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Case Report

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Successful thrombolysis for acute ischaemic stroke in haemodialysis

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Abstract

Stroke is a leading cause of death worldwide and is associated with significant morbidity in survivors. Early thrombolytic therapy in acute ischaemic stroke has been shown to dramatically improve patient outcomes. Although the age-adjusted incidence of stroke is 5–10 times greater in haemodialysis patients, the use of thrombolysis for this indication in this group of patients has not been described to date. We present a case where alteplase was used successfully for acute ischaemic stroke in a patient established on maintenance haemodialysis in the setting of an international randomized controlled trial and advocate caution with the use of systemic thrombolytics despite the favourable outcome seen with this case.

Keywords: alteplase; haemodialysis; stroke

Introduction

Intravenous rtPA remains the only proven treatment for acute ischaemic stroke in the general population. Patients with end-stage renal disease (ESRD) on dialysis have a 5–10-fold higher incidence of stroke than the general population with an overall incidence rate of 13–33 per 1000 patient-years [1,2]. Haemorrhagic stroke subtype is more frequent in patients on dialysis (≥30%) [3]. This may reflect the bleeding diathesis of uraemia [4] as well as the effects of anticoagulation for vascular access and dialysis circuit patency, the prevalence and degree of hypertension, and the established ethnic variations.

Patients with ESRD have been traditionally excluded from the large prospective randomized controlled trials that form the evidence base for treatment of vascular disease, including stroke, in the general population. The paradoxical effect of this apparent 'renalism' [5] is to potentially restrict access to beneficial therapies in a cohort that would have derived the greatest benefit. In addition, extrapolating outcome data derived from studies in the general population to patients on haemodialysis is not always fruitful. In one of the few adequately powered large prospective randomized controlled trials in haemodialysis (HD), atorvastatin did not reduce the incidence of stroke in stark contrast to studies in the general population [6]. At present, the use of thrombolytic therapy for acute ischaemic stroke in HD patients has not been described.

Case report

We present the case of a 73-year-old male of South Asian ethnicity. He had a prior diagnosis of progressive chronic kidney disease secondary to obstructive uropathy and recurrent urosepsis, and a hydronephrotic left kidney requiring insertion of a J-J ureteric stent in June 2009. In addition, he had type 2 diabetes mellitus, ischaemic heart disease (myocardial infarction March 2009) and a diagnosis of hypertension. He did not have a history of cardiac dysrhythmia, a prothrombotic diathesis or cerebrovascular disease. There was no family history of renal or cerebrovascular disease. He was not on maintenance antiplatelet agents or oral anticoagulants. He was a non-smoker and did not consume any alcohol. Following emergency admission to the intensive care unit with pulmonary oedema, oliguria and a serum creatinine of 10.2 mg/dL (899 μmol/L), he was established on maintenance thrice weekly HD via a right internal jugular tunnelled cuffed central venous catheter (TesioCath™, MedComp, Harleysville, PA, USA) 2.5-months prior to presentation with an acute stroke.

He presented to his local emergency department with acute right hemiparesis and aphasia of a 90-min duration. He had undergone routine HD 24-h with no complications prior to presentation. On arrival, his blood pressure (BP) was 190/87 mmHg, capillary blood glucose was 86.5 mg/dL (4.8 mmol/L) and his Glasgow Coma Score (GCS) was 15/15. He was in sinus rhythm on his electrocardiogram. An urgent CT scan of his brain revealed an acute ischaemic stroke affecting the superior parasagittal cortex of the left frontal lobe. There was no evidence of intracranial haemorrhage. At that point, he was transferred immediately to his local acute stroke centre. On arrival, his BP was 176/75 mmHg. Clinical examination revealed a mild right facial droop, evidence of a right hemiparesis (power 3/5 in the upper limb and power 0/5 in the lower limb) with increased muscle tone in the upper limb, lower limb hyperreflexia and an upgoing plantar response in the lower limb.

He was dysphasic with receptive and expressive elements. No cardiac murmurs or carotid bruits were detected, and he was clinically euvolaemic. Calculated total NIH stroke score was 8. His laboratory examinations are presented in Table 1.

There were no absolute contraindications to thrombolysis, and he was eligible for trial enrolment. Following informed consent, he underwent randomization and received 54 mg rtPA (0.9 mg/kg—weight estimated at 60 kg) as per trial protocol (10% bolus followed by an infusion). rtPA (Actilyse™, Boehringer Ingelheim Ltd, Bracknell, Berkshire, UK) was delivered at 4-h after symptom onset. A repeat CT brain scan was performed 24-h after thrombolysis which showed a small area of haemorrhagic transformation within the original infarct and no other interval change (Figure 1). He remained clinically stable although required sodium valproate (600 mg b.d.) and clobazam (5 mg o.d.) for intermittent left upper limb myoclonus which responded well to therapy. Echocardiography revealed only borderline left ventricular hypertrophy. A 24-h Holter during the interdialytic period revealed sinus rhythm with a 1-h paroxysm of asymptomatic atrial fibrillation that terminated spontaneously. There was no significant carotid stenosis on Doppler ultrasonography. Four days after admission, he was transferred to our specialist renal stroke rehabilitation unit where he was an inpatient for the following month. During this time, power in his upper limb improved to 4/5 proximally and 3/5 distally, and in his lower limb to 4/5 proximally. His dysphasia improved, but he was left with a residual mild expressive deficit. He was discharged home 5 weeks after his initial admission and remains stable on maintenance HD.

