



Case Report

# Successful Intravenous Thrombolysis for Acute Ischemic Stroke of the Anterior Circulation in a Patient Taking Ticagrelor: A Case Report and Literature Review

Paternoster Lionel<sup>1\*</sup>, Emmanuelle Levecque<sup>1</sup>, Roudebush Cédric<sup>2</sup>, Jose Antonio Elozegi<sup>1</sup>, Marie Dagonnier<sup>1</sup>

<sup>1</sup>Department of Neurology, CHU Ambroise Paré, Mons, Belgium

<sup>2</sup>Faculté de Médecine ULB, Université Libre de Bruxelles (ULB), Brussels, Belgium

\*Corresponding author: Paternoster Lionel, Department of Neurology, CHU Ambroise Paré, Mons, Belgium

**Citation:** Lionel P, Levecque E, Cédric R, Elozegi JA, Dagonnier M (2024) Successful intravenous thrombolysis for acute ischemic stroke of the anterior circulation in a patient taking ticagrelor: A case report and literature review. Int J Cerebrovasc Dis Stroke 7: 172. DOI: <https://doi.org/10.29011/2688-8734.100172>

**Received Date:** 10 January, 2024; **Accepted Date:** 13 January, 2024; **Published Date:** 18 January, 2024

## Abstract

**Background:** Ticagrelor is an antiplatelet agent widely used in the treatment of coronary acute syndrome and was recently found to be of interest in secondary prevention of minor stroke and transient ischemic attack. One retrospective study considers ticagrelor as a safe option for secondary prevention after moderate or severe acute ischemic stroke. The eligibility for intravenous thrombolysis in patients pretreated with ticagrelor is controversial. Literature on the safety of intravenous thrombolysis for ischemic stroke in patients taking ticagrelor is limited to eight cases, of which two cases of symptomatic intracranial hemorrhage, one case of asymptomatic intracranial hemorrhage and one case of retropharyngeal hematoma have been reported. **Case presentation:** We report a 57-year-old patient who was hospitalized for ST-segment elevation myocardial infarction and treated by ticagrelor. Four days later, he presented an anterior circulation ischemic stroke clinically expressed by right hemiparesis with mutism. The patient was successfully treated by intravenous thrombolysis with an improvement of the National Institutes of Health Stroke Scale from 12 to 1 at 24 hours<sup>0</sup>. No complications have been observed post-treatment. **Conclusions:** This is the second reported case of successful intravenous thrombolysis for an ischemic stroke of the anterior circulation in a patient pretreated with ticagrelor. This case reinforces the urgent need for further investigations on the safety of intravenous thrombolysis in patients pretreated with ticagrelor as the number of such cases is expected to increase in the future.

**Keywords:** Ticagrelor; Intravenous thrombolysis; Acute ischemic stroke; Acute stroke management

**Abbreviations:** AIS: Acute Ischemic Stroke; CT: Computed Tomography; IVT: Intravenous Thrombolysis; MRI: Magnetic Resonance Imaging; NIHSS: National Institutes of Health Stroke Scale

## Background

Ticagrelor is a recent antiplatelet agent that reversibly inhibits the ADP P2Y<sub>12</sub> receptor [1]. It is widely used in the treatment of coronary acute syndromes [2]. The literature on intravenous thrombolysis for ischemic stroke in patients taking ticagrelor is limited to eight cases [3-7]. Two cases of symptomatic intracranial hemorrhage, one case of asymptomatic intracranial hemorrhage

and one case of retropharyngeal hematoma have been reported [3-5].

Since the SOCRATES [8] and THALES [9] trials, interest for ticagrelor in secondary prevention of minor stroke or transient ischemic attack has emerged. The use of ticagrelor following moderate or severe acute ischemic stroke is presumed to be a safe option according one retrospective study [10].

The number of patients who suffer acute ischemic strokes while taking ticagrelor is likely to increase in the future. However, the eligibility for intravenous thrombolysis remains controversial. According to international stroke guidelines, the use of intravenous thrombolysis in acute ischemic stroke treatment is recommended notwithstanding a single or dual antiplatelet therapy pretreatment [11]. However, no study has investigated the safety of intravenous thrombolysis in patients taking ticagrelor.

