

## Case report

# Successful use of tenecteplase in massive pulmonary embolism with cardiopulmonary resuscitation immediately following tracheostomy

W. ABDULLA and U. NETTER

**Summary :** The use of thrombolytics for the treatment of massive pulmonary embolism with cardiopulmonary resuscitation is being controversially discussed. This is one of the first reports on the successful use of tenecteplase in a 59-year-old man who survived a massive pulmonary embolism after tracheostomy followed by a 30-minute cardiopulmonary resuscitation without cerebral damage. In such a dramatic clinical event, the immediate and simple use of this modern thrombolytic appears to be a justifiable last-resort treatment option until controlled studies in sufficiently sized patient populations will have proven or refuted its efficacy and safety.

**Key words :** Pulmonary embolism ; resuscitation ; thrombolysis ; tenecteplase, tracheostomy.

## INTRODUCTION

Because of expected bleeding complications following resuscitation, the use of thrombolytics has for a long time only been cautiously employed in conditions of resuscitations due to acute myocardial infarction and massive pulmonary embolism (1). Nevertheless, a number of case reports and small clinical studies on the successful use of thrombolytics during resuscitation following massive pulmonary embolism continue to be published (2, 3, 4).

This case study is one of the first publications, on the successful use of tenecteplase for massive pulmonary embolism with resuscitation. It adds to already published case reports on patients with massive pulmonary embolism without the need for resuscitation. In these case studies, patients were successfully treated with bolus administration of tenecteplase (5) or catheter-directed thrombolysis using tenecteplase (6). The carrying out of the thrombolysis immediately after tracheostomy is of great interest in this case report.

## CASE PRESENTATION

A 59-year-old man (weight 85 kg, height 185 cm) was referred to the hospital because of increasing respiratory failure. There was a one-year history of increasing muscle weakness in arms and legs and weight loss of about 16 kg over the last 6 years. For the last 6 months, the patient had reported shortness of breath. One week before the current admission, amyotrophic lateral sclerosis (ALS) had been diagnosed in another hospital. Five days later, increasing respiratory failure due to ALS developed and the patient was referred to our hospital for further management.

At the time of admission, the patient was comatose and in acute respiratory failure. The patient was intubated and put on a respirator improving his condition within hours. He was cooperative and alert. A urinary catheter was placed via the urethra with some difficulties and subsequent moderate bleeding, which stopped. Prophylaxis for thrombosis was carried out daily with subcutaneous injection of dalteparin sodium 5000 IU anti-Xa and intense physiotherapeutic measures. During the following days, attempts to wean the patient off the respirator failed because of persistent respiratory muscle weakness.

W. ABDULLA, M.D., Sc.D. ; U. NETTER, M.D.  
Department of Anaesthesiology and Intensive Care Medicine.  
Klinikum Bernburg.  
Teaching Hospital, Martin Luther University Halle-Wittenberg.

**Corresponding author and requests for reprints :** Prof. Dr. W. Abdulla, Klinik fuer Anaesthesiologie und Intensivmedizin, Klinikum Bernburg, Kustrenaer Str. 98, D-06406 Bernburg.  
Tel. : +49-3471-341370. E-mail : walied.abdulla@t-online.de.

A percutaneous tracheostomy (Ciaglia Blue-Rhino® Set EZ Pass® Hydrophilic Coating, William Cook Europe, DK-4632 Bjaeverskov, [www.cookgroup.com](http://www.cookgroup.com)) was performed 12 days after referral. An x-ray taken 5 hours later revealed a diffuse opacity in the middle and lower parts of the left lung. Before bronchoscopy could be performed, the patient's condition worsened and oxygen saturation dropped suddenly to 30%. Respiratory sounds over the left lung were greatly diminished. Meanwhile, an arterial line had been established for continuous haemodynamic monitoring of the patient. Because of a suspected pneumothorax, a chest drainage tube was inserted in the left anterior axillary line, which did not reveal air or blood. Hypoxaemia persisted despite ventilation with 100% oxygen (pH 7.15, PaO<sub>2</sub> 26.6 mmHg or 3.55 kPa, PaCO<sub>2</sub> 78.76 mmHg or 10.5 kPa, base deficit 4.1 mmol/L, standard bicarbonate 19.8 mmol/L), systolic blood pressure was 50 mmHg and heart rate 60 beats per minute. Ventricular complexes observed on the ECG monitor widened followed by asystole.

