·临床病理讨论·
Clinicopathological conference

# Chest pain caused by pulmonary embolism

(the 25th case)

People Hospital, Beijing University

## Case presentation

The patient is a female of 82 years old. She was admitted on April 10, 2007, because of "hypertension for thirty years, chest distress and short breath for two weeks, which were aggravated for one week"

The patient was found to have hypertension in health examination thirty years ago. The highest blood pressure was 180/100mmHg. She took some hypotensive agents, but the blood pressure was not controlled well. Three years ago, she felt dizziness and headache repeatedly, without vertigo. The symptoms often occurred during tiredness and emotional fluctuation, and were relieved after rest. In Fuwai Hospital, she was diagnosed as primary hypertension and atrial fibrillation, and was treated with hypotensive agents. The symptoms, were relieved later. In recent three years, the treatment was irregular and the blood pressure was about 160/100mmHg.

Two weeks ago, she got pharyngodynia followed by chest distress and short breath, which did not cause chest pain, dyspnea and awakening during night. The symptoms were not relieved after anti-inflammatory treatment. In recent week, the chest distress and short breath were aggravated, causing waking up during night and she could not lie down. The symptoms were relieved after sitting up. No sweating and palpitation, no cough, expectoration or hemoptysis, no nausea and vomiting, no syncope and amaurosis. One day before admission, she suddenly felt chest distress and short breath after urination, and had chest pain and restlessness. The heart rate was 120 bpm, the blood pressure was 160/100mmHg. Instant blood gas analysis: pH 7.48, $PCO_2$ 35 mmHg, $PO_2$ 49 mmHg, $SiO_2$ 87%, BE 2.8mmol/L. Myocardial enzyme test was normal. D-dimer 834μg/L. Chest computerized tomography showed emboli in right inferior pulmonary artery and its branches, one branch of right upper pulmonary artery, and left upper pulmonary artery, bilateral pleural effusion, infection in right middle and inferior lung and left inferior lung, atelectasis of right inferior lung and heart enlargement.

Past history: Appendectomy for appendicitis 27 years ago, cholecystectomy for cholecystitis 17 years ago. "Bone split" during external injury 4 years ago, which healed after plaster external fixation treatment for 4 months. Sometimes she felt swelling in left leg.

Physical examination on admission: T 36.0℃, P 120 bpm, R 22 /min, BP 140/100 mmHg. General condition was fair, no engorgement of jugular vein was seen, pulmonary respiration sound was clear, there were some moist rales in both inferior lungs. Dull percussion note was found under 8 intercostal space in right side. There was enlargement of heart boundary at left side, heart rate 136 bpm and rhythm was irregular, intensity of first heart sound varied. No pathological murmur was heard in all heart valve areas, P2>A2. No murmur was heard in tricuspid valve area. No pericardial friction sound was heard. Abdomen was soft, liver and spleen were not palpable. Operation scars could be seen under right costal margin and McBurney point. There was light pitting edema in both lower extremities. The circumference of two

收稿日期:2007-07-23

作者单位:100044 北京市,北京大学人民医院心内科
作者简介:吴彦,男,1963年4月生,北京市人,医学博士,主任医师。
E-mail:wy86463331@sina.com

legs(10cm below patella): right side 31.5cm, left side 30cm.

laboratory tests: Tab 1～Tab 3

Electrocardiogram: atria fibrillation, left ventricle high voltage.

Echocardiogram(2007-04-17): left atrium diameter 4.44 cm, left ventricle diastolic-end diameter 4.67 cm, left ventricle systolic-end diameter 2.26 cm, left ventricle ejection fraction 53%. Right atrium longitudinal diameter 5.46 cm, right atrium transverse diameter 3.63 cm. Estimated pulmonary artery systolic pressure 39 mmHg. Conclusion: left atrium enlargement, ascending aortectasia, tricuspid regurgitation (moderate degree), aortic valve regurgitation(mild to moderate degree), pulmonary artery hypertension(light).

Chest X-ray(2007-04-13): Bilateral pleural effusion, more severe in right side; heart shadow enlargement.

