Case Reports

Cerebrovascular Diseases

Published online: March 20, 2006

Cerebrovasc Dis 2006;21:419–421
DOI: 10.1159/000092131

Effective Treatment with Abciximab for Consecutive Bilateral Middle Cerebral Artery Occlusion

Volker Puetz[a], *Matthias Weise*[b], *Ruediger von Kummer*[c], *Georg Gahn*[a]

Departments of [a]Neurology, [b]Internal Medicine, and [c]Institute of Neuroradiology, Technical University Dresden, Dresden, Germany

Introduction

Intravenous thrombolysis with alteplase (rt-PA) is the treatment of choice for ischemic stroke within 3 h of symptom onset [1]. Meta-analysis of the major thrombolytic stroke trials suggest a small, but still significant, benefit if given within 3–6 h [2–4]. Based on the results of a recent trial, the glycoprotein IIb/IIIa receptor antagonist abciximab may be a treatment option for this time window [5].

Potentially viable penumbral tissue may be present well beyond 6 h, in isolated cases even up to 48 h [6]. Modern imaging techniques like magnetic resonance imaging (MRI) using diffusion-weighted (DWI) and perfusion imaging (PI) may identify the penumbra and permit improved patient selection [7, 8]. Nevertheless, the best treatment for these patients has not yet been defined. This particularly applies to patients with recurrent or new symptoms after an initially successful thrombolysis where an early second thrombolytic therapy is debatable.

We report on a patient with acute left middle cerebral artery (MCA) occlusion occurring after thrombolysis with rt-PA for right MCA occlusion, whom we successfully treated with intravenous abciximab 17.5 h after onset of new symptoms.

Case Report

A 62-year-old woman was admitted to our hospital with acute onset of left-sided hemiparesis. On admission, she had left-sided hemiplegia and facial palsy with minor dysarthria – National Institutes of Health Stroke Scale (NIHSS) 11. Cerebral computed tomography (CCT) and CT angiography demonstrated right MCA mainstem occlusion but no early ischemic changes. We initiated thrombolysis with rt-PA (0.9 mg/kg) 165 min after symptom onset. With this therapy, the patient improved to NIHSS 5.

However, 1 h after termination of thrombolysis, she developed a sudden decline of consciousness. Since a repeat CCT ruled out intracranial hemorrhage (ICH), we suspected non-convulsive status epilepticus and gave intravenous lorazepam (6 mg) and valproic acid (bolus administration 900 mg, followed by 6-hour infusion 100 $mg \cdot h^{-1}$). Electroencephalographic (EEG) monitoring was technically not feasible. The patient remained stuporous requiring intubation and mechanical ventilation the next morning. MRI demonstrated a new occlusion of the left MCA and the left internal carotid artery (ICA), as confirmed by duplex ultrasound. The right MCA appeared recanalized (fig. 1). In the presence of only small DWI lesions, PI showed a perfusion deficit of the complete left MCA territory resulting in a large PI/DWI mismatch. Therefore, we initiated treatment with intravenous abciximab (bolus administration 0.25 mg/kg, followed by 12-hour infusion therapy 0.125 $\mu g \cdot kg^{-1} \cdot min^{-1}$) 17.5 h after onset of new symptoms.

Duplex sonography performed after the abciximab infusion demonstrated persistent occlusion of the left ICA but recanalization of the left MCA. The patient initially remained comatous. Repeated CCTs on days 1, 3 and 5 after thrombolysis ruled out ICH or major ischemia. EEG ruled out seizure activity, and there was no evidence for metabolic coma. She subsequently regained consciousness and was extubated after 11 days.

Further workup revealed a stalked thrombus in the left atrial ear (transesophageal echocardiography) and intermittent atrial fi-

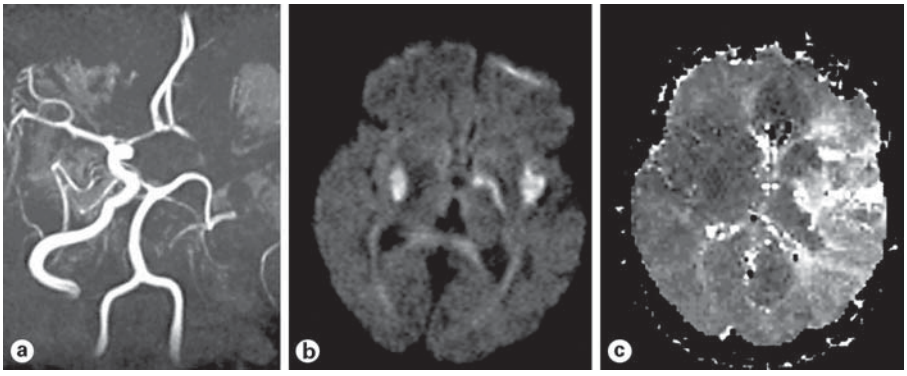

Fig. 1. MRI was performed 16.5 h after clinical deterioration: MR angiography demonstrates new occlusions of the left MCA and ICA while the right MCA is recanalized (**a**). DWI shows bilateral ischemic lesions in the basal ganglia and left insular ribbon (**b**). PI demonstrates a perfusion deficit of the complete left MCA territory resulting in a PI/DWI mismatch (**c**).

