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## Case report

# First case of ischemic stroke which happened during continuous intravenous infusion of rt-PA

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## ABSTRACT

Catheter-directed thrombolysis (CDT) is one of the methods in the treatment of patients with acute lower limb ischemia. It is based on intrathrombus infusion of one of the thrombolytic agents. The most common complication of CDT is bleeding.

We present a patient with left lower limb ischemia, treated by CDT, in which symptoms of stroke, proved to have ischemic etiology, started during continuous intra-arterial infusion of rt-PA. As the patient presented with the history of atrial fibrillation, the most probable mechanism of stroke was related to detachment of possible intra-atrial thrombus. Ischemic stroke which happened during intra-arterial thrombolysis with rt-PA has never been mentioned in literature yet and the case stands for the statement that very effective causative treatment of ischemic stroke with rt-PA is not sufficient to “prevent” ischemic stroke if used in very small doses.

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## 1. Introduction

Catheter-directed thrombolysis (CDT) is an alternative method to surgical thrombolectomy, anticoagulant therapy and amputation in the treatment of patients with acute lower limb ischemia. It is used both in acute embolic ischemia and arterial or graft thrombosis [1]. It is based on intrathrombus infusion of one of the thrombolytic agents – the major three that are in use today are urokinase (UK), alteplase (rt-PA – recombinant tissue plasminogen activator) and reteplase (mucin of t-PA) [2].

CDT is recommended if a patient suffers from acute or sub-acute ischemia and does not manifest severe loss of sensory and motor function [1,3]. Patients with immediate limb threat often require emergent operation, however in some patients with cardiovascular risks of general anesthesia, thrombolysis may be the best option [4].

## 2. Case report

An 82-year-old, right-handed, Caucasian woman was admitted to the Department of General Surgery because of ischemia

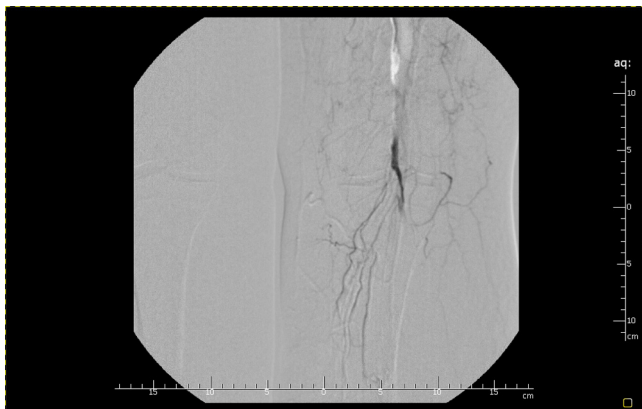
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of the left lower limb. This patient was previously (for 2 weeks) treated in the Department of Internal Medicine of another hospital because of dyspnea and swelling of the lower limbs. She presented there with a history of chronic coronary heart disease, myocardial infarction, fixed left bundle branch block, chronic heart failure, hypertensive disease, chronic obstructive pulmonary disease, hypercholesterolemia and diabetes mellitus. Physically, on admission to the Department of Internal Medicine the patient was in a severe general condition with clinical symptoms of circulatory and respiratory insufficiency in the course of infection and exacerbation of chronic obstructive pulmonary disease. ECG revealed atrial tachycardia with atrio-ventricular block 2:1, cardiac rhythm of 135/min. Over 15 days the patient improved but in the morning on the following day, the patient complained about pain of the left lower limb at rest. The left leg was cool and the patient reported numbness on the dorsal part of the foot while examined. There was also no pulse found below the left knee. Duplex Doppler of the lower limb vessels revealed patent left popliteal artery with moderately impaired flow, which was monophasic, highly resistant, with slightly lower velocity than on the right side. Proximal segments of the left shin arteries were also patent, but distally – about 5 cm below the knee the Doppler ultrasound signal was absent, which indicated occlusion of those arteries. Angio-CT of the lungs was performed to exclude pulmonary embolism. ECG showed atrial fibrillation (AFib). The dose of enoxaparin was increased to 120 mg/day (60 mg bid). Afterwards the patient was translocated to the Department of Surgery of our hospital and soon after admission the procedure of percutaneous catheter directed intra-arterial thrombolysis (CDT) was initiated. Using the cross-over method catheter ending was introduced into the thrombus in the tibial truncus and the left tibial artery. At 00:30 thrombolytic treatment was started – the patient received a single bolus of 5 ml of Actilyse (rt-PA), and then intravenous infusion of 15 ml of Actilyse along with 800 mg of heparin infusion were set up. About 7:00 am the next day a nurse recorded the patient was unresponsive, without logical verbal contact. Overall until that time the patient received in total about 12 ml of Actilyse. A consulting neurologist evaluated the patient as conscious but without any verbal contact, with “floating” eyeballs, gazing to the left. Also features of a lesion of the pathways of the right



**Fig. 1 – Angiography of the left lower limb with thrombembolization.**



**Fig. 2 – CT scan of the brain at the day of stroke of the patient.**

facial nerve, paresis of the right limbs and Babinski sign on the right were found (Figs. 1 and 2).