Chest computerized tomography(2007-04-10): embolism in right inferior pulmonary artery and its branches, one branch of right upper pulmonary artery, and left upper pulmonary artery. Bilateral pleural effusion and infection in right middle and

Tab 1 Blood

| | WBC ($\times10^9$/L) | Ne (%) | RBC ($\times10^{12}$/L) | HB (g/L) | PLT ($\times10^9$/L) |
|---|---|---|---|---|---|
| 2007-04-10 | 10.921 | 87.91 | 4.48 | 122 | 293 |
| 2007-04-12 | 11.91 | 86.6 | 4.035 | 118.4 | 284.6 |
| 2007-04-13 | 10.11 | 85.52 | 3.949 | 116.2 | 286.1 |
| 2007-04-14 | 8.59 | 80.75 | 4.018 | 116.7 | 276.6 |
| 2007-04-16 | 6.84 | 81.05 | 4.112 | 117.5 | 336.6 |
| 2007-04-17 | 5.56 | 68.76 | 3.88 | 112.3 | 287.2 |
| 2007-04-19 | 6.57 | 68.82 | 4.405 | 125.4 | 335.3 |

Tab 2 Blood gas analysis

| | pH | $PCO_2$ (mmHg) | $PO_2$ (mmHg) | $HCO_3$ | BE | $SiO_2$ (%) | Oxygen inhalation |
|---|---|---|---|---|---|---|---|
| 07-04-10 3pm | 7.48 | 35 | 49 | 26.1 | 2.6 | 87 | No oxygen inhalation |
| 07-04-10 5pm | 7.47 | 36 | 89 | 26.2 | 2.5 | 97 | Nose oxygen 7l/min |
| 07-04-119am | 7.48 | 37 | 57 | 27.6 | 4.1 | 91 | Nose oxygen 4l/min |
| 07-04-11 9pm | 7.576 | 33.1 | 52 | 31 | 8.9 | 91.4 | Mask oxygen 5l/min |
| 07-04-12 11am | 7.549 | 36.3 | 82.8 | 32 | 9.4 | 99.9 | Mask oxygen 5l/min |
| 07-04-12 8pm | 7.526 | 36.7 | 83.5 | 30.6 | 8.1 | 100 | Mask oxygen 5l/min |
| 07-04-13 3pm | 7.524 | 37 | 72.4 | 30.8 | 7.8 | 99.4 | Mask oxygen 5l/min |
| 07-04-16 1pm | 7.498 | 39.7 | 69.3 | 31.2 | 7.7 | 98.3 | Mask oxygen 5l/min |
| 07-04-17 11am | 7.559 | 32.8 | 70.6 | 29.6 | 7.1 | 100 | No oxygen inhalation |

Tab 3 Blood coagulation analysis

| | PT (s) | APTT (s) | INR | D-Dimer (μg/L) | Warfarin (mg) |
|---|---|---|---|---|---|
| 2007-04-10 | 15 | 30.9 | 1.33 | 834 | 5 |
| 2007-04-11 | 25.1 | 39.9 | 2.62 | 800 | 2.5 |
| 2007-04-12 | 34 | 45.8 | 4.031 | 365.86 | 2.5 |
| 2007-04-13 | 29.7 | 48.4 | 3.354 | 432.707 | 0 |
| 2007-04-14 | 32.6 | 49.4 | 3.77 | 1400 | 0 |
| 2007-04-16 | 24.7 | 42.5 | 2.61 | 458.539 | 1.25 |
| 2007-04-17 | 24.3 | 40.9 | 2.55 | 506.486 | 1.25 |
| 2007-04-18 | 22.2 | 2.257 | 1.25 | | |
| 2007-04-19 | 21.2 | 2.12 | 1.25 | | |

inferior lung and left inferior lung, right inferior lung atelectasis and heart enlargement.

Ultrasound scan of arteries of both lower extremities(2007-04-19): multiple sclerotic plagues in arteries of both lower extremities, light stenosis of left femoral artery, stenosis of arteries of both dorsa pedis with decreased blood flow rate.

Ultrasound scan of veins of both lower extremities(2007-04-19): No abnormality was found in femoral veins, deep and superficial femoral veins, great saphenous vein and popliteal vein.

Myocardial infarction markers (2007-04-11): CKMB<1.0μg/L, MYO85.8μg/L, TNI<0.05μg/L.