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

1015–9770/06/0216–0419$23.50/0

Accessible online at:
www.karger.com/ced

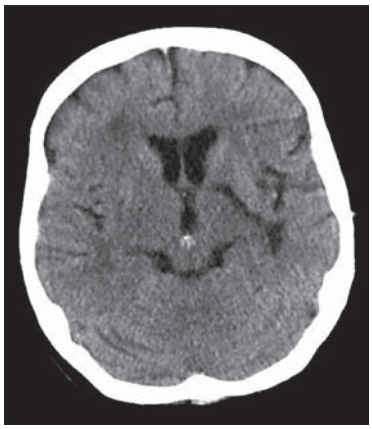

Fig. 2. Repeat CCT performed 2 months after thrombolytic therapy shows infarctions in the basal ganglia bilaterally, in the left insular ribbon and the internal capsule, identical to the DWI lesions on initial MRI. The asymptomatic left temporo-occipital ICH seen on routine MRI 3 weeks after thrombolysis is completely resorbed.

brillation (Holter ECG) strongly suggesting recurrent cardiac embolism. Therefore, we commenced secondary prophylaxis with subcutaneous low-molecular-weight heparin (nadroparin 0.7 ml/day) 2 days after thrombolysis with abciximab. An asymptomatic left temporo-occipital ICH seen on routine MRI 3 weeks after thrombolysis was rated as a complication of anticoagulation but did not result in therapeutic alterations.

Two months later, we saw the patient in our outpatient clinic. She had a minor right-sided hemiparesis and was independent without help (NIHSS 2, modified Rankin Scale 1). The final infarction volume corresponded to the DWI lesions on the initial MRI. The ICH had resolved completely (fig. 2). Subsequently, the patient was started on warfarin.

Discussion

In acute ischemic stroke, the identification of an ischemic penumbra may result in a therapeutic dilemma, because treatment beyond 6 h after symptom onset has only been studied in a phase II study so far [9]. Nevertheless, the penumbra may be present for up to 48 h [4], and consequently, thrombolytic therapy may be justified.

The glycoprotein IIb/IIIa receptor anatagonist abciximab has been safely applied up to 24 h after the onset of ischemic stroke [10]. So far, abciximab has not proven its efficacy, but showed a nonsignificant shift in favorable functional outcomes as measured by the modified Rankin Scale score at 3 months (odds ratio 1.20; p = 0.33; 95% CI 0.84–1.70) [5]. Therefore, abciximab is expected to play a major role in future stroke therapy [11].

In this case report, abciximab was applied 17.5 h after the onset of new symptoms following fibrinolysis with rt-PA for right-sided MCA occlusion. The long time lag until a diagnosis of recurrent stroke was reached was caused by initial misinterpretation of symptoms. Non-convulsive status epilepticus at stroke onset may have contributed to the clinical deterioration, but was not proven because EEG monitoring was technically not feasible. Several EEGs performed in the postacute phase showed no epileptic activity. Nevertheless, seizure at stroke onset should not be regarded as an absolute contraindication to thrombolysis in the presence of potentially salvageable tissue [12].

The demonstration of left MCA occlusion and PI/DWI mismatch proved that recurrent stroke was the main reason for the secondary clinical deterioration of the patient. This situation was presumably caused by recurrent cardiac embolism. Few case reports outline the risk of rt-PA in the setting of myocardial infarction or ischemic stroke to break up or detach cardiac thrombotic material and promote recurrent embolism [13, 14]. This mechanism might also have been relevant in our patient. However, in a recent series of 5 stroke patients with a cardiac thrombus undergoing thrombolysis with rt-PA, there was no increased risk of recurrent embolism [15].

Despite the prolonged time window and prior rt-PA treatment, therapy with abciximab was safe, because no ICH occurred. The ICH seen on MRI 3 weeks after thrombolysis was related to anticoagulation with low-molecular-weight heparin because it did not show on prior CCTs. Abciximab was also effective because the final infarction volume corresponded to the initial DWI lesion, the occluded MCA was recanalized early, and the patient had a good clinical outcome.