We present a case of intravenous thrombolysis in an acute stroke patient taking ticagrelor for an ST-segment elevation myocardial infarction. A literature review for intravenous thrombolysis in acute ischemic stroke patients pretreated with ticagrelor was conducted by searching PubMed using the keywords stroke, intravenous thrombolysis and ticagrelor.

### Case Presentation

We present a 57-year-old patient who was hospitalized for ST-segment elevation myocardial infarction and treated by ticagrelor (90mg) twice daily. Upon admission, he underwent percutaneous coronaryography showing severe tritronic atheromatosis.

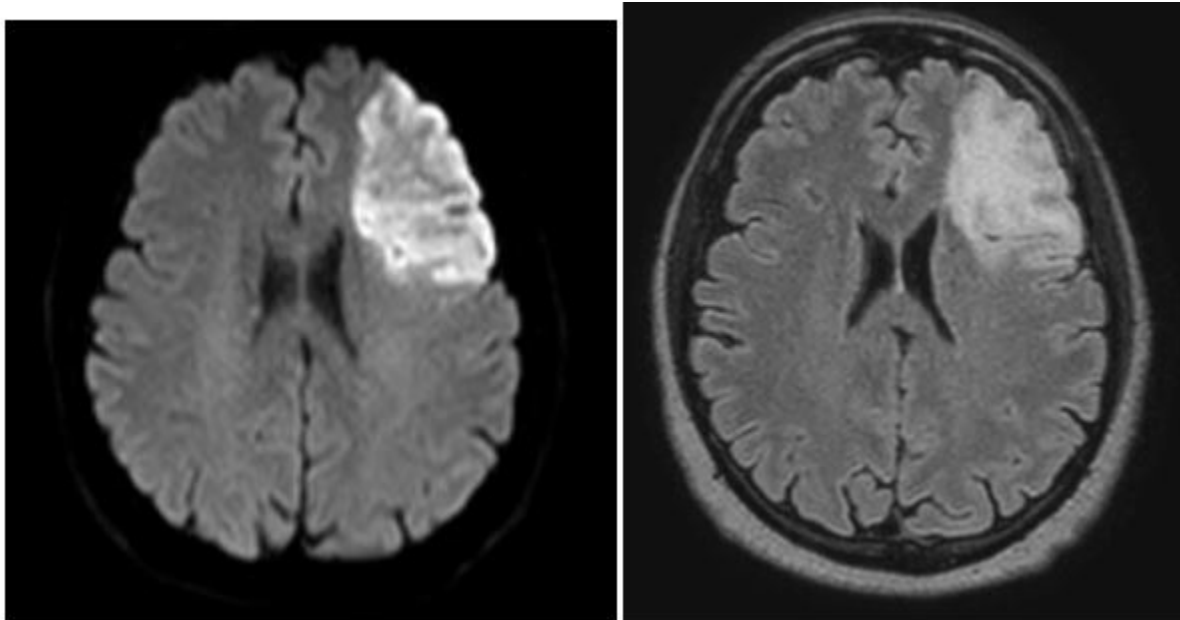
Four days later, he developed sudden right hemiparesis and mutism. His National Institutes of Health Stroke Scale (NIHSS) was 12 for right facial weakness, right hemiparesis, mutism, partial alteration of consciousness and partial gaze palsy. Brain computed tomography did not demonstrate any acute ischemic damage (Figure 1). He received 0.9 mg/kg intravenous alteplase 15 minutes after symptoms were discovered and was last seen asymptomatic 90 minutes prior to discovery. 24 hours after intravenous thrombolysis, his NIHSS score improved to 1 (mild dysarthria) and brain CT demonstrated left frontal hypodensity without hemorrhage (Figure 2). A magnetic resonance imaging six days later demonstrated left frontal infraction (Figure 3). Aspirin therapy at 80 mg once a day was started and ticagrelor was continued at 90 mg twice daily. He was eventually discharged home with mild aphasia as his only neurological deficit (NIHSS: 1).



**Figure 1:** Initial brain computed tomography.



**Figure 2:** 24-hour post intravenous thrombolysis computed tomography demonstrating a left frontal hypodensity without hemorrhage.