Brain natriuretic peptide: 2007-04-11 7am: 14961ng/L; 2007-04-12: 206ng/L; 2007-04-13: 122ng/L.

Blood biochemical tests(2007-04-10): albumin 32.3g/L, total protein 58.7g/L, high density lipoprotein cholesterol 0.83mmol/L, low density lipoprotein cholesterol 1.88 mmol/L, creatinine 60 μmol/L, lactate dehydrogenase 260U/L.

Blood biochemical tests(2007-04-14): albumin 27.2g/L, total protein 52.8g/L, high density lipoprotein cholesterol 0.92mmol/L, low density lipoprotein cholesterol 2.82 mmol/L, creatinine 71 μmol/L, lactate dehydrogenase 313U/L.

Emergency blood tests (2007-04-16): urea 4.7mmol/L, natrium 140.6 mmol/L, potassium 3.44 mmol/L, blood sugar 8.59mmol/L, creatinine 77μmol/L, calcium 1.89mmol/L, chlorine 107mmol/L, $CO_2$ 29mmol/L.

Admission diagnosis: pulmonary embolism, hypertension(grade 3, high risk), atrial fibrillation, enlargement of heart boundary at left side, after cholecystectomy, after appendectomy, cardiac dysfunction NYHA class 3, upper respiratory tract infection.

Treatment: diltiazem 90mg qd, metoprolol 67.5mg qd, fosinopril 10mg qd, continuous venous pumping of nitrate to control blood pressure, low molecular weight heparin, warfarin 1.25 mg qd and diuretics.

## Case summary

An elderly female with 30 years history of uncontrolled hypertension, sustained atrial fibrillation, chest distress and short breath for two weeks, which were aggravated for 1 week, chest pain and restlessness for 1 day, low oxygen partial pressure, high D-dimer. Chest computerized tomography showed embolism in right inferior pulmonary artery and its branches, one branch of right upper pulmonary artery, and left upper pulmonary artery. Bilateral pleural effusion and infection in right middle and inferior lung and left inferior lung, right inferior lung atelectasis and heart enlargement.

## Clinicopathological discussion

*Professor Chen Hong*: there are many mechanisms of pulmonary embolism to cause short breath. Big embolus causes short breath due to anoxia of the body and small embolus causes wide bronchial spasm. And many small emboli can cause severe symptom. The emboli may originate from leg vein, because the patient had gastrocnemius muscle tenderness, which should not be neglected during physical examination. In addition, the cause of bilateral pleural effusion and hypoalbuminemia should be sought. The patient had nocturnal paroxysmal dyspnea in the past, this may be the result of pleural effusion and not necessarily caused by heart failure.

*Associate professor Jin Xinxin*: Pulmonary embolism may be not acute, because chest distress and short breath occurred 2 weeks ago, which should be differentiated from symptoms of heart failure. Electrocardiagram and echocardiogram are helpful to diagnosis.

*Professor Xie Jiyan*: Although chest CT showed multiple small pulmonary emboli, the chest pain and low oxygen partial pressure may be caused by big embolus. Big embolus can undergo autolysis and cause misdiagnosis.

*Professor Guo Danjie*: Since the patient had symptoms of low oxygen partial pressure, high D-dimer, and especially the findingings of chest CT examination, the diagnosis of pulmonary embolism is definite. Thrombolytic therapy can be used for big embolism and unstable hemodynamics. But the chest CT did not find big embolism, and there was no disorder of hemodynamics, so there was no indication of thrombolysis therapy in this patient.

*Associate professor Sun Yihong*: The diagnosis of pulmonary embolism is definite, but the source of embolus is uncertain. The venous thrombus of gastrocnemius muscle is not prone to cause pulmonary embolism, but the embolus of proximal part of gastrocnemius muscle vein can cause small pulmonary embolism. The patient had atrial fibrillation for a long time which can cause thrombosis in left atrium. If foramen ovale reopens, the left atrial embolus also can cause pulmonary embolism.

*Professor Hu Dayi*: The patient has no thrombolysis indication, but anticoagulation therapy must be used. Warfarin is the best choice, but the dosage is hard to control due to individual variation of sensitivity. The beginning dosage for old patient is 2.5—3.0 mg/day and the dose is regulated according to INR (stable at 2.0-3.0).

