

Clinical and Laboratory Findings in Patients with Pulmonary Embolism in Phramongkutkla Hospital

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Abstract

Pulmonary embolism (PE) was believed to be a rare disease and often misdiagnosed in Thailand. Only a few cases of PE in Thai patients have been reported. The purpose of this study was to describe the characteristics of history, physical examination and laboratory investigations in Thai patients with PE. Forty-nine patients diagnosed as PE in Phramongkutkla Hospital between 1994 and 1998 were included in the study. All patients underwent complete history, physical examination and appropriate laboratory studies. The mean age of this patient group was 53 years. Thirty-four per cent of these patients were first suspected of lung embolism while the others were misdiagnosed as congestive heart failure, myocardial infarction, pneumonia or septic shock. The most common syndrome was isolated dyspnea. Interestingly, chronic thromboembolic pulmonary hypertension which is uncommonly found in western countries was diagnosed in 12 per cent of our patients. Dyspnea, pleuritic pain, leg swelling, cough, tachypnea, tachycardia and increased pulmonary component of second heart sound were common symptoms and signs. A high-probability ventilation/perfusion lung scan and deep vein thrombosis were demonstrated in 93 per cent and 55 per cent of our patients, respectively. The mortality rate was 10 per cent.

Key word : Pulmonary Embolism, Deep Vein Thrombosis Lung Scan, Hypercoagulable

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Pulmonary embolism (PE) was believed to be a rare disease and often misdiagnosed in Thailand(1). Only a few cases of PE in Thai

patients have been reported since 1967(2-8). Recently, PE has become more interesting for many reasons, including the following. Firstly, labora-

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tories used to confirm the diagnosis of PE, such as lung scan, pulmonary angiography and spiral computed-tomography, have become more available(9). Secondly, prevalence of vascular diseases, including coronary artery disease, have increased steadily. Lastly, many clinicians have become more aware and have the capability to make the diagnosis of this disease.

The mortality attributable to PE depends on many factors but could be up to 30 per cent in untreated patients, more than 10 times the annual mortality for patients treated with anticoagulant drugs(10). Early diagnosis is crucial, therefore, characteristics of PE are needed. The purpose of this analysis was to evaluate disease characteristics including clinical, risk factors and laboratory findings of PE in Thai patients.

MATERIAL AND METHOD

Study population

The study was conducted from January 1994 to December 1998. All patients who were diagnosed with PE in Phramongkutkla Hospital were prospectively included in the study protocol. Diagnosis of PE was established by angiography, spiral computed-tomography, or high clinical suspicion with high probability of ventilation-perfusion lung scanning. The high clinical likelihood was based on appropriate symptoms and signs, the presence of predisposing factors, and the absence of other diseases to account for these. Patients' data including history, physical examination, predisposing factors and laboratory findings were carefully completed as soon as the diagnosis was confirmed. The patients were closely followed-up for at least 3 months to evaluate the course of the disease and the mortality rate.

Syndrome of PE

The syndrome of PE was classified into 4 groups, as follows.

1. Pulmonary infarction or hemorrhage was defined as patients with pleuritic pain or hemoptysis in the absence of circulatory collapse.

2. Isolated dyspnea was specified as dyspnea in the absence of hemoptysis, pleuritic pain, shock or loss of consciousness.

3. Circulatory collapse was defined as loss of consciousness or shock (blood pressure < 80 mm Hg)(11,12).

4. Chronic thromboembolic pulmonary hypertension (CTEPH) was characterized by gradual onset of shortness of breath, occurring over months to years, with or without a prior history of pulmonary emboli and evidence of right ventricular failure(13-15).

Chest Radiograph

Chest radiographs were obtained within 24 hours after the admission or the onset of symptoms. The majority of patients were obtained in the posteroanterior projection with the upright position. Radiographs were considered to be abnormal if one or combinations of the following abnormalities were demonstrated: pulmonary parenchyma abnormality, pleural effusion, pleural based opacity, elevated diaphragm, decreased pulmonary vascularity, prominent central pulmonary artery, cardiomegaly, Westermark's sign or pulmonary edema.