In conclusion, therapy with abciximab can be a treatment option in selected patients even if given beyond 6 h after symptom onset and after prior thrombolysis with rt-PA.

References

1 Tissue plasminogen activator for acute ischemic stroke: the National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. N Engl J Med 1995;333:1581–1587.

2 Hacke W, Brott T, Caplan L, Meier D, Fieschi C, von Kummer R, Donnan G, Heiss WD, Wahlgren NG, Spranger M, Boysen G, Marler JR: Thrombolysis in acute ischemic stroke: controlled trials and clinical experience. Neurology 1999;53:S3–S14.

3 Wardlaw J, del Zoppo G, Yamaguchi T: Thrombolysis for acute ischemic stroke (Cochrane review). Cochrane Database Syst Rev 2000;2: CD000213.

4 Hacke W, Donnan G, Fieschi C, Kaste M, von Kummer R, Broderick JP, Brott T, Frankel M, Grotta JC, Haley EC Jr, Kwiatkowski T, Levine SR, Lewandowski C, Lu M, Lyden P, Marler JR, Patel S, Tilley BC, Albers G, Bluhmki E, Wilhelm M, Hamilton S; ATLANTIS Trials Investigators; ECASS Trials Investigators; NINDS rt-PA Study Group Investigators: Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS rt-PA stroke trials. Lancet 2004;63:768–774.

5 Abciximab Emergent Stroke Treatment Trial (AbESTT) Investigators: Emergency administration of abciximab for treatment of patients with acute ischemic stroke: results of a randomized phase 2 trial. Stroke 2005; 36:880–890.

6 Donnan GA, Howells DW, Markus R, Toni D, Davis SM: Can the time window for administration of thrombolytics in stroke be increased? CNS Drugs 2003;17:995–1011.

7 Schellinger PD, Fiebach JB, Jansen O, Ringleb PA, Mohr A, Steiner T, Heiland S, Schwab S, Pohlers O, Ryssel H, Orakcioglu B, Sartor K, Hacke W: Stroke magnetic resonance imaging within 6 hours after onset of hyperacute cerebral ischemia. Ann Neurol 2001;49:460–469.

8 Rother J, Schellinger PD, Gass A, Siebler M, Villringer A, Fiebach JB, Fiehler J, Jansen O, Kucinski T, Schoder V, Szabo K, Junge-Hulsing GJ, Hennerici M, Zeumer H, Sartor K, Weiller C, Hacke W; Kompetenznetzwerk Schlaganfall Study Group: Effect of intravenous thrombolysis on MRI parameters and functional outcome in acute stroke <6 h. Stroke 2002; 33:2438–2445.

9 Hacke W, Albers G, Al-Rawi Y, Bogousslavsky J, Davalos A, Eliasziw M, Fischer M, Furlan A, Kaste M, Lees KR, Soehngen M, Warach S; DIAS Study Group: The Desmoteplase in Acute Ischemic Stroke Trial (DIAS): a phase II MRI-based 9-hour window acute stroke thrombolysis trial with intravenous desmoteplase. Stroke 2005;36:66–73.
10 Abciximab in acute ischemic stroke: a randomized, double-blind, placebo-controlled, dose escalation study. The Abciximab in Ischemic Stroke Investigators. Stroke 2000;31:601–609.
11 Lapchak PA, Araujo DM: Therapeutic potential of platelet glyocoprotein IIb/IIIa receptor antagonists in the management of ischemic stroke. Am J Cardiovasc Drugs 2003;3:87–94.
12 Selim M, Kumar S, Fink J, Schlaug G, Caplan LR, Linfante I: Seizure at stroke onset: should it be an absolute contraindication to thrombolysis? Cerebrovasc Dis 2002;14:54–57.
13 Yasaka M, Yamaguchi T, Yonehara T, Moriyasu H: Recurrent embolization during intravenous administration of tissue plasminogen activator in acute ischemic stroke. A case report. Angiology 1994;45:481–484.
14 Bautista RED: Embolic stroke following thrombolytic therapy for myocardial infarction in a patient with preexisting ventricular thrombi. Stroke 1995;26:324–325.
15 Derex L, Nighoghossian N, Perinetti M, Honnorat J, Trouillas P: Thrombolytic therapy in acute ischemic stroke patients with cardiac thrombus. Neurology 2001;57:2122–2125.

