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Post haemodialysis stroke thrombolysis, to give or not to give?

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Abstract

With every increment of glomerular filtration rate (GFR) by 10%, there is an elevated risk of stroke by 7%. Stroke death is also 9 times higher in end stage renal failure (ESRF) patients as compared to the general population. Certain studies have described that intravenous thrombolysis in ESRF patients with acute ischaemic stroke has no added benefit with increased risk of bleeding while some still recommend intravenous thrombolysis (IVT) as it improves neurological outcome. We describe two cases of acute ischaemic stroke at 0 hours post haemodialysis (HD) and 3.5 hours post HD. A 62-year-old gentleman with underlying hypertension and ESRF, presented 3.5 hours after haemodialysis with National Institute of Health Stroke Scale (NIHSS) of 7. Computed Tomography Angiography (CTA) showed a right distal M1 non occlusive thrombus and IV Alteplase 40mg was given. NIHSS post IVT at 6hours showed improvement to 3 and 0 upon discharge. Current mRS is 0. Upon undergoing 3hours of haemodialysis, a 66-year-old gentleman with underlying Hepatitis C and ESRF had an acute stroke with NIHSS of 10. CTA showed left M2 occlusion and IV Alteplase 50mg was given. NIHSS 6hours post IVT is 7 and 4 upon discharge. Complications include, oozing over his left BCF and minimal sulcal subarachnoid haemorhage. Current mRS is 1. In conclusion, post dialysis patients who suffer from an acute stroke, may be given intravenous thrombolysis as to improve their clinical outcome. In this study, both patients were given a lower dose of Alteplase (0.6mg/kg) and had favourable outcomes.

Keywords: Acute ischaemic stroke, post haemodialysis, intravenous thrombolysis, end stage renal failure

INTRODUCTION

End stage renal failure (ESRF) is a significant loss of renal function with a permanent glomerular filtration rate (GFR) of less than 15 ml/min. This subjects a patient to renal replacement therapy, either by haemodialysis, ambulatory peritoneal dialysis or kidney transplant to improve morbidity and mortality.

Globally, the incidence of ESRF is increasing. According to international comparisons of the United States Annual Data Report, 8 reporting countries or regions with the highest incidence of ESRF were situated in Asia.[1] In Malaysia, according to the Malaysian 30th Dialysis and Transplant Registry the incidence of ESRF undergoing renal replacement therapy has increased from 34,272 in 2013 to 53,164 in 2022.[2]

Cerebral vascular disease is the leading cause of death in Malaysia in 2014 with an approximate of 15.2% of total deaths, followed by ischaemic heart disease (14.8%) and lower respiratory tract infections (9.3%).[3] In a stroke data analysis study done from 2009-2017, from the 9361 of first ever stroke patients admitted to hospitals in Malaysia, 36.2% were discharge with independent activities of daily living (ADL), 53.1% had functional dependence, while 10.8% succumbed at the time of discharge.[4]

The increasing trend in prevalence in both ESRF and cerebral vascular disease, especially acute ischaemic stroke in the context of this discussion, is well attributed to the increase in prevalence of non-communicable disease (NCD) in Malaysia— namely diabetes, hypertension, and dyslipidaemia in which 8.1% of Malaysian has all three NCDs while up to 9.9% of Malaysians lives with a combination of two types of NCDs.[5]

Acute ischemic stroke (AIS) accounts for 70-80% of stroke in dialysis patients with remaining being haemorhagic stroke.[6] An increased incidence of stroke is particularly seen in the first month of

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initiation of haemodialysis, with a study showing up to 7 times higher incidence in stroke compared to baseline, with a rapid decrease in 1-2months after initiation and stabilized at twice the baseline rate in 1 year upon initiation of haemodialysis (HD).[7] With every increment of glomerular filtration rate by 10%, there is an elevated risk of stroke by 7%.[8]

Up to now, use of intravenous thrombolysis (IVT) in ESRF patient is controversial. While Recombinant tissue plasminogen activator (rTPA) such as Alteplase has no contraindication to be used in ESRF patients, but its reported high risk of bleeding post IVT preclude most neurologists from using them. There are several risk factors that contributes to bleeding risks in ESRF patients namely uraemia, concomitant use of antiplatelets, regular exposure to heparin during dialysis as well as effects of hypovolaemia and hypertension in this population.[6]

In this report, we describe two end stage renal failure patients with acute ischaemic stroke who presented early to our stroke unit in Hospital Seberang Jaya, Penang, Malaysia and were treated with intravenous thrombolysis with good outcomes.

CASE REPORTS

Patient 1

62-year-old gentleman with underlying hypertension and ESRF on regular HD. Patient completed HD at 7.30pm and 3.5 hours later, presented with a left sided body weakness and slurring of speech. National Institute of Health Stroke Scale (NIHSS) on arrival was 9 then 7 prior to IVT. Computed Tomography Angiography (CTA) brain up to the arch of aorta showed a right distal M1 non occlusive thrombus. Blood pressure prior to IVT was 123/72, activated partial thromboplastin time (APTT) was 26 and the International normalized Ratio (INR) was 1.1. Patient was subsequently given IV Alteplase 40mg (4mg bolus and 36mg over 1 hour) using his dry weight of 61kg (0.65mg/kg). Total dose of Alteplase was rounded off to facilitate process of preparation and delivery of the medication. NIHSS post IVT at 6hours showed improvement to 3 and 0 upon discharge. Current Modified Rankin Score (mRS) is 0.