Lung scans

Ventilation and/or perfusion lung scans were done using the standard method that was previously described(11,16). Scanning was performed within 24 hours on weekdays or 48 hours on weekends when pulmonary thromboembolism was suspected. Interpretation by using the modified PIOPED criteria was done by experienced radiologists(17).

Arterial blood gases and A-a gradient

Arterial blood gases were performed while breathing room air within 24 hours of entry into the study. Patients who had prior cardiopulmonary disease were excluded. Prior cardiopulmonary disease was defined as a history of or evidence of congestive heart failure, valvular heart disease, chronic obstructive pulmonary disease, pneumonia, adult respiratory distress syndrome and other chronic lung diseases. The alveolar arterial oxygen (A-a) gradient was calculated according to the following equation:

$$\text{A-a gradient (mm Hg)} = 150 - 1.25 \text{ PaCO}_2 - \text{PaO}_2$$

The normal range of A-a oxygen gradient was equal or less than 20 mm Hg(18).

Statistical methods

Data are expressed as mean \pm SD or proportions.

RESULTS

Forty-nine patients were diagnosed with PE. The mean age was 53 ± 17.8 years (mean \pm SD) and ranged from 21 to 88 years. Clinical characteristics of the patients are described in Table 1. The most common predisposing factor for PE in this report was immobilization (24 % of patients). Hypercoagulable state was found in 6 patients (12%) including protein C deficiency (3 cases), antithrombin III deficiency (1 case), activated protein C resistance (1 case) and primary antiphospholipid antibody syndrome (1 case). Less common predisposing factors were cardiac disease (12%), malignancy (10%), trauma (6%) and surgery (4%). Absence of predisposing factors was observed in 9 patients (18%).

Only 34 per cent of these patients were first suspected of lung embolism while others were misdiagnosed as congestive heart failure, acute myocardial infarction, pneumonia or septic shock. Among patients who died of PE, death within 3 months occurred in 5 of 49 (10%).

Table 1. Clinical characteristics and predisposing factors of the patients. (n=49)

Predisposing factors	Number	%
Immobilization	12	24
Hypercoagulable state	6	12
Congestive heart failure or myocardial infarction	6	12
Malignancy	5	10
Nephrotic syndrome	3	6
Trauma	3	6
Surgery	2	4
Others	3	6
No predisposing factors	9	18
Total	49	100

Syndromes of PE

There are four subgroups of PE with distinctive features (Table 2). Isolated dyspnea was the most common syndrome and found in 45 per cent of the patients. CTEPH is the result

of single or recurrence of PE which fails to achieve embolic resolution. This condition, once was believed to be a rare disease in the United States, has become recognized with increasing frequency(19). Six cases (12%) in this study were diagnosed as CTEPH.

Table 2. Syndromes of PE.

	Number	%
Isolated dyspnea	22	45
Pleuritic pain or hemoptysis	17	35
Chronic thromboembolic pulmonary hypertension	6	12
Circulatory collapse	4	8
Total	49	100

Symptoms and signs

The common clinical features of patients with PE in this study were dyspnea, tachypnea, tachycardia, pleuritic pain, clinical signs of deep vein thrombosis (DVT), cough and increased pulmonary component of second heart sound (Table 3, 4). Dyspnea was the most common symptom (92%). Pleuritic pain, which was characterized as chest pain aggravated by deep inspiration, occurred in 39 per cent of the patients. The most common sign in our patients was tachypnea (92%). Tachycardia was found in 69 per cent of PE patients. Finally, clinical signs of deep vein thrombosis (DVT) could be detected approximately in one-fourth of this patient group.

Table 3. Symptoms of PE patients.

	Number	%
Dyspnea	45	92
Pleuritic pain	19	39
Leg swelling	16	33
Cough	12	24
Angina like pain	8	16
Hemoptysis	7	14
Palpitation	6	12
Leg pain	5	10
Wheezing	2	4
Total	49	100

Table 4. Signs of PE patients.

