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Are all intracranial mass lesions always a contraindication for thrombolytic therapy?

顱內佔位性病變是否總是溶栓治療的一個禁忌？

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Thrombolytic therapy is regarded as the first treatment choice in haemodynamically unstable patients with pulmonary embolism. Intracranial tumors have long been considered as a contraindication to thrombolytic therapy due to the risk of intracerebral haemorrhage. In this report, we presented a 76-year-old female patient with meningioma and massive pulmonary embolism who had received thrombolytic therapy despite a contraindication of intracranial mass. The patient completed the thrombolytic therapy without having complication. (Hong Kong j.emerg.med. 2014;21:98-102)

溶栓治療被認為是血流動力學不穩定的肺栓塞患者的第一治療選擇。因腦出血的危險，顱內腫瘤一直被視為溶栓治療的禁忌。在這份報告中，一個有腦膜瘤的76歲女性大面積肺栓塞患者，儘管有顱內佔位性病變的禁忌，我們也給了溶栓治療。患者完成了溶栓治療，並且沒有併發症。

Keywords: Adult, cardiogenic shock, meningioma, pulmonary embolism, treatment outcome

關鍵詞：成人、心源性休克、腦膜瘤、肺栓塞、治療結果

Introduction

Pulmonary embolism (PE) is an acute life-threatening cardiopulmonary emergency due to the occlusion of pulmonary arteries. Massive PE often results in systemic hypotension, hypoperfusion, mental status changes and obstructive shock, which have a high mortality rate. If a patient has massive PE with unstable haemodynamics, thrombolytic therapy is regarded as the first choice of treatment.[1] However, intracranial tumours have long been considered as an absolute contraindication to thrombolytic therapy because of the risk of intracranial haemorrhage. Here, we describe a patient who had meningioma and new onset acute massive PE, and received thrombolytic therapy in our emergency department (ED).

Case

A 76-year-old female patient was admitted to ED with a complaint of syncope. Clinically she had moderate hypotension and mild tachypnea. Her vital findings on admission were: blood pressure was 84/51 mmHg, pulse rate was 85/min, respiratory rate was 20/min, temperature was 37.5ºC and oxygen saturation was 98 percent on room air. On physical examination, she was conscious, co-operative, and oriented; her Glasgow Coma Score (GCS) was 15 and other systemic examinations were normal. An electrocardiography revealed sinus rhythm with right bundle branch block.

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No acute pathological finding was detected on chest radiograph. Blood values had slight alterations as indicated in Table 1. In her medical history, she had recently diagnosis of meningioma just a week ago. Computed tomography (CT) of brain was ordered and a right occipital lobe meningioma (17x18 mm) compatible with her previous CT scan was detected. There was no oedema or haemorrhage in the brain due to the mass lesion (Figure 1).

The patient had persistent moderate hypotension and hypocapnia despite an initial oyxgen and fluid treatment. The probability of pulmonary embolism was calculated via both clinical decision rules (CDR): Simplified Wells Score and Revised Geneva Score.[2,3] In this patient, the risk factors for PE were medical history of malignancy, hypocapnia and age over 65. According to clinical decision rules, she was scored 1 point on simplified Wells rule and 2 points on simplified Geneva score. Although she had a low likelihood to develop PE according to the clinical decision rules, a computed tomography pulmonary angiogram (CTPA) was ordered because of her persistent, unexplained hypotension and hypocapnia The CTPA demonstrated filling defects in the bilateral main pulmonary arteries which were consistent with the diagnosis of PE (Figure 2). An immediate echocardiography also revealed a dilated right ventricle. Low molecular weight heparin (LMWH) therapy with enoxaparin 6000 IU q12h was administered early.