**Figure 3:** Magnetic resonance imaging six days later demonstrating left frontal infraction with a hyperintensity on axial diffusion (A) and axial FLAIR (B) sequences.

The patient had no residual neurological deficits at a 1-year follow up.

### Discussion and Conclusions

A literature review for intravenous thrombolysis in acute ischemic stroke patients pretreated with ticagrelor was conducted by searching PubMed using the keywords stroke, intravenous thrombolysis and ticagrelor. Only eight cases have been described to date [3-7]. The main characteristics of each patient are illustrated in Table 1. Three of them developed clinical complications, two deadly hemorrhagic transformations (Godier et al. 2015; Lo et al. 2016) and one retropharyngeal hematoma (Lo et al. 2016) while one patient presented an asymptomatic intraparenchymal hemorrhage (Wright et al. 2019). Each of those cases involved the anterior cerebral circulation. Our case is the second patient taking ticagrelor who was treated by intravenous thrombolysis for an anterior circulation ischemic stroke without complication. It is worth noting that only one case also benefited from mechanical thrombectomy (Rizzo et al. 2021). Onset to needle time is missing in three patients (Godier et al. 2015; Lo et al. 2016).

	Gender	Vascular territory	Complication	Discharge outcome	NIHSS at admission	24 hour – NIHSS	Follow-up visit NIHSS	Ticagrelor dose	Other active treatment	Thrombolysis agent	Onset to needle time	Therapy at discharge
Godier et al. 2015	Male	Middle cerebral artery	Hemorrhagic transformation	Death	Unknown	Unknown	Not applicable	90 mg BID	Aspirin	Alteplase	Unknown	Not applicable
Lo et al. 2016	Female	Middle cerebral artery	Hemorrhagic transformation	Death	2	Death	Not applicable	Unknown	Unknown	Alteplase	90 minutes	Not applicable

Lo et al. 2016	Male	Middle cerebral artery	Retropharyngeal hematoma	Inpatient rehabilitation unit	17	Unknown	Unknown	Unknown	Unknown	Alteplase	Unknown	Unknown
Wright et al. 2019	Male	Basilar artery	None	Home	10	1	0	90 mg BID	Aspirin	Tenecteplase	65 minutes	Aspirin and clopidogrel
Wright et al. 2019	Male	Middle cerebral artery	Asymptomatic intraparenchymal hemorrhage	Home	5	5	0 (at 4 months)	Unknown	Aspirin and heparin 5000 UI	Alteplase	Unknown	Aspirin and ticagrelor
Landzberg et al. 2021	Male	Basilar artery	None	Home	3	1	0 (at 3 day)	60 mg BID	Aspirin	Alteplase	110 minutes	Aspirin and ticagrelor
Landzberg et al. 2021	Male	Vertebral artery	None	Skilled nursing facility	18	Unknown	Unknown	90 mg BID	Aspirin	Alteplase	170 minutes	Not available
Rizzo, Federica et al. 2021	Male	Middle cerebral artery	None	Home	4	1	1 (at 3 months)	90 mg BID	Aspirin	Alteplase	230 minutes	Aspirin and ticagrelor
Paternoster et al. 2023	Male	Middle cerebral artery	None	Home	12	1	0 (at 1 year)	90 mg BID	Unknown	Alteplase	Unknown	Aspirin and ticagrelor

**Table 1:** Main characteristics of published cases of intravenous thrombolysis in acute ischemic stroke.

The increasing use of ticagrelor raises the question of intravenous thrombolysis eligibility in case of acute ischemic stroke. According to international stroke guidelines, intravenous thrombolysis for acute ischemic stroke treatment is recommended notwithstanding single or dual antiplatelet therapy pretreatment [12]. Conflicting data exists on the safety of intravenous thrombolysis for acute ischemic stroke in patients taking dual antiplatelet therapy [13,14]. A recent meta-analysis demonstrated that the increase in symptomatic intracranial hemorrhage and mortality initially reported does not persist after adjusting for confounding variables [15]. Pending further studies on the safety of intravenous thrombolysis in patients taking ticagrelor, such decisions must be made on a case-by-case basis.

