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Thrombolysis in Acute Ischemic Stroke after Idarucizumab for Dabigatran Etexilate Reversal in Elderly: a Case Report

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Abstract

Introduction—Dabigatran is one of the nonvitamin K antagonist oral anticoagulants. Thrombolytic treatment with intravenous recombinant tissue plasminogen activator is contraindicated in patients taking a DOAC. Idarucizumab was recently approved for dabigatran-activity reversing in severe bleeding, emergency surgery, or urgent procedures, but many attempts have been made to use idarucizumab in patients presenting with acute ischemic stroke in order to be eligible for thrombolysis.

Case—Our patient was an 89-year-old woman with severe aphasia who was treated with dabigatran for nonvalvular atrial fibrillation. She received an infusion of idarucizumab followed by thrombolytic therapy, with complete remission of symptoms after 24 hours.

Discussion—Idarucizumab is a safe option for patients with acute ischemic stroke treated with dabigatran; otherwise eligibles for thrombolysis, even in very old people like our patient.

Introduction

Dabigatran etexilate is a specific, reversible thrombin inhibitor, approved for stroke prevention in patients with nonvalvular atrial fibrillation [1] and for treatment of deep vein thrombosised pulmonary embolism [2].

Dabigatran, as well as the others nonvitamin K antagonist oral anticoagulators (NOACs), had the disadvantage of no antidote capable of rapid reversal of anticoagulant action.

In October 2015, Idarucizumab [3] was approved, a fragment of monoclonal antibody capable of reversing dabigatran activity within few minutes.

This antibody fragment demonstrated prompt and durable reversal of the anticoagulant effects of dabigatran in animal studies, and in phase I studies of young and elderly individuals, as well as in renally impaired volunteers [4,5].

Idarucizumab has currently the indication for severe bleeding and for emergency surgery or urgent procedures, but no stroke guidelines suggest its use before intravenous (i.v.) thrombolysis at the moment [6–8].

Thrombolytic treatment with recombinant tissue plasminogen activator (t-PA) is controindicated in patients taking a DOAC.

From 2015 to present, many attempts have been made to use Idarucizumab for rapid reversal of Dabigatran anticoagulation action in patients with acute ischemic stroke, in order to allow the use of i.v. t-PA [9,10].

Case

An 89-year-old woman with a history of hypertension, ischemic cardiopathy, type 2 diabetes mellitus, chronic obstructive pulmonary disease, and nonvalvular atrial fibrillation treated with dabigatran 110 mg twice daily was admitted in the emergency department because of the appearance of speech disturbance started at 12.45 am, proved by the doughter. At the stroke unit valuation, we found a severe expressive aphasia, and she scored four on the NIHSS.

A head CT scan showed no signs of bleeding or hyperacute ischemia. The laboratory tests showed an activated partial thromboplastin time of 38.80 seconds, a mild

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hyponatremia, and an eGFR of 38 ml/min (Cockcroft-Gault). No contraindications for i.v. fibrinolysis were found. She was taking antihypertensive therapy (angiotensin-receptor blocker plus thiazide diuretic), proton pump inhibitor, digoxin, and combination of long-acting beta2-agonist plus corticosteroid inhalator. She had a modified rankin score of 1.

After informed written consensus, we administered two vials of 2.5 g of idarucizumab as rapid i.v. infusion and after 5 min, at 16.45 pm, 4 hours after the symptoms onset, we started i.v. thrombolysis with t-PA (40 mg, 0.9 mg/kg), 10% in 10 min and 90% infused in 60 min.

She had a clinical improvement, with NIHSS at 2 hours of 2, and after 24 hours, she returned to her prestroke neurological baseline. Computer tomography at 24 hours showed no evidence of hemorrhage. We performed a magnetic resonange 48 hours after the beginning of symptoms, which did not find signs of acute ischemic areas. During the pressure monitoring, we found a not well-controlled arterial hypertension, confirmed by patient's relatives.

At the discharge, we decided to continue with dabigatran 110-mg BID, because of the clinical context (patient more than 80 years, weight less than 60 kg, eGRF less than 50 ml/min), and we improved antihypertensive treatment.

Discussion

NOACs do not exclude the occurrence of embolic brain infarcts [9]. While i.v. t-PA is becoming a standard of treatment of stroke, this therapy is currently contraindicated by guidelines in patients on DOACs. Thus, idarucizumab administration prior to i.v. thrombolysis in stroke may be a treatment option in patients taking dabigatran. To our knowledge [10–17], this patient is the oldest person treated with idarucizumab for rapid dabigatran reversal before the use of t-PA in a patient with acute ischemic stroke. She had an excellent clinical course, with the resolution of neurological symptom that the patient had at the admission. She had no hemorrhagic complications nor thrombotic manifestations. In this case, idarucizumab administration seems to have no procoagulant effects; in addition, no adverse reactions including hypokalemia, delirium, constipation, pyrexia, and pneumonia were developed.

Our case is a further proof of idarucizumab utility in the acute ischemic stroke context and shows that even in old age people the use of idarucizumab for dabigatran-reversal should be considered among the possible options.

Conclusion

This is the first case described of thrombolysis after idarucizumab dabigatran neutralization in a person older than 85 years; we show that dabigatran reversal by idarucizumab seems to be safe either in old age. Large studies should be performed to examine the occurrence of sICH, recurrent infarction, and thrombosis.

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Not applicable.

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