Table 1. Laboratory findings of the patient

	Patient's values	Normal limits
Glucose	127	83-110 mg/dl
Urea nitrogen (BUN)	34	9.8-20.1 mg/dl
Creatinine	1.2	0.6-1.1 mg/dl
Troponin	0.8 (0 hour) 1.4 (6 hours)	0-0.3 ng/dl
White blood cell	18.3 (69.1% neutrophils)	4.0-10.3 $10^3/\mu L$
Haemoglobin	12.9	12.0-16.0 g/dL
Platelet	186	156-373 $10^3/\mu L$
pH	7.44	7.35-7.45
pCO_2	31.3	35-45 mmHg
pO_2	81.1	83-108 mmHg

During the observation within ED, the patient continued to have hypotension with her blood pressure dropped to 72/51 mmHg despite aggressive saline infusion. She was tachycardic (140 beats/min), tachypnoeic (40 breaths/min) and with an oxygen saturation of 80%. She gradually lost her consciousness; and her GCS was 9 in total as E2M5V2. In view of her unstable haemodynamic status due to massive PE, an immediate thrombolytic therapy was planned despite of her meningioma. As the patient was still unconscious, the first-degree relatives



Figure 1. Brain CT scan showing parafalcine mass (arrows).

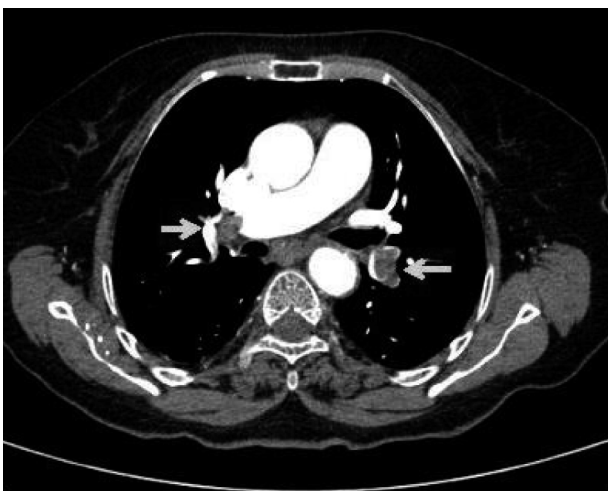


Figure 2. Chest computed tomographic angiogram showing thrombus in bilateral main pulmonary arteries (arrows).

of the patients were broadly informed about the high risk of cerebral haemorrhage due to the patient's medical history of intracranial mass; however, they were also informed that unless the patient received thrombolytic therapy, her current medical situation carried a high risk of death as well. After the approval of patient's relatives, 100 mg of recombinant tissue plasminogen activator (rt-PA) was administered to the patient as a two-hour infusion. Within 5 to 10 minutes after the initiation of thrombolytic therapy, the patient's blood pressure raised to 136/72 mmHg, pulse rate was 72/min, respiratory rate was 16/min, oxygen saturation was 97% and her GCS was again 15. Thrombolytic therapy was successfully completed after two hours. Her vital signs were in normal limits and no complication was recorded. She was admitted to hospital with intact neurological findings. She was discharged on the 20th day of her hospitalisation under LMWH treatment for coumadin optimisation.

Discussion

PE is a cardiovascular emergency and can progress to a life-threatening problem when massive PE occurs. Diagnosis and treatment strategies may vary depending on the clinical situation and presence of haemodynamic instability.

Diagnosis of PE is based on clinical findings in combination with laboratory tests and imaging studies, usually CTPA. A clinical practice guideline recommended that validated CDR should be used to estimate pretest probability of pulmonary embolism and to interpret test results before imaging studies.[2] There are two validated CDRs: the Wells rule and the revised Geneva score.[3,4] Simplified versions of both of these scores also have been developed. A recent comparison of these four (Wells rule, revised Geneva score, simplified Wells rule, and simplified revised Geneva score) revealed that all four CDRs show similar performance for exclusion of acute PE in combination with a normal d-dimer result.[5] Although there were low scores according to CDRs for our patient, CTPA revealed the diagnosis of PE.

In massive PE cases, blood pressure levels may be within normal limits within the first 12-48 hours. However, cardiac arrest usually follows severe hypotension that is resistant to aggressive intravenous fluid treatment.[6] In our case, even though the patient had massive PE, her haemodynamic status was within normal range after fluid treatment and had findings of right ventricular loading on echocardiography. Her haemodynamics became abnormal during the ninth hour of observation.