Computed tomography revealed numerous, diffuse areas of reduced density that might correspond to post-ischemic lesions – new ischemic areas might have been masked by them. Moreover, the lenticular nucleus on the left was slightly faded and its density was reduced. There were no signs of intracranial hemorrhage.

Over the day the general state of the patient was slightly better – she was conscious, trying to comply with the commands. Complete motor aphasia and paralysis of left limbs were still present. The patient was transferred to the Department of Neurology. Initially the patient was in medium-heavy general state, neurologically stable, with efficient respiration and circulation. AFib was still being observed – the patient was given beta-blocker (metoprolol) via intravenous drip. Moreover, acetylsalicylic acid (75 mg po), enoxaparin (40 mg bid sc), mannitol (100 ml qid iv), furosemide iv, and ipratropium bromide with salbutamol via nebulization were administered.

On the next day of hospitalization at 7:40 cardiac arrest happened. There were neither spontaneous respirations nor palpable carotid pulses. Cardiopulmonary resuscitation was begun immediately with 100% oxygen by bag-valve-mask and closed chest cardiac compressions. The patient was intubated. Atropine and adrenaline were administered. Tracheal intubation and mechanical ventilation were substituted for bag-valve-mask ventilation. Resuscitation was successful, but there were 2 more cardiac arrests. Dopamine and dobutamine were administered via intravenous drip. The patient was unconscious and unresponsive to pain. Periodically, bradycardia about 30/min and systemic blood pressure about 60/40 mmHg were observed. Despite treatment, bradycardia worsened, periodically there was no carotid and femoral pulse. At 10:20 the patient was declared dead.

### 3. Discussion

Complications of CDT are recorded in about 30% of patients. Bleeding is the most common (11.3%) complication (access site

hematoma, skin and subcutaneous, as well as cerebral hematomas, gastro-intestinal and renal bleeding, hematuria). Intracranial hemorrhage is the most dangerous complication of thrombolytic treatment. Other complications are distal or proximal embolization, peri-catheter thrombosis, compartment syndrome, lymphocele, and pseudoaneurysm.

*Ischemic stroke during intra-arterial infusion of rt-PA* has never been mentioned in literature yet. There is, however, 1 publication addressing 3 cases of ischemia of the brain after thrombolysis of an occluded limb artery, but in all 3 cases the thrombolytic agent used was streptokinase [5].

Here we describe a patient in whom two complications of atrial fibrillation took place almost simultaneously – embolic arterial occlusion of the left lower limb and ischemic stroke as an expression of arterial thromboembolism. The patient's medical history showed several risk factors of ischemic stroke: arterial hypertension, diabetes mellitus, hypercholesterolemia, obesity related to sedentary lifestyle, as well as chronic coronary heart disease. *Symptoms of stroke*, which happened to be of ischemic etiology, *started during continuous intravenous infusion of rt-PA*. This *effective for revascularization treatment* is used specifically in acute phase of ischemic stroke, independently of etiology, and therefore it is surprising that *ischemic stroke occurred during the therapy of choice of ischemic stroke*. It has to be admitted, however, that the dose of rt-PA used in the described case was significantly smaller than the dose used to treat stroke. On the other hand, “treating ischemic stroke” is a different situation from “no stroke with potential of ischemic stroke”. This means that a small dose of potent thrombolytic agent cannot prevent ischemic stroke which is probably due to cardiac embolus. It has to be speculated that probably rt-PA applied for treatment of ischemed limb in a patient with AFib provoked stroke in the mechanism of possible detaching a thrombus or thrombi from the left atrium, which then became an embolus or emboli in the brain arteries. It seems that in such situation as occlusion of a peripheral artery of a limb in a patient with AFib embolectomy is a safer procedure than thrombolysis. This can lower the risk of stroke “despite” or “because” of systemic thrombolytic treatment.

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## Conflict of interest

None declared.

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## Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

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