	Number	%
Tachypnea	45	92
Tachycardia	34	69
Increased pulmonary component of second heart sound	14	29
Deep vein thrombosis	13	27
Crackles	10	20
Temperature > 38.5°C	8	16
Diaphoresis	8	16
Homan's sign	3	6
Third heart sound	1	2
Total	49	100

Chest radiograph

Chest radiographs were abnormal in 40 of 49 patients (82%) (Table 5). The common radiographic abnormalities were prominent central pulmonary artery, pleural effusion, cardiomegaly and pulmonary parenchymal abnormality. Decreased pulmonary vascularity and Westermark's sign, that are characteristics of PE, were uncommonly found in this study.

Table 5. Chest radiograph.

	Number	%
Prominent central pulmonary artery	22	45
Pleural effusion	18	37
Cardiomegaly	18	37
Pulmonary parenchymal abnormality or atelectasis	15	31
Pleural based opacity	7	14
Decreased pulmonary vascularity	6	12
Westermark's sign	1	2
Elevated diaphragm	1	2
Normal	9	18
Total	49	100

Lung scan

Lung scans were performed in 46 patients and the results were reported as normal, high, intermediate and low probability. Three patients were too ill to be studied by lung scans so that

angiogram or CT scan was an alternative method. High probability occurred in 43 of 46 patients (93%). Three cases (7%) were interpreted as intermediate probability and the diagnosis of PE was confirmed by pulmonary angiogram. No patient with normal or low probability of lung scans had PE.

Table 6. Electrocardiography.

	Number	%
Sinus tachycardia	20	42
Nonspecific ST changed or T-wave abnormalities	19	40
S1Q3T3	15	32
Right axis deviation	7	15
Pulmonary P wave	6	13
Others	9	19
Normal ECG	9	19
Total	47	100

Identification of deep vein thrombosis

Identification of DVT was done in 40 patients by ultrasonography, venogram or radioisotope scanning. Femoral and/or popliteal vein thrombosis were found in 22 patients (55%). DVT could not be detected in 18 of 40 patients with PE (45%).

Electrocardiography (ECG)

Analysis of the ECG in 47 patients with PE is shown in Table 6. Sinus tachycardia, which is defined as heart rate > 100/min, was the most common ECG finding in 20 of 47 (42%) patients. Normal ECG occurred less frequently and was found in 9 patients (19%). Nonspecific ST segment or T-wave abnormalities were presented in 19 of 47 (40%) and S1Q3T3 were also found in 15 cases (32%).

Arterial blood gas analysis

Arterial blood gas analysis was performed in 44 patients of PE respective of the presence of cardiopulmonary disease. The partial pressure of oxygen in arterial blood (PaO₂), measured while patients were breathing with

room air, was 68.85 ± 9.98 mm Hg (mean \pm SD). The A-a oxygen gradient was 44.77 ± 15.69 mm Hg (mean \pm SD) among patients with PE. In addition, normal values of the A-a gradient were found in 7 per cent of patients with PE.

DISCUSSION

PE is a common disease responsible for 10 per cent of all deaths in hospitals in western countries(20). The cumulative probability of PE and DVT by the age of 80 years was 10.7 per cent(21). Prevalence of PE at autopsy has not changed over three decades, while the diagnosis was unsuspected in 70 per cent of patients who died from this disease (22). Death from PE is not common if the appropriate treatment is promptly started(10). Diagnosis of PE is an important issue in clinical practice. The clinical features, though having a poor predictive value, might reinforce the need for further investigation(23). Therefore, we would like to present characteristics of history, physical examination and laboratory investigation in Thai patients with PE.