Dr. V. Puetz, Department of Neurology
Technical University Dresden, Fetscherstrasse 74
DE–01307 Dresden (Germany)
Tel. +49 351 458 3565, Fax +49 351 458 4365
E-Mail volker.puetz@neuro.med.tu-dresden.de

Cerebrovasc Dis 2006;21:421–422
DOI: 10.1159/000092132

Limb-Shaking Transient Ischemic Attack Induced by Middle Cerebral Artery Stenosis

Wei-Jian Jiang[a], *Feng Gao*[a], *Bin Du*[a], *Trilochan Srivastava*[b], *Yong-Jun Wang*[a]

[a] Neurovascular Angioplasty Team, Department of Neurology and Neuroradiology, Beijing Tiantan Hospital, Capital University of Medical Sciences, Beijing, China, and [b] All India Institute of Medical Sciences, New Delhi, India

A 71-year-old female presented with a 3-month history of episodic shaking movements of the left leg. She had a history of hypertension for the past 10 years. These recurrent episodes would usually begin with a sensation of 'weakness' involving predominantly her left leg, and at times, the left arm. This was followed by the involuntary, focal, arrhythmic shaking movements of her left leg for about 30–45 s without spread to other limbs or body parts. The whole event would last for less than 5 min. Her consciousness was not impaired during the attacks. These attacks would occur during prolonged standing and walking. There were 4–5 attacks per day with increased frequency in the last month. The general physical and neurological examinations were normal. Her blood pressure was 155/70 mm Hg and there was no orthostatic hypotension. The ambulatory electroencephalographic monitoring was normal. Diffusion-weighted MRI revealed hyperintense lesions in the right border zone between the anterior cerebral artery (ACA) and middle cerebral artery (MCA) (fig. 1a). Magnetic resonance angiogram showed severe focal stenosis of the right MCA and absence of bilateral ACA (fig. 1b). Perfusion CT showed delayed time to peak and mean transit time, increased relative cerebral blood flow, and slightly decreased relative cerebral blood flow in right anterior frontal lobe, the right anterior and posterior border zone and the right basal ganglia (fig. 1c). Digital substraction angiography showed severe focal stenosis of the M1 segment of the right MCA and absence of bilateral ACA. The right border zone (between ACA and MCA) was shifted internally, suggestive of the right ACA territory being compensated partially by the leptomeningeal collateral vessels from the right MCA (fig. 1d). Extracranial segment of the right internal carotid artery was normal. The patient was diagnosed as a case of

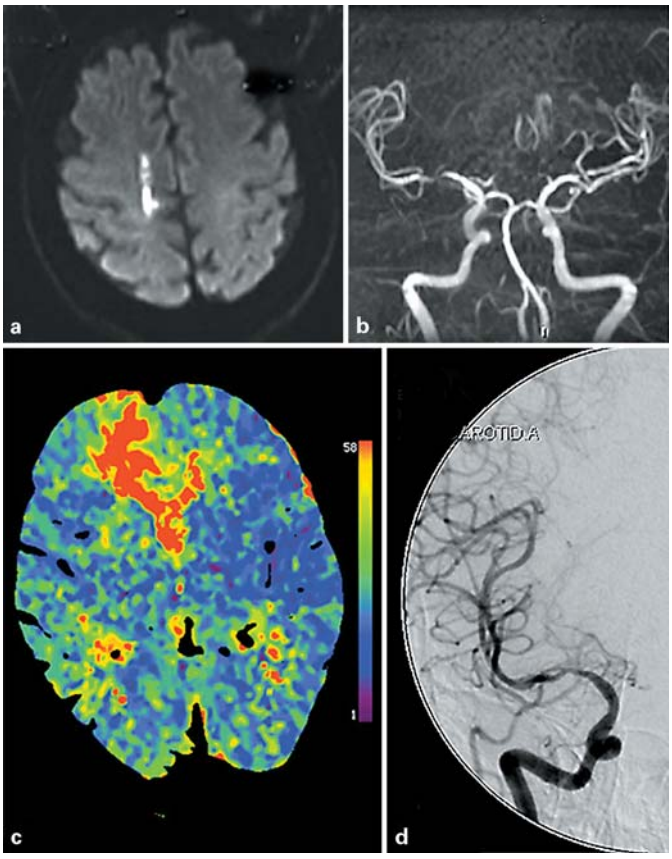

Fig. 1. a Diffusion-weighted MRI revealed high signal intensity lesions in the right watershed territory between the ACA and MCA. **b** Magnetic resonance angiogram showed severe focal stenosis of the right MCA and absence of bilateral ACA. **c** Perfusion CT showed delayed mean transit time in the right anterior frontal lobe, the right anterior and posterior border zone, and the right basal ganglia. **d** Digital substraction angiography showed severe focal stenosis of the M1 segment of the right MCA and absence of the ACA. The right border zone (between the ACA and MCA) shifted internally, suggestive of the right ACA territory being compensated partially by the leptomeningeal collateral vessels from the right MCA.