Epinephrine 0.2 mg and atropine 0.5 mg were administered without immediate success and external cardiac massage was started. The sudden drop in oxygen saturation combined with a drop in blood pressure and heart rate made a massive pulmonary embolism most likely to be the cause for this acute event. D-dimers determined later were 4701 ng/mL for this time point and supported the suspected diagnosis. As a last-resort treatment, 8000 U of tenecteplase (Metalyse®, Boehringer Ingelheim, D-55216 Ingelheim am Rhein, Germany) were administered as a bolus dose via a central venous line followed by a bolus of 5000 IU of heparin. External cardiac massage was continued for 30 minutes and the patient's condition stabilized with oxygen saturation increasing to 89%. Shortly thereafter, sinus rhythm was established with a heart rate of 130 beats per minute. The systolic blood pressure reached a peak of 175 mmHg within 5 minutes and then declined to values between 100 mmHg and 140 mmHg. 200 mmol NaHCO<sub>3</sub> were given and ventilation was optimized.

A massive haemorrhage from the urethra was observed, whereas bleeding from the chest tube and the tracheostoma was minimal. Haemoglobin dropped to 9.8 g/dL. The patient received 5000 IU of protamine sulfate, 7 units of blood, and 6 units of fresh frozen plasma within the next 4 hours and the haemorrhage stopped.

The patient's condition improved and 12 hours later the patient was awake and in stable

cardiopulmonary condition. Because of a massive opacity of the right lung on x-ray, a bronchoscopy was performed, during which a large blood clot was removed from the carina. This procedure was repeated several times over the next 24 hours. Phenprocoumon therapy was started (INR 2.5 to 3.5).

The patient recovered uneventfully except for ALS. He was fully oriented in space and time and gave no indication of any mental impairment. He was referred to a specialized neurological unit 5 days after the event for further follow-up of ALS and use of a permanent ambulatory respirator.

## DISCUSSION

The incidence of pulmonary embolism is 1 in 1000 in the general population (7). In western industrialised countries, the rate of cardiopulmonary resuscitations for out-of-hospital cardiac arrest is between 40 and 90 per 100,000 inhabitants (8). Massive pulmonary embolism and acute myocardial infarction are the causes for cardiac arrest in 50 to 70% of cases (9). Mortality in patients with pulmonary embolism has not decreased during the last 20 years (10) and is around 100% in patients with massive pulmonary embolism and hypotension (11). About 90% of patients with fatal pulmonary embolism die within one to two hours after the occurrence of the first symptoms (12). These facts underline the importance and need for more efficacious therapeutic strategies in these patients.

There is no doubt about the benefit of thrombolysis in high-risk patients with pulmonary embolisms, i.e., patients with cardiogenic shock, decreased tissue and organ perfusion, low arterial pressure and respiratory failure (13). Compared with surgical embolectomy, the advantage of thrombolysis is its immediate availability without the need for a cardiosurgical unit and respective time for preparation.

Thrombolytic agents dissolve pulmonary emboli and are thus a causal therapy for the underlying disease leading to cardiac arrest (1, 3). In cases of massive pulmonary embolism, external cardiac massage causes a mechanical fragmentation of the embolus, which enlarges the area of action for the thrombolytic agent. This may explain the relatively fast onset of action of thrombolytics, which have been observed during thrombolysis with resuscitations (1). In addition, thrombolytics administered during resuscitation have shown to

improve cerebral microcirculatory reperfusion in preclinical models (14, 15).

Tenecteplase has a number of advantages compared with streptokinase, urokinase and tissue plasminogen activator, which are approved treatments for pulmonary embolism. These advantages include a simpler mode of administration via bolus injection, faster onset of action, longer half-life, increased fibrin specificity and higher resistance to inhibition by plasminogen activator 1 (PAI-1) (16, 17, 18, 19). Compared with alteplase in patients with acute myocardial infarction, there was no difference in the incidence rates of intracranial haemorrhage with tenecteplase administration; however, the risk for extracranial haemorrhage was reduced with tenecteplase treatment (20).

In this patient tenecteplase treatment was successful in the treatment of massive pulmonary embolism and a 30-minute cardiopulmonary resuscitation. The patient recovered without any neurological deficit, except for the known ALS. However, tenecteplase contributed to a bleeding complication from the urethra related to a urinary catheter manipulation 13 days prior to the event. The haemorrhage was eventually managed by transfusions of blood and fresh frozen plasma as well as by administration of protamine as the specific antidote for reversal of heparinization and prompt shortening of whole-blood clotting time. There were no other major bleeding sites. Sufficiently powered, randomised, controlled studies are still lacking to prove or refute the efficacy and safety of thrombolytics in general and tenecteplase in particular in massive pulmonary embolism with cardiopulmonary resuscitation.

#### CONCLUSION

This case study reports on the successful use of tenecteplase in a 59-year-old man who survived a massive pulmonary embolism followed by a 30-minute cardiopulmonary resuscitation without cerebral damage. In such a dramatic clinical event, the immediate and simple use of this modern thrombolytic appears to be a justifiable last-resort treatment option until controlled studies in sufficiently sized patient populations will have proven or refuted its efficacy and safety.