## Comments

*Professor Hu Dayi*: pulmonary embolism can be diagnosed according to clinical presentation and chest CT. The problems are the necessity of thrombolytic therapy and identification of the source of the embolus. (1) Pulmonary embolism is a common high risk disease, the mortality is about 30% in untreated patients but only 2%-8% in treated patients. Big pulmonary embolism should be treated immediately. In the past, more than 50% of lung without perfusion, or embolism in more than 2 pulmonary lobar arteries could be considered as large pulmonary embolism. However, in severe heart and pulmonary disease patients, small embolism with obstruction of arteries of 1-2 pulmonary segments can cause severe pathophysiological effects. So, the new definition of large pulmonary embolism is the pulmonary embolism accompanied by shock or hypotension (systolic blood pressure $<$ 90mmHg or decrease by more than 40mmHg for 15min or longer, except these symptoms caused by new arrhythmia, low blood volume or septicemia). The definite diagnosis is the prerequisite for thrombolytic therapy. This patient can not be diagnosed as large pulmonary embolism, so she had no indication of thrombolysis, but anticoagulation therapy can be used. (2) Ninety per cent of pulmonary emboli come from thrombi of deep veins of lower limbs, and phlebography can find thrombi in deep veins of lower limb in 70% pulmonary embolism patients. The sensitivity and specificity of ultrasound for proximal deep vein thrombosis are higher than 95% in symptomatic patients. In this patient, the difference in circumference of two legs, tenderness at gastrocnemius region and the appearance of mild pitting edema of both lower extremities suggested the thrombus came from lower limbs, although no abnormality was found in femoral vein, deep and superficial femoral veins, great saphenous vein and popliteal vein by ultrasound scan of veins of both lower extremities. Warfarin should be used at least for 3 months.

(Translator: WU Yan)

# 肺栓塞导致急性胸痛一例

## 1 病例摘要

患者女性，82 岁。主因“发现血压升高 30 年，胸闷气短 2 周，加重 1 周”以“高血压、肺栓塞”于 2007 年 4 月 10 日入院。患者 30 年前体检发现血压升高，当时为 180/100mmHg，服用药物（具体不详）控制血压，血压控制不理想。3 年前患者反复出现头晕、头痛，非撕裂样，无视物旋转，多于劳累及情绪波动时出现，休息后缓解。曾在阜外医院就诊，诊为“原发性高血压，心房纤颤”，予降压治疗，症状明显缓解。近 3 年来用药不规律，血压控制在 160/100mmHg。2 周前患者咽痛后出现明显胸闷气短，无夜间憋醒，无胸痛及呼吸困难，在当地医院行抗炎治疗效果不理想。1 周来患者胸闷气短加重，有夜间憋醒，夜间不能平卧，坐起后症状缓解。发作时无出汗、心悸，无咳嗽、咳痰、咳血，无恶心、呕吐，无晕厥及黑蒙。1d 前患者小便后突发胸闷憋气，胸痛明显，

（下转第 442 页）

AT1 receptors in neointima of rat aorta. J Clin Invest, 1992,90:1707-1712.

[16] Takeda K, Ichiki T, Tokunou T, et al. Peroxisome proliferator-activated receptor in vascular in smooth muscle cells. Circulation, 2000, 102:1834-1839.

[17] Pasceri V, Wu HD, Willerson JT, et al. Modulation of vascular inflammation *in vitro* and *in vivo* by peroxisome proliferator-activated receptor-gamma activators. Circulation, 2000, 101:235.

[18] Marx N, Froehlich T, Siam L, et al. Antidiabetic PPAR-gamma-activator rosiglitazone reduces MMP-9 serum levels in type 2 diabetic patients with coronary artery disease. Arterioscler Thromb Vasc Biol, 2003, 23:283-288.

[19] Ricote M, Li AC, Willson TM, et al. The peroxisome proliferator-activated receptor-gamma is a negative regulator of macrophage activation. Nature, 1998, 391:79-82.

[20] Rajesh G, Yuvraj K, Ahmad A, et al. Troglitazone reduce reactive oxygen species generation by leukocytes and lipid peroxidation and improves flow-mediated vasodilatation in obese subjects. Hypertension, 2000, 36: 430-435.