The treatment of PE depends on haemodynamic stability. Patients who are haemodynamically stable should receive anticoagulation therapy. LMWH can be administered initially and have less bleeding complications than intravenous unfractionated heparin (IV UFH). Massive PE with haemodynamic instability or systemic hypoperfusion is an absolute indication for thrombolytic therapy.[7-10] There are three thrombolytic agents currently approved by the Food and Drug Administration (FDA) for use in patients with acute PE: alteplase, urokinase, and streptokinase. Alteplase among the new generation fibrinolytics, is the only agent which has been approved by the American FDA and it requires a total of 100 mg infusion within two hours.[11,12] The evidence-based clinical practice guidelines of American College of Chest Physicians suggest IV UFH over subcutaneous LMWH in patients in whom thrombolytic therapy is being considered or planned. On the other hand the CLOT trial suggested that LMWH therapy might be favoured over oral anticoagulation in patients with an underlying malignancy.[13]

In this case, LMWH was the first treatment of choice in the ED. However after completion of the thrombolytic therapy, LMWH was continued instead of IV UFH. Oral anticoagulation was started during hospitalisation. However, optimum dose adjustment could not be achieved successfully and she was discharged on LMWH therapy on the 20th day.

Patients with massive PE often decompensate suddenly. Once haemodynamic instability has developed, mortality is extremely high where the risk of early death

(the mortality rate in hospital or within 30 days) is more than 15%.[14,15] The overall mortality rate within 90 days in patients with systolic blood pressure <90 mmHg was 43-62% and 13-16% in normotensive patients.[16] The mortality rate in patients receiving anticoagulant therapy was detected as 29%, in patients undergoing surgical embolectomy as 24% and in patients receiving thrombolytic therapy as 11%. The mortality rate in untreated patients is almost 100%.[17] Major haemorrhage at a rate of 13% and lethal intracranial haemorrhage at a rate of 1.8% can be seen as complications following thrombolytic therapy in PE.[18,19]

Since patients with intracranial masses have high risk of haemorrhage, thrombolytic therapy has not been recommended. Other treatment modalities such as transvenous or open surgical embolectomy have been favored for who thrombolytic is contraindicated. However, these surgical procedures require expertise. In medical care settings where surgical embolectomy cannot be performed, treatment choices become quite limited for a PE patient who has haemodynamic instability and could not receive thrombolytic therapy. In literature, there were few reports of patients with intracranial mass who had received thrombolytic therapy.[20-23] Three of these cases were treated with systemic thrombolytic therapy for acute myocardial infarction without awareness of the existing intracranial tumour (one pituitary adenoma, two meningiomas).[20,21] Two cases with known tumours (acoustic schwannoma and meningioma) treated for acute cerebrovascular events did not have any complications.[22] On the other hand an intracranial haemorrhage after thrombolytic therapy for acute stroke was reported in a patient with an intracranial tumour (glioblastoma multiforme).[23]

In our case, we had to make a critical decision. We were aware of the patient's recent diagnosis of meningioma and the patient had massive PE with haemodynamic instability. Despite the lack of evidence that thrombolytic therapy could improve mortality, only a benefit in those at highest risk of recurrence or death had been reported in a meta-analysis that included the trials which compared thrombolysis with heparin for the initial treatment of pulmonary embolism.[22] Meningioma, as being outside of the brain parenchyma, encouraged us to give thrombolytic so that the patient might have a chance for a rescue operation if a bleeding complication had occurred.

