Diagnosis and management of pulmonary thromboembolic disease

Chronic pulmonary thromboembolic disease is one of the most underdiagnosed causes of chronic breathlessness and is not uncommon in elderly patients in hospital. About a quarter of cases of pulmonary thromboembolic disease result in pulmonary hypertension, which can be cured if referred to appropriate centres.

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Pulmonary embolism is not uncommon. The estimated prevalence of this acute condition in patients in hospital is about 1%. The prevalence at autopsy is about 15%, and can be the cause or contributing cause of death in about 37% of cases. In the remaining 63% of cases, it can be an incidental finding.[1] Various recent studies show the incidence of venous thromboembolism as about one in 1000 people per year.[2,3] Pulmonary embolism can be difficult to diagnose and is easily missed in clinical practice. In one study, nearly 40% of patients who had deep venous thrombosis but no symptoms of pulmonary embolism had evidence of pulmonary embolism on lung scans.[4]

Diagnosis

Diagnosis of pulmonary embolism is a challenge for clinicians and, dependent on sensitivity and specificity, various tests can be used to confirm or exclude pulmonary embolism.[5] Investigations that effectively confirm pulmonary embolism because of their high sensitivity include intraluminal filling defect in pulmonary angiography or helical CT and ventilation-perfusion scan (V-Q scan) showing high probability if the patient has moderate or high clinical probability. Similarly, investigations helpful for exclusion of this disorder include normal pulmonary angiogram, normal V-Q scan and a normal D-dimer test with low clinical suspicion.[6]

Box 1: Case report

A 65-year-old man presented to the medical admissions department with an acutely swollen and painful right leg. The assessing doctor had clinical suspicion of deep-vein thrombosis. Investigation with venous and arterial Doppler scan then revealed an acute deep-vein thrombosis with acute paradoxical embolus in the right leg.

At this point, review of his clinical notes showed that he was being investigated as an out-patient for symptoms of New York Heart Association class II heart failure. His chest X-ray and lung-function tests at that investigation were normal, and he was mildly hypoxic on arterial blood gas testing. ECG had shown right-axis deviation with widespread t-wave inversion in the inferoseptal leads. Transthoracic ECG had shown grossly dilated right ventricle and atrium with hypertrophy and impaired systolic function.

During our assessment, ECG showed R-waves in lead V1, right bundle branch block was noted, and widespread inverted t-waves were seen in leads II, III, AVF, and V1–V5. CT pulmonary angiogram then confirmed extensive proximal pulmonary emboli. Pulmonary arterial pressure was raised to an estimated 87 mmHg. Transoesophageal echo showed a patent foramen ovale.

After discharge with anticoagulation treatment, the patient's symptoms worsened progressively to functional class III–IV symptoms in follow-up clinic visits. The final diagnosis at this point was severe pulmonary arterial hypertension due to recurrent pulmonary emboli (chronic thromboembolic pulmonary hypertension). He was referred to the National Pulmonary Hypertension Service and was assessed for further treatment by pulmonary and coronary angiogram, among other investigations. He was eventually referred for pulmonary endarterectomy with bosentan as bridging therapy and successful surgery was done at Papworth Hospital.

One month after surgery the patient showed remarkable symptomatic improvement of heart failure from class IV to class I. His estimated pulmonary artery systolic pressure was down to 30 mmHg and he had no clinical signs of pulmonary hypertension. He was eventually discharged from the clinic because he had no symptoms over the subsequent few months.

To achieve greatest clinical and cost efficiency from the available investigations, choice of initial diagnostic test is of utmost importance. Multiple guidelines are used worldwide,[5] and in the UK, the British Thoracic Society's guidelines[6] are followed. The most important decision to make is that of clinical probability of pulmonary embolism, on which the choice of further investigation depends. Probability should be clearly assessed and documented in every case of suspected pulmonary embolism.

A way of assessing risk is probability of pulmonary embolism scored between 0 (low probability), 1 (intermediate probability) and 2 (high probability). If pulmonary embolism is more likely than any alternative diagnosis, a score of +1 is given and if the patient has a major risk factor for venous thromboembolism a further rating of +1 is given. According to guidelines from the British Thoracic Society, major risk factors for venous thromboembolism include recent immobility, major surgery, leg fracture, previous deep-vein thrombosis or pulmonary embolism, obstetric or metastatic cancer, but does not include oestrogen-containing medication, travel, known thrombophilia, obesity, or minor surgery, which are considered as minor risks.