## Declarations

### Ethics approval and consent to participate

Not applicable.

### Consent for publication

Written informed consent for publication was obtained from the patient.

### Availability of data and materials

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

## Funding

Not applicable.

## Authors' contributions

L.P. is the main writer. L.P. was in charge the patient during the hospitalization and performed the literature review. E.L. was in charge of the patient during the hospitalization and commented the article. C.R. performed the literature review and commented the article. M.D. was in charge of the patient during the hospitalization and commented the article. J.E. was in charge of the patient during the hospitalization and commented the article.

## Acknowledgements

Not applicable.

## References

1. Angiolillo DJ, Rollini F, Storey RF, Bhatt DL, James S, et al. (2017) International expert consensus on switching platelet P<sub>2</sub>Y<sub>12</sub> receptor-inhibiting therapies. *Circulation* 136: 1955–1975.
2. Valgimigli M, Bueno H, Byrne RA, Collet JP, Costa F, et al. (2018) 2017 ESC focused update on dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS: The Task Force for dual antiplatelet therapy in coronary artery disease of the European Society of Cardiology (ESC) and of the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 39: 213–260.
3. Godier A, Taylor G, Gaussem P (2015) Inefficacy of platelet transfusion to reverse ticagrelor. *N Engl J Med* 372: 196–197.
4. Lo KY, Biby S, Sethi P, Campbell BC (2016) Symptomatic intracerebral and systemic hemorrhage after stroke thrombolysis in patients taking ticagrelor. *Int J Stroke* 11: NP71-72.
5. Wright SL, Jahangiri B, Smyth DW, Fink JN, Ho R, et al. (2020) Successful intravenous thrombolysis for ischemic stroke as a complication of coronary intervention in patients with ticagrelor pretreatment. *J Clin Neurosci Off J Neurosurg Soc Australas* 71: 283–286.
6. Landzberg DR, English S, Frankel M, Navalkale D (2021) Stroke thrombolysis in patients taking ticagrelor -two successful cases and a review of the literature. *J Stroke Cerebrovasc Dis Off J Natl Stroke Assoc* 30: 105520.
7. Rizzo F, Mezzapesa DM, Chiumarulo L, Parisi M, Loizzo ND, et al. (2021) Successful intravenous thrombolysis and endovascular treatment for acute ischemic stroke in a patient pretreated with ticagrelor: a case report and literature review. *Clin Drug Investig* 41: 653–657.
8. Johnston SC, Amarenco P, Albers GW, Denison H, Easton JD, et al. (2016) Ticagrelor versus aspirin in acute stroke or transient ischemic attack. *N Engl J Med* 375: 35–43.
9. Johnston SC, Amarenco P, Denison H, Evans SR, Himmelmann A, et al. (2020) Ticagrelor and aspirin or aspirin alone in acute ischemic stroke or TIA. *N Engl J Med* 383: 207–217.
10. English SW, Landzberg DR, Bhatt NR, Frankel MR, Navalkale D (2021) Safety of ticagrelor in moderate and severe acute ischemic stroke: A single-center retrospective review. *J Stroke Cerebrovasc Dis Off J Natl Stroke Assoc* 30: 105767.
11. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, et al. (2018) 2018 Guidelines for the early management of patients with acute ischemic stroke: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 49: e46–110.
12. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, et al. (2019) Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 50: e344–418.
13. Xian Y, Federspiel JJ, Grau-Sepulveda M, Hernandez AF, Schwamm LH, et al. (2016) Risks and benefits associated with prestroke antiplatelet therapy among patients with acute ischemic stroke treated with intravenous tissue plasminogen activator. *JAMA Neurol* 73: 50–59.
14. Tsvigoulis G, Goyal N, Kerro A, Katsanos AH, Krishnan R, et al. (2018) Dual antiplatelet therapy pretreatment in IV thrombolysis for acute ischemic stroke. *Neurology* 91: e1067–1076.
15. Malhotra K, Katsanos AH, Goyal N, Ahmed N, Strbian D, et al. (2020) Safety and efficacy of dual antiplatelet pretreatment in patients with ischemic stroke treated with IV thrombolysis: A systematic review and meta-analysis. *Neurology* 94: e657–666.