#### CONFLICT OF INTEREST STATEMENT

There are no conflicts of interest.

#### References

1. Padosch S. A., Motsch J., Boettiger B. W., *Thrombolysis during cardiopulmonary resuscitation*, ANAESTHESIST, **51**, 516-532, 2002.
2. Grabner C., Wahl U., Reineke H., *Successful cardiopulmonary resuscitation using high-dose bolus injection of rt-PA in massive pulmonary embolism*, ANAESTHESIOLOG INTENSIVMED NOTFALLMED SCHMERZTHER, **36**, 306-308, 2001.
3. Boettiger B. W., Boehrer H., Bach A., Motsch J., Martin E., *Bolus injection of thrombolytic agents during cardiopulmonary resuscitation for massive pulmonary embolism*, RESUSCITATION, **28**, 45-54, 1994.
4. Newman D. H., Greenwald L., Callaway C. W., *Cardiac arrest and the role of thrombolytic agents*, ANN. EMERG. MED., **35**, 472-480, 2000.
5. Caldicott D., Parasivam S., Harding J., Edwards N., Bochner F., *Tenecteplase for massive pulmonary embolus*, RESUSCITATION, **55**, 211-213, 2002.
6. Sze D. Y., Carey M. B., Razavi M. K., *Treatment of massive pulmonary embolus with catheter-directed tenecteplase*, J. VASC. INTERV. RADIOL., **12**, 1456-1457, 2001.
7. Goldhaber S. Z., *Pulmonary embolism*, N. ENGL. J. MED., **339**, 93-104, 1998.
8. Boettiger B. W., Grabner C., Bauer H., et al., *Long term outcome after out-of-hospital cardiac arrest with physician staffed emergency medical services, the Utstein style applied to a mid-sized urban/suburban area*, HEART, **82**, 1674-1679, 1999.
9. Zipes D. P., Wellens H. J., *Sudden cardiac death*, CIRCULATION, **98**, 2334-2351, 1998.
10. Goldhaber S. Z., de Rosa M., Visani L., *International cooperative pulmonary embolism registry detects high mortality rate*, CIRCULATION, **96** (Suppl 1,1-159), 882-888, 1997.
11. Jerjes-Sanchez C., Ramirez-Rivera A., de Lourdes Garcia M., et al., *Streptokinase and Heparin versus Heparin Alone in Massive Pulmonary Embolism, A Randomized Controlled Trial*, J. THROMB. THROMBOLYSIS, **2**, 227-229, 1995.
12. Stein P. D., Hull R. D., Raskob G., *Risks for major bleeding from thrombolytic therapy in patients with acute pulmonary embolism. Consideration of noninvasive management*, ANN. INTERN. MED., **121**, 313-317, 1994.
13. Goldhaber S. Z., *Thrombolysis in pulmonary embolism, a debatable indication*, THROMB. HAEMOST., **86**, 444-451, 2001.
14. Fischer M., Boettiger B. W., Popov-Cenic S., Hossmann K. A., *Thrombolysis using plasminogen activator and heparin reduces cerebral no-reflow after resuscitation from cardiac arrest, an experimental study in the cat*, INTENSIVE CARE MED, **22**, 1214-1223, 1996.
15. Lin S. R., O'Connor M. J., Fischer H. W., King A., *The effect of combined dextran and streptokinase on cerebral function and blood flow after cardiac arrest, an experimental study on the dog*, INVEST. RADIOL., **13**, 490-498, 1978.
16. Keyt B. A., Paoni N. F., Refino C. J., et al., *A faster-acting and more potent form of tissue plasminogen activator*, PROC. NATL. ACAD. SCI. U S A, **91**, 3670-3674, 1994.
17. Refino C. J., Paoni N. F., Keyt B. A., et al., *A variant of t-PA (T103N, KHRR 296-299 AAAA) that, by bolus, has increased potency and decreased systemic activation of plasminogen*, THROMB. HAEMOST., **70**, 313-319, 1993.
18. Collen D., Stassen J. M., Yasuda T., et al., *Comparative thrombolytic properties of tissue-type plasminogen activator and of a plasminogen activator inhibitor-1-resistant glycosylation variant, in a combined arterial and venous*

- thrombosis model in the dog*, THROMB. HAEMOST., **72**, 98-104, 1994.
19. Benedict C. R., Refino C. J., Keyt B. A., *et al.*, *New variant of human tissue plasminogen activator (TPA) with enhanced efficacy and lower incidence of bleeding compared with recombinant human TPA*, CIRCULATION, **92**, 3032-3040, 1995.
  20. Assessment of the Safety and Efficacy of a New Thrombolytic Investigators, *Single-bolus tenecteplase compared with front-loaded alteplase in acute myocardial infarction, the ASSENT-2 double-blind randomised trial*, LANCET, **354**, 716-722, 1999.