Generally, D-dimer testing is done only if the calculated clinical probability is low or intermediate, and if the result is negative, pulmonary embolism is excluded reliably.[7] For patients with high clinical probability of this condition, CT pulmonary angiogram is the initial investigation recommended, and if positive, is confirmatory. Isotope lung scanning may be considered as the initial imaging investigation in absence of significant symptomatic concurrent cardiopulmonary disease or abnormal chest radiographic findings.

Management

Heparin constitutes the mainstay of management and should be given to patients with moderate-to-high likelihood of pulmonary embolism, unless contraindicated, and anticoagulation with warfarin should be started after diagnosis is confirmed. Once anticoagulation is established, it should be continued for 4–6 weeks for temporary risk factors, 3 months for primary idiopathic risk factors, and at least 6 months for others.[7] Filters in the inferior vena cava are mainly used for cases in which anticoagulation is either contraindicated or unsuccessful in preventing recurrence of pulmonary embolism and continuing deep-vein thromboses.

Thrombolysis

Thrombolysis for pulmonary emboli is at present recommended only for massive pulmonary embolism with haemodynamic shock that is severe enough to cause cardiac arrest.[7] The evidence supporting this recommendation is from a small study done in 1995 which looked at eight patients with shock related to massive pulmonary embolism.[8] The four patients on heparin died, whereas the four receiving thrombolysis survived.

Predicting prognosis

Echocardiogram of right ventricular function has an important prognostic role in pulmonary embolism. A finding of right ventricular hypokinesis with normal systemic arterial pressure predicts an adverse clinical outcome. In patients who underwent echocardiography, a finding of right ventricular hypokinesis was associated with a doubling of the mortality rate at 14 days and with a rate at 3 months of 1·5 times that in patients without hypokinesis. The overall mortality rate at 1 year was 15%; however, the mortality rate at 1 year was three times higher in patients with right ventricular dysfunction than in those with normal right ventricular function.[9,10] The mortality rate increases as right ventricular failure worsens.[11]

Chronic thromboembolic pulmonary hypertension

The main complication of unresolved or acute pulmonary embolism is chronic thromboembolic pulmonary hypertension, which is underdiagnosed with an incidence higher than is generally appreciated.[12] It is characterised by

Box 1: Alternative diagnoses

- Dissection of the aorta
- Pericardial tamponade
- Lung cancer
- Primary pulmonary hypertension
- Rib fracture
- Pneumothorax
- Costochondritis
- Musculoskeletal pain
- Pneumonia or bronchitis
- Asthma
- Exacerbation of COPD
- Myocardial infarction
- Pulmonary oedema
- Anxiety

intraluminal thrombus organisation and fibrous stenoses or complete obstructions of the pulmonary arterial branches, causing persistently raised pressure in the pulmonary artery, and progressive right heart failure. The treatment of choice for this condition is surgical pulmonary endarterectomy, which can cure the disorder. It is a major surgical procedure associated with significant risks, and cannot be done in a substantial proportion of patients, because of either the distal location of pulmonary thromboemboli or severe comorbidity.

A preoperative period of at least 3 months of adequate anticoagulation is mandatory. Patients considered for surgery are usually have symptoms of class III or IV heart failure. The surgical accessibility of thromboembolic lesions is heavily dependent on the experience of the surgical team. Preoperative assessment is done by pulmonary angiography. Worldwide mortality rates vary between 5% and 24%;[13] the lower mortality is usually seen in centres with more experience in such procedures.

Most patients with functional class III or IV before the operation achieve class I or II with a good exercise capacity after surgery.[14] Cardiac output is increased and oxygenation can be returned to normal. Right heart function and tricuspid competence assessed by echocardiography is also significantly and persistently improved. Long-term survival after endarterectomy is very favourable compared with medical treatment or lung transplantation, with a 5-year survival rate of 75% to 80%. After endarterectomy, the 5-year survival is 75–80%,[15] whereas in a registry of the US National Institutes of Health, the median survival with medical management was reported as 2·8 years, with 1-year, 3-year, and 5-year survival rates of 68%, 48%, and 34%, respectively.[16] Other surgical options include atrial septostomy and, eventually, lung and heart-lung transplantation.

Conclusion

Pulmonary thromboembolism remains a very difficult diagnosis to make. When a diagnosis is made, as well as treating the acute condition with anticoagulation, following-up patients and monitoring them closely for development of chronic thromboembolic pulmonary hypertension is important. Monitoring can be done with serial chest X-ray, ECG, and echocardiogram, and if evidence of pulmonary hypertension is seen, early referral to a local expert group is recommended for further evaluation and monitoring of pulmonary hypertension. Chronic thromboembolic pulmonary hypertension remains an extremely under-recognised condition in hospital practice and this is very important as it can be potentially curable if the lesion is amenable to pulmonary thromboendarterectomy.

I have no conflict of interest.

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