Stroke Therapy in the 21st Century: A Case Report

Uta Meyding-Lamadé[1], Burc Bassa[1], Christian Jacobi[1], Bodo Kress[2], Corinna Schranz[1]

[1]Department of Neurology and [2]Department of Neuroradiology, Krankenhaus Nordwest, Frankfurt, Germany.

Abstract:

This is a case report of a typical stroke patient, who was treated recently in our hospital (Frankfurt Nordwest, Germany). Modern stroke care concept is discussed in this report.

Keywords: *Stroke, Thrombolysis, Stroke Unit, Secondary prevention*

Case Report:

An 80-year-old patient complained of vertigo during breakfast. Few minutes later he was not able to respond to the questions from his wife and almost fell off the chair due to a right sided weakness. His wife was not sure of what to do and decided to wait. As the patient had not improved after 2 hours, she then called the ambulance.

The ambulance arrived about 2.5 hours since the onset of the symptoms. The ambulance driver, trained dealing with neurological emergency suspected acute stroke. They brought the patient immediately to our stroke unit at Department of Neurology, Krankenhaus Nordwest, Frankfurt, Germany.

At the Stroke Unit the patient was first examined by the stroke neurologist, who found an alert patient with a marked non-fluent aphasia. Other neurological findings were a right sided facial palsy, a moderate hemiparesis and hypoaesthesia of the right sided limbs. Vital signs showed an elevated blood pressure (170/95mmHg), a normal heart rate (77/min) and a normal breathing rate. Body temperature was 37.3°C.

ECG demonstrated atrial fibrillation and showed pacer activity. Lab values were normal except an insignificant increase of INR (1.23). His medical history revealed an arterial hypertension, a coronary heart disease with two stents. Medication prior to admission was: bisoprolol 2.5mg, L-Thyrox 150µg, ASA 85mg, ramipril 2.5mg, hydrochlorothiazide 25mg .

Ten minutes after admission a cranial computer tomography (CCT) (Figure 1a) was performed, showing no clear effacement, but a hyperdensity of the temporal branch of the left middle cerebral artery (MCA). Despite the early time window

Corresponding author: Professor Dr.Uta Meyding-Lamadé, Krankenhaus Nordwest, Department of Neurology, Frankfurt, Germany

diffusion-MRI (Figure 1c) was performed to increase treatment safety in this elderly patient.

Figure 1a) Computertomography at admission showing a thrombotic occlusion of a temporal branch of the distal MCA left side

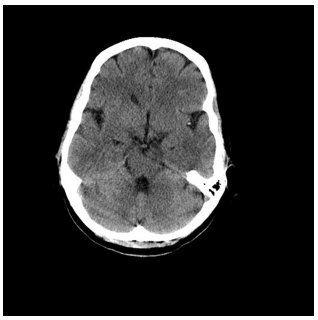


Figure 1b) MR-Angiography before thrombolysis showing a proximal occlusion of the left MCA

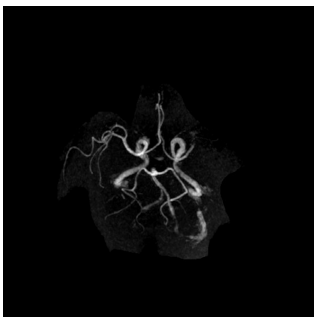
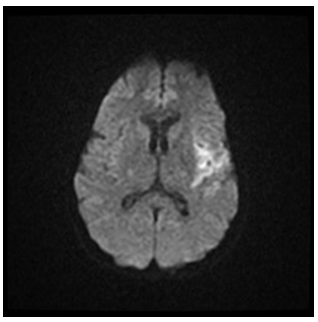


Figure 1c) Diffusion MRI before thrombolysis with a diffusion abnormality in the parietotemporal lobe less than 1/3 of the MCA territory



As clinically suggested it showed a diffusion abnormality in the left parieto- temporal lobe less than a third of the entire media territory. MR-angiography (Figure 1b) demonstrated an occlusion of the proximal MCA on the left side. No intracranial bleeding was detectable in either method.

Because our patient was admitted within 4.5 hours, CCT excluded intracerebral haemorrhage and no other contraindications could be detected. He was treated immediately with 60mg rt-PA (Alteplase) intravenously (0.9 mg/kg body weight, 10% as bolus, remaining dose as infusion over 60min).

A few hours later the neurological symptoms improved significantly. The patient was able to move all limbs and the aphasia was also in regression. Corresponding to the clinical findings, the follow up CCT a day later showed only a small infarction of the left sided lateral basal ganglia and a small parietocortical infarction.

