular dysfunction.¹⁰

The usefulness of low molecular weight heparins e.g. enoxaparin has caught the attention of clinicians because of improved bioavailability, predictable anticoagulation, ease of administration, and lack of need for monitoring anticoagulation. It is safe and equipotent or superior when compared with unfractionated heparin or warfarin. It allows clinicians to treat PE in an out-patient setting.¹¹

Acknowledgement

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