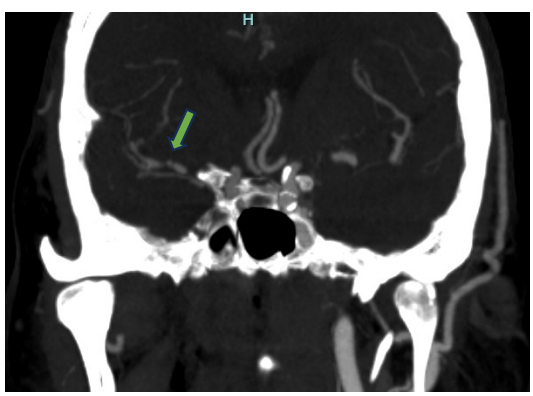

Figure 1: Arrow showing right distal M1 non occlusive thrombus seen in case 1, coronal view

Patient 2

A 66-year-old gentleman with underlying Hepatitis C and ESRF, on regular HD at Hospital Seberang Jaya Haemodialysis Unit was undergoing regular HD until at 3hours of ongoing dialysis, became unresponsive. NIHSS upon arrival to Emergency Department 15minutes later was 10. CTA showed left M2 occlusion. Blood pressure prior to IVT was 149/75, APTT value was 31 and INR was 1.2. IV Alteplase 50mg was given (4.5mg bolus and 45.5mg over 1 hour) using his dry weight 74kg (0.67mg/kg). Similarly, as the previous case, total dose of Alteplase was rounded off to facilitate process of preparation and delivery of the medication. NIHSS 6hours post IVT is 7 and 4 upon discharge. Patient, however had oozing over his left brachiocephalic fistula (BCF) after 30minutes of Alteplase administration which resolved with compression bandage and a minimal sulcal subarachnoid haemorrhage which did not worsen on serial CT brain post IVT. He was then discharged home at Day 4 post stroke with

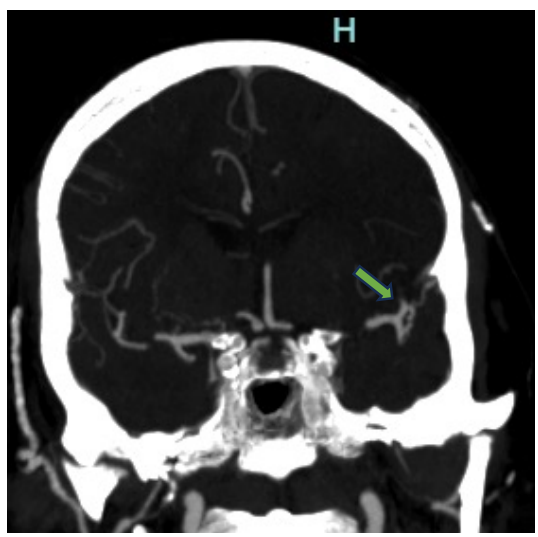

Figure 2: Arrow showing left proximal M2 thrombus seen in case 2, coronal view

anticoagulant for a newly diagnosed atrial flutter. Current mRS is 1.

DISCUSSION

Multiple studies have shown that poorer GFR contributes to poorer outcome of IVT including poor functional status, death and symptomatic intracranial haemorhage.[9] A large collaborative cohort study involving 11 large European stroke centres (4780 patients) concluded that patients with chronic kidney disease receives no additional benefit from IVT as compared to non-thrombolysed patients.[9] This may be due to chronic kidney disease patients have reduced fibrinolysis rates because of higher clot rigidity and lesser clot permeability.[10]

Both patients described above were chronic haemodialysis patients in which both patients were initiated HD over 1 year prior to presentation. One patient had no bleeding complication while one had bleeding from his BCF which was resolved by compression bandage and an asymptomatic subarachnoid haemorrhage.

Both patients presented within 4.5H time frame, which may have contributed to their successful IVT and good outcomes. Patient 2 was a patient undergoing haemodialysis at the inhouse haemodialysis unit of Seberang Jaya Hospital, hence a prompt stroke activation assisted his arrival of only 15 minutes to our stroke unit upon symptoms onset. This is in keeping with various stroke guidelines and studies that have shown that IV alteplase administration within 4.5H results in more favourable outcomes.[11] A narrative study from Japan also described benefits of IVT in ESRF with AIS, although a joint decision with nephrologist may also help in making a sound decision.[12]

A slightly lower dose of IV Alteplase 0.6mg/kg were used in both cases in keeping with the Japanese Alteplase Clinical Trials 2006 which concluded that the dose of 0.6mg/kg is non inferior in terms of efficacy and safety when compared to the dose of 0.9mg/kg in previous studies done in North America and the European Union.[13] Moreover, keeping in consideration the Japanese Stroke Society's recommendation for administration of rTPA in patients receiving anticoagulants, both patients had INR of <1.7 and APTT of less than 1.5 times of baseline value (both cases had APTT <40) in order to reduce any possible risk of complications post IVT especially as both patients presented right after receiving heparinised haemodialysis.[14] Similarly, 2019 American Stroke Association also recommends IV alteplase in ESRF patients while a prolonged APTT results in higher hemorrhagic risks.[11] Both cases did not undergo mechanical thrombectomy.

In conclusion, in cases of acute ischaemic stroke in ESRF patients, careful decision making must be done, taking into consideration patient's premorbid condition, blood parameters, post stroke care and rehabilitation to increase the possibility of a favourable outcome post IVT. While there is no contraindication for the usage of rTPA in patients with GFR of <15, several studies have shown that bleeding risks is higher in this population compared to those with normal GFR. In this limited case report of two patients, we used a lower dose of Alteplase (0.6mg/kg), paired with INR<1.7, APTT <40, in ESRF individuals with good premorbid status, and outcome was favourable.

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