[21] Majithiya JB, Paramar AN, Balaraman R. Pioglitazone, a PPARgamma agonist, restore endothelial function in aorta of streptozotocin-induced diabetic rats. Cardiovasc Res, 2005, 66:150-161.

[22] Tao L, Liu HR, Gao E, et al. Antioxidative, antinitrative, and vasculoprotective effects of a peroxisome proliferator-activated receptor-gamma agonist in hypercholesterolemia. Circulation, 2003, 108:1834-1839.

[23] Inoue I, Goto S, Matsunaga T, et al. The ligands/activators for peroxisome proliferators-activated receptor alpha (PPARalpha) and PPARgamma increase $Cu^{2+}$, $Zn^{2+}$-superoxide dismutase and decrease $p^{22phox}$ message expression in primary endothelial cells. Metabolism, 2001, 50:3-11.

[24] Bagi Z, Koller G, Kaley G, et al. PPARgamma activation, by reducing oxidative stress, increases NO bioavailability in coronary arterioles of mice with type 2 diabetes. Am J Physiol Heart Circ Physiol, 2004, 286: H742-H748.

[25] Negro R, Dazzi D, Hassan H, et al. Pioglitazone reduces blood pressure in non-dipping diabetic patients. Minerva Endocrinol, 2004, 29:11-17.

(上接第438页)

表现烦躁，当时心率120次/min，血压160/100mmHg，急查动脉血气分析：pH7.48，$PCO_2$ 35mmHg，$PO_2$ 49mmHg，$SiO_2$ 87%，BE 2.8mmol/L，心梗三项：正常。D-二聚体834μg/L，螺旋CT肺血管成像：右下肺动脉及其分支、右上肺动脉一分支、左上肺动脉内血栓，双侧胸腔积液合并右中下肺及左下肺感染，右下肺压迫性膨胀不全，心脏增大。

入院查体：体温36.0℃，心率120次/min，呼吸22次/min，血压140/100mmHg。一般状况可，颈静脉无充盈，两肺底可闻及少量湿啰音。右肺第八肋间下叩诊浊音。心界左大，心率136次/min，律不齐，第一心音强弱不等，心脏各瓣膜区未闻及病理性杂音，P2＞A2。未闻及心包摩擦音。腹软，肝脾未触及。右侧肋缘下可见一7cm纵行手术瘢痕。麦氏点处可见一5cm斜形手术瘢痕。双下肢轻度可凹性水肿。双下肢径线（髌骨下10cm）：右下肢31.5cm，左下肢30cm。

## 2 临床病理讨论

根据临床表现和CT检查可以诊断为肺栓塞。需进一步明确是否需要溶栓治疗及栓子来源。(1)肺栓塞已经成为一种常见高危疾病，未经治疗的患者死亡率约为30%，诊断明确并接受充分治疗的患者病死率可下降至2%～8%。特别是大面积肺栓塞应当紧急救治。以往根据肺灌注显像显示50%以上的肺无灌注或栓塞≥2个肺叶动脉者成为大面积肺栓塞。而严重心肺疾病的患者即使较小的栓塞堵塞1～2个肺段也会引起严重的病理生理效应。因此较新的定义是将伴有休克或低血压（收缩压＜90mmHg或下降超过40mmHg持续15min以上，除外新发生心律失常，低血容量或败血症所致的上述症状）的肺栓塞定义大面积肺栓塞，该诊断是决定溶栓治疗的先决条件。该患者显然不适合，因此没有溶栓指征，可采用抗凝治疗。(2)90%的肺栓塞栓子来自下肢深静脉血栓，肺栓塞患者进行静脉造影发现70%存在深静脉血栓。对于有症状的患者，超声诊断近端深静脉血栓的敏感性和特异性均超过95%。该患者双下肢轻度可凹性水肿，双下肢径线不一致，有腓肠肌部位压痛，仍应考虑血栓来自下肢，尽管双下肢静脉彩超显示双下肢股静脉、股深股浅静脉、大隐静脉汇入部、腘静脉血流通畅，腔内未见异常回声。华法令抗凝治疗至少3个月。

（参加讨论医师：陈红、金新新、解基严、郭丹杰、孙艺红、胡大一）

（吴彦 整理）