As carotid duplexsonography showed no stenosis or occlusion, the most probable reason for the embolic stroke was atrial fibrillation. For secondary prevention, the patient was initially put on low molecular heparin (Enoxaparin 40mg BID). Later, anticoagulation with Phenprocoumon was initiated.

Public awareness

Most people are not aware of stroke symptoms and important time is lost. The interval from symptom onset to first call for medical help is the main cause of prehospital delay. Major reasons for delayed contact include not only lack of awareness of stroke symptoms and recognition of their severity, but also denial of the disease and the hope that symptoms would resolve. In Europe up to 50% of the patients do not realize stroke symptoms. This suggests that educating the population to recognize stroke symptoms, and changing people's attitudes to acute stroke, may reduce the delay from stroke onset to emergency medical service (EMS) involvement. While most people agree that stroke is an emergency, and that they would seek medical help immediately, in reality only up to 50% call EMS. In many cases the first contact is with a family member or with a general practitioner; in some studies between 45% and 48% of patients were referred via a general practitioner [1].

Patient referral

Once stroke symptoms are suspected, patients or their proxies should call Emergency Medical service (EMS). The EMS system should have an electronic validated algorithm of questions to diagnose stroke during the phone interview. The ambulance dispatchers and paramedics should be able to diagnose stroke using simple instruments such as the Face-Arm-Speech-Test (Table 1) [2]. They should also be able to identify and provide appropriate help for patients with early complications or co-morbidities of stroke, such as impaired consciousness, seizures, vomiting, or haemodynamic instability. Suspected stroke victims should be transported without delay to the nearest stroke unit. Patients with onset of stroke symptoms within 4.5 hours should be given priority in evaluation and transportation.

Table 1) Face-arm-speech-test

Item	Yes	No	Uncertain
Speech impairment	☐	☐	☐
Facial Palsy	☐	☐	☐
Arm weakness	☐	☐	☐
If at least one symptom is present, this patients is suspected of having a stroke			

Stroke Units and telemedicine

A stroke unit consists of a discrete area of a hospital ward that exclusively takes care of stroke patients and is staffed by a specialist multidisciplinary team [1]. The core disciplines of the team are medicine, nursing, physiotherapy, occupational therapy, speech and language therapy and social workers. Treatment in a stroke unit reduces mortality and care-dependency by 25-30% compared to treatment in general wards. All types of patients, irrespective of gender, age, stroke subtype and stroke severity, appear to benefit from treatment in stroke units [3]. Although stroke unit care is more costly, it reduces post-acute inpatient care costs and is therefore cost-effective.

In remote or rural areas without a close meshed stroke unit coverage telemedicine can improve

access to treatment. Telemedicine, as part of a regional stroke treatment concept, has been demonstrated to be a feasible, valid and reliable means of facilitating thrombolysis delivery to patients in distant or rural hospitals, where timely air or ground transportation is not feasible. The quality of treatment, complication rates, and short and long term outcomes are similar for acute stroke patients treated with rtPA via a telemedicine consultation at local hospitals and those treated in academic centres [4, 5].

Early/general stroke treatment

First of all it is important for stroke patients to keep or to bring their vital signs (blood pressure, body temperature, blood oxygen content, blood glucose level, fluid balance) in the normal range. Blood pressure monitoring and treatment is a controversial area in stroke management. Patients outside the highest and lowest levels of blood pressure recommended in the first 24 hours after stroke are more likely to have early neurological decline and poorer outcomes. It is still undetermined whether blood pressure should be lowered after acute stroke, and whether antihypertensive therapy should be continued or stopped in the first few days after stroke. In the absence of reliable evidence from clinical trials, many clinicians have developed protocols for the management of extremely high blood pressure. In some centres it is common practice to begin cautious blood pressure reduction when levels exceed 220 mmHg systolic and 120 mmHg diastolic. In patients undergoing thrombolysis it is common practice to avoid systolic blood pressures above 185 mmHg. Most recommended drugs for treatment are i.v. labetalol and urapadil [1].

Hyperglycaemia occurs in up to 60% of stroke patients without known diabetes and is associated with larger infarct volumes and cortical involvement, and with poor functional outcome. Despite the lack of data it is common practice in stroke units to reduce blood glucose levels exceeding 180 mg/dl (10 mmol/l). Hypoglycaemia (<50mg/dl [2.8 mmol/l]) should be treated by intravenous dextrose bolus or infusion of 10–20% glucose [1].

Raised body temperature should prompt a search for infection and treatment where appropriate. Studies with antipyretic medication have been inconclusive, but treatment of raised body temperature (>37.5°C) with paracetamol is common practice in stroke patients [1].