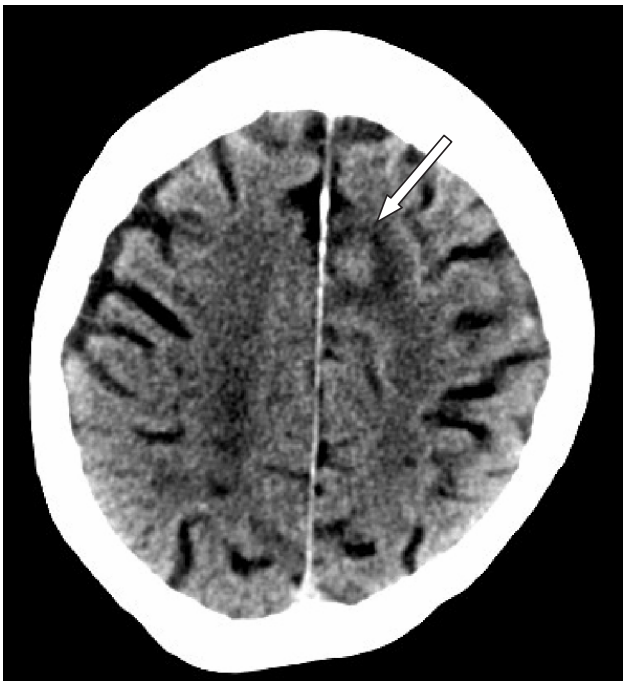

Fig. 1. Single representative axial section through the brain post-thrombolysis. Within the parasagittal cortex of the left frontal lobe in the anterior cerebral artery territory is an ischaemic infarct with a small amount of haemorrhagic transformation (area of increased attenuation marked with the arrow).

Discussion

rtPA (alteplase) is a glycoprotein that becomes activated on binding to fibrin, converting plasminogen to plasmin and leading to fibrinolysis. It is rapidly cleared from the circulation following administration undergoing predominantly hepatic clearance. When administered within 3-h of symptom onset in the seminal placebo-controlled National Institute of Neurological Disorders and Stroke (NINDS) rtPA study, it resulted in a significantly better neurological outcome at 3 months [7]. Analysis of pooled results of six randomized controlled trials of intravenous rtPA showed that the best outcomes occurred in patients treated within 2-h of symptom onset and suggested a benefit extending to 4.5-h. This was confirmed in a subsequent randomized controlled trial, ECASS III [8]. Although mortality did not differ between the two groups, 52.4% patients in the rtPA arm recovered with no disability after 90% vs 45.2% in the placebo arm (P = 0.04). There was, however, a higher rate of symptomatic intracerebral haemorrhage in the rtPA arm (2.4% vs 0.2%, P = 0.008) in keeping with prior studies. A Cochrane systematic review suggested a benefit associated with rtPA up to 6-h from symptom onset [9], and this is currently under study [10].

Use of rtPA is contraindicated in cases where there is a 'known haemorrhagic diathesis' or severe uncontrolled arterial hypertension (defined as 185/110 mmHg) as well as 'administration of heparin within the previous 48-h and a thromboplastin time exceeding the upper limit of normal for laboratory'. The manufacturer advises caution in 'all situations where there is a high risk of haemorrhage' [11].

The use of warfarin in HD patients with atrial fibrillation or for maintenance of arteriovenous graft patency will preclude some patients from receiving rtPA despite a study demonstrating a higher incidence of stroke in patients on this therapy. High rates of coronary and peripheral arterial disease and its treatment with percutaneous interventions in ESRD lead to a significant proportion of patients on single or dual maintenance antiplatelet therapy. Clinicians need to be aware of the high rates of occult gastrointestinal bleeding in HD patients as well as considering uraemia as a state of mild haemorrhagic diathesis. Heparin is routinely used

Table 1. Laboratory tests at time of presentation

Haemoglobin	15.9 g/dL
Total leucocyte count	7.5×10^9/mL
Platelet count	161×10^9/mL
Sodium	136 mmol/L
Potassium	4.7 mmol/L
Urea	12.2 mmol/L
Creatinine	462 μmol/L
Albumin	44 g/L
Total cholesterol	2.2 mmol/L
C-reactive protein	2 mg/L
INR	1.1
APTT	27.8 s
Fibrinogen	4.00 g/L

for dialysis circuit anticoagulation. Although the effect of unfractionated heparin can be monitored using the activated partial thromboplastin time (APTT), this is not the case for low-molecular-weight heparins (e.g. tinzaparin and enoxaparin) that are increasingly used for this indication.

To our knowledge, this is the first reported case of intravenous thrombolysis for treatment of acute ischaemic stroke in a haemodialysis patient. The outcome for this patient was favourable; however, we would advise extreme caution with the use of rtPA (alteplase) and treatment delivered on a case-by-case basis.

Conflict of interest statement. None declared.

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