In the present study, predisposing factors were found in the majority of these patients (82%). The most common predisposing factor was immobilization which was similar to reports from other countries(11,24,25). Hypercoagulable state (e.g. protein C deficiency, protein S deficiency, antithrombin III deficiency, activated protein C resistance and primary antiphospholipid antibody syndrome) was measured in patients who did not have any predisposing factors. A hypercoagulable state was found in 12 per cent of this patient group. However, the tests for factor V Leiden mutation and hyperhomocysteinemia, which were suggested by a previous review article,(26) could not be done routinely in our hospital. There was no apparently predisposing factor in 18 per cent of patients that was comparable to 10-20 per cent reported earlier(24). So, the presence of risk factors that were found in the majority of our patients may lead to the clinical diagnosis of PE. On the other hand, the absence of risk factors in PE patients should alert the clinician to do a workup for the hypercoagulable state.

Interestingly, only 34 per cent of patients with PE were first suspected of lung embolism

while others were misdiagnosed as congestive heart failure, myocardial infarction, pneumonia or septic shock. Therefore, PE is undoubtedly underdiagnosed in our clinical practice and possibly leads to a life threatening problem.

It is helpful to consider a possible diagnosis of PE in terms of the mode of presentation. We classified the syndrome of PE into 4 groups. The severity of acute thromboembolism was graded as mild with the pulmonary infarction syndrome to moderate with the isolated dyspnea to severe with circulatory collapse(12). Isolated dyspnea was the most common syndrome in this study. Forty five per cent of our patients presented with the sudden onset of unexplained shortness of breath. The syndrome of pleuritic pain or hemoptysis, that was the most prevalent mode of presentation in North America(11), occurred in 17 of 49 patients (35%) in the present study. Apart from this, circulatory collapse was as uncommon as in other studies but contributed to a poorer prognosis than the other modes(11,12).

CTEPH, that was characterized by gradual onset of shortness of breath and evidence of right heart failure, occurred in 6 of 49 (12%). This mode of presentation was believed to be uncommon in the United States and was demonstrated in approximately 450 of the 500,000 PE patients each year(19). However, it was recognized more frequently in our patient group. Typically, these patients had the history of progressive dyspnea on exertion while diagnostically it was initially overlooked and patients were left untreated over months to years. Therefore, CTEPH was not an uncommon syndrome in our study and may be caused by unrecognized pulmonary thromboembolism by physicians for many months or years. In addition, patients who present with dyspnea on exertion and right ventricular failure should alert the physician to exclude PE.

Clinical features of PE are nonspecific and mimic other diseases. Dyspnea and tachypnea were the most common clinical manifestations in this study, only 1 patient (2%) had neither of these. The absence of these important clinical features nearly ruled out the diagnosis of PE. Furthermore, unilateral leg edema which suggested deep vein thrombosis and guided to the diagnosis of PE was detected in 27 per cent of these patients.

Chest radiograph was abnormal in 82 per cent of our patients and it was similar to the number reported by Stein *et al*(11). Prominent central pulmonary artery, that suggested pulmonary hypertension, was the most common radiographic abnormality and might have resulted from the delayed diagnosis. Pleural effusion, cardiomegaly or pulmonary parenchymal abnormalities could be detected in approximately one-third of these patients. Notably, decreased pulmonary vascularity or Westermark's sign, which suggest the disease, were uncommon and this finding was in agreement with other reports (11,27). Although a plain chest radiograph rarely gives the direct clue for diagnosis of PE, however, it might be helpful in terms of exclusion of other cardiopulmonary diseases. It also provides information that helps in interpreting the lung scan.

Lung scan is a traditional non-invasive diagnostic test for PE. Patients with a high probability of scan and high clinical suspicion by the time of diagnosis had a 96 per cent chance of having the embolism(28). The presence of pre-existing cardiac or pulmonary disease did not impair diagnostic utility of lung scans(16). Ninety-three per cent of this patient group had a high probability of lung scans. Only 3 patients (7%) had intermediate probability of scans and the diagnosis was confirmed by pulmonary angiogram or echocardiogram. The results indicate that normal or low probability lung scans with a low clinical likelihood have a low chance of PE.

Over 90 per cent of emboli originate from the proximal leg veins even in the absence of clinical findings of DVT(24,29). In this study, DVT was identified by ultrasonography, venogram or radionuclide scanning. Fifty-five per cent of patients had a clot detected in the femoral and/or popliteal vein while only 50 per cent of these patients had clinical findings of DVT. These data indicate that in suspicious cases, concomitant

presence of DVT strongly suggests diagnosis of PE. On the other hand, if clinical features of DVT cannot be detected, PE will not be totally excluded.