Acute stroke imaging

Patients with suspected TIA or stroke should have clear priority over other patients for brain imaging, because time is crucial. Investigation of TIA is equally urgent, because up to 10% of these patients will suffer stroke within the next 48 hours [6]. Diagnostic imaging must be sensitive and specific in detecting stroke pathology, particularly in the early phase of stroke. CT is usually sufficient to guide routine thrombolysis and is the most cost-effective strategy for imaging acute stroke patients. Overall, CT is less sensitive than multimodal MRI, but equally specific, for early ischaemic changes. Early CT changes in ischaemic stroke include decrease in tissue x-ray attenuation,

tissue swelling with effacement of cerebrospinal fluid spaces, and arterial hyperattenuation, which indicates the presence of intraluminal thrombus with high specificity [7]. The presence of early signs of ischaemia on CT should not exclude patients from thrombolysis within the first 3 hours, though patients with a hypoattenuating ischaemic lesion which exceeds one third of the middle cerebral artery (MCA) territory may benefit less from thrombolysis.

Modern, multimodal MRI-techniques including diffusion, T2* and perfusion imaging have the advantage of higher sensitivity for early ischaemic changes than CT [8]. This higher sensitivity is particularly useful in the diagnosis of posterior circulation strokes and lacunar or small cortical infarctions. MRI can also detect small and old haemorrhages for a prolonged period with T2* (gradient echo) sequences. However, DWI can be negative in patients with definite stroke and the usefulness could not be demonstrated in randomized clinical trials [9].

Specific stroke treatment

Thrombolytic therapy with intravenous rtPA (Alteplase) is the only proven specific acute stroke therapy, which was evaluated in several randomized, placebo controlled trials. The treatment was approved based on the results of the NINDS-trial within a 3 hour time window [10]. Three years ago the ECASS III trial showed that this treatment is effective and safe also in a 3 to 4.5 hour time window [11]. Recently the combined analysis of NINDS and ECASS III again demonstrated that rtPA is effective and safe in the time window of 4.5 hours after symptom onset [12]. This analysis also confirms the clear correlation between the onset-to-treatment-time (OTT) and the treatment effect; the earlier the treatment the better the outcome. The most feared risk of thrombolytic therapy is intracerebral haemorrhage, because it commonly leads to a clinical deterioration. The above mentioned analysis found a 5.2% risk for symptomatic intracerebral haemorrhage, which is around 5 times higher than in-patients treated with placebo. It is important that there was no significant interaction between the bleeding risk and the OTT. The NNT to achieve a favourable clinical outcome (patient with no or only mild symptoms) after 3 months is 7. European regulatory agencies do not advocate rtPA treatment in patients with severe stroke (NIHSSS $\geq$25), extended early ischaemic changes on CT-scan, or age above 80 years (unlike the US labelling). Nevertheless, observational studies suggest that rtPA given within 3 hours of stroke onset is safe and effective in patients over 80 years of age[13].

In individual cases (time window > 4.5h) or stroke patients with an uncertain time window the use of multimodal imaging criteria may be helpful for patient selection [14]. Interventional techniques aiming to remove occluding clots with mechanical retrievers are under development and are useful treatment options for patients with very severe strokes.

Secondary prevention

Secondary prevention depends on the etiological classification of the stroke and the individual risk factor profile. The etiological workup should be carried out during the initial 24 hours by ultrasound

and laboratory testing, as the risk of recurrence is highest during the first hours and days.

In our case, the patient suffered his stroke from cardioembolic origin due to atrial fibrillation. For patients with permanent or paroxysmal atrial fibrillation (AF) and concomitant vascular risk factors an oral anticoagulation with a target INR between 2.0 and 3.0 is recommended [1]. Anticoagulation in elderly patients with Warfarin is important, because they have a particular high risk of suffering from embolic stroke and the BAFTA-trial has confirmed that warfarin is also safe in those patients [15]. However, treatment with warfarin bears some problems, for example the need for regular blood tests, the multiple interactions with other drugs and a small therapeutic range. In the near future new drugs like direct thrombin-inhibitors are expected as a promising alternative. The ReLy study examined two dosages of dabigatran in the prevention of stroke recurrence in patients with atrial fibrillation and a prior stroke or TIA. The lower dosage had the same effectiveness as warfarin but was safer in terms of severe bleeding complications, the higher dosage was more effective with comparable bleeding complications [16].

Conclusion

Optimization of the prehospital phase, public education for stroke recognition, immediate admission to a stroke unit may lead to a better strokecare. The only effective acute therapy (rtPa, Alteplase) is now available for patients during the 4.5 hours window with adherence to the inclusion- and exclusion criteria. Treatment at a specialized stroke centre has proven to save lives and reduces morbidity, that help enabling more patients to live an independent life after their stroke.

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