References

1. Buller HR, Agnelli G, Hull RD, Hyers TM, Prins MH, Raskob GE. Antithrombotic therapy for venous thromboembolic disease: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004;126 (3 Suppl):401S-28S.
2. Qaseem A, Snow V, Barry P, Hornbake ER, Rodnick JE, Tobolic T, et al. Current diagnosis of venous thromboembolism in primary care: a clinical practice guideline from the American Academy of Family Physicians and the American College of Physicians. Ann Fam Med 2007;5(1):57-62.
3. Wells PS, Anderson DR, Rodger M, Stiell I, Dreyer JF, Barnes D, et al. Excluding pulmonary embolism at the bedside without diagnostic imaging: management of patients with suspected pulmonary embolism presenting to the emergency department by using a simple clinical model and d-dimer. Ann Intern Med 2001;135(2): 98-107.
4. Klok FA, Mos IC, Nijkeuter M, Righini M, Perrier A, Le Gal G, et al. Simplification of the revised Geneva score for assessing clinical probability of pulmonary embolism. Arch Intern Med 2008;168(19):2131-6.
5. Douma RA, Mos IC, Erkens PM, Nizet TA, Durian MF, Hovens MM, et al. Performance of 4 Clinical Decision Rules in the Diagnostic Management of Acute Pulmonary Embolism: A Prospective Cohort Study. Ann Intern Med 2011;154(11):709-18.
6. Goldhaber SZ, Elliott CG. Acute pulmonary embolism: part I: epidemiology, pathophysiology, and diagnosis. Circulation 2003;108(22):2726-9.
7. Konstantinides S. Pulmonary embolism: impact of right ventricular dysfunction. Curr Opin Cardiol 2005;20 (6):496-501.
8. Torbicki A, Perrier A, Konstantinides S, Agnelli G, Galiè N, Pruszczyk P, et al. Guidelines on the diagnosis and management of acute pulmonary embolism: the Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC). Eur Heart J 2008;29(18): 2276-315.
9. Hirsh J, Guyatt G, Albers GW, Harrington R, Schünemann HJ. Executive summary: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). Chest 2008;133(6 Suppl):71S-109S.
10. Dong B, Jirong Y, Liu G, Wang Q, Wu T. Thrombolytic therapy for pulmonary embolism. Cochrane Database Syst Rev 2006;19(2):CD004437.

11. Nijkeuter M, Hovens MM, Davidson BL, Huisman MV. Resolution of thromboembolism in patients with acute pulmonary embolism: a systematic review. Chest 2006;129:192-7.
12. Laporte S, Mismetti P, Decousus H, Uresandi F, Otero R, Lobo JL, et al. Clinical predictors for fatal pulmonary embolism in 15,520 patients with venous thromboembolism: findings from the Registro Informatizado de la Enfermedad TromboEmbolica venosa (RIETE) Registry. Circulation 2008;117(13): 1711-6.
13. Lee AY, Levine MN, Baker RI, Bowden C, Kakkar AK, Prins M, et al. Low-molecular-weight heparin versus a coumarin for the prevention of recurrent venous thromboembolism in patients with cancer. N Engl J Med 2003;349(2):146-53.
14. Goldhaber SZ, Visani L, De Rosa M. Acute pulmonary embolism: clinical outcomes in the International Cooperative Pulmonary Embolism Registry (ICOPER). Lancet 1999;353(9162):1386-9.
15. Kasper W, Konstantinides S, Geibel A, Olschewski M, Heinrich F, Grosser KD, et al. Management strategies and determinants of outcome in acute major pulmonary embolism: results of a multicenter registry. J Am Coll Cardiol 1997;30(5):1165-71.
16. Kucher N, Rossi E, De Rosa M, Goldhaber SZ. Massive pulmonary embolism. Circulation 2006;113(4):577-82.
17. Rose PS, Punjabi NM, Pearse DB. Treatment of right heart thromboemboli. Chest 2002;121(3):806-14.
18. Goldhabert SZ, Kessler CM, Heit JA, Elliott CG, Friedenberg WR, Heiselman DE, et al. Recombinant tissue-type plasminogen activator versus a novel dosing regimen of urokinase in acute pulmonary embolism: a randomized controlled multicenter trial. J Am Coll Cardiol 1992;20(1):24-30.
19. Kanter DS, Mikkola KM, Patel SR, Parker JA, Goldhaber SZ. Thrombolytic therapy for pulmonary embolism. Frequency of intracranial hemorrhage and associated risk factors. Chest 1997;111(5):1241-5.
20. Jaffe R, Reichman JM, Weiss AT, Zahger D. Thrombolysis in the presence of an intracranial meningioma. Chest 1997;111(1):258.
21. Rubinshtein R, Jaffe R, Flugelman MY, Karkabi B, Lewis BS. Thrombolysis in patients with a brain tumour. Heart 2004;90(12):1476.
22. Neil W, Ovbiagele B. Intravenous thrombolysis in ischemic stroke patients with intracranial neoplasms: two cases and a literature review. Case Rep Med 2011; 2011:503758.
23. Grimm SA, DeAngelis LM. Intratumoral hemorrhage after thrombolysis in a patient with glioblastoma multiforme. Neurology 2007;28;69(9):936.