ECG abnormalities were common findings and sinus tachycardia was the most common finding in this study. T-wave abnormality, which reflected the severity of PE was identified in 40 per cent of cases. This finding was recently reported to be the most common ECG abnormality in patients with PE(11,30). Nineteen per cent of our patients had a normal ECG. Although ECG findings of PE are not specific enough for diagnosis of the disease, they help physicians to exclude other diseases. Furthermore, The partial pressure of oxygen was approximately 68 ± 10 mm Hg (mean \pm SD) and A-a oxygen gradient was 44 ± 16 mm Hg. Only 7 per cent of this patient group had a normal A-a gradient. This finding indicates that the normal value of gradient could not exclude the diagnosis of PE, however, the chance of it being PE is low.

In conclusion, PE was initially believed to be a rare condition in Thailand. We reported 49 cases of PE in Thai patients who were admitted in Phramongkutkla Hospital during the last 5 year period. Clinical manifestations of PE were reviewed and had some differences from those previously reported in the literature. It is important to diagnose this disease and promptly start the appropriate treatment. Finally, clinicians should develop their own strategies for selecting the appropriate investigations in order to avoid a delayed diagnosis and may reduce the mortality rate of PE.

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โรคหลอดเลือดที่ปอดอุดตันที่ได้รับการวินิจฉัยที่โรงพยาบาลพระมงกุฎเกล้า

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โรคหลอดเลือดที่ปอดอุดตันเป็นโรคที่วินิจฉัยได้ยากและผิดพลาดได้บ่อย ถึงแม้จะเป็นโรคที่อาจพบได้เสมอในเชิงปฎิบัติทั่วไป แต่ถูกประสงค์ของการศึกษาเนื่องจากความซับซ้อนของอาการ, อาการแสดง และการสืบค้นทางห้องปอด ปฎิบัติการที่สำคัญในผู้ป่วยจำนวน 49 รายที่ได้รับการวินิจฉัยโรคนี้ และรับไว้รักษาในโรงพยาบาลพระมงกุฎเกล้า ระหว่างปี พ.ศ. 2537-2541 โดยที่ข้อมูลต่าง ๆ ของผู้ป่วยจะถูกบันทึกทันทีเมื่อได้รับการวินิจฉัยว่าเป็นโรคหลอดเลือดที่ปอดอุดตัน ผลการศึกษานั้นพบว่า อายุเฉลี่ยของผู้ป่วยคือ 53 ปี อัตราส่วนระหว่างผู้หญิงต่อผู้ชายใกล้เคียงกัน ประเด็นที่สำคัญคือผู้ป่วยเพียงร้อยละ 34 เท่านั้นที่ได้รับการลงสัญญาเป็นโรคดังนี้แต่เริ่มต้น ในขณะที่ผู้ป่วยส่วนใหญ่ถูกวินิจฉัยผิดเป็นโรคหัวใจล้มเหลว, กล้ามเนื้อหัวใจขาดเลือด, ปอดอักเสบ หรือ ภาวะซึมจากการติดเชื้อในกระแสเลือด นอกจากนี้ ผู้ป่วยที่มีลักษณะอาการของหลอดเลือดที่ปอดอุดตันแบบเรื้อรัง ซึ่งพบได้ไม่น้อยนักจากการรายงานของต่างประเทศ กลับพบได้ถึงร้อยละ 12 ในผู้ป่วยกลุ่มนี้ การสืบค้นทางห้องปฎิบัติการพบว่า ventilation/perfusion lung scan มีลักษณะที่เข้าได้กับโรคหลอดเลือดที่ปอดอุดตันถึงร้อยละ 93 ผู้ป่วยมีหลอดเลือดดำที่ขาอุดตันร้อยละ 55 อัตราการเสียชีวิตจากโรคนี้สูงถึงร้อยละ 10

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