



## Ticagrelor Induced Angioedema: A Case Report

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### ABSTRACT

Ticagrelor is a new direct-acting oral antiplatelet drug, which reversibly Inhibits the adenosine diphosphate receptor P2Y12. Ticagrelor is a cyclopentyl triazole pyrimidine derivative. This medication showed a better outcome without increasing the bleeding risk compared to other antiplatelet agents. The major ticagrelor clinical trials reveal the common adverse events were dyspnoea, bleeding, and ventricular pauses. Here we present a case with angioedema following the ticagrelor intake. The Patient treated with the antihistamines and steroid and importantly stoppage of the drug ticagrelor. The recovery is prompt with no other complication and at the same time, the dual antiplatelet therapy was not interrupted, It continued with clopidogrel. The next day patient was completely improved and discharged to home with aspirin and clopidogrel. About hypersensitivity reaction of ticagrelor explained to the patient.

**Keywords:** Ticagrelor, Case report, Angioedema.

### CASE PRESENTATION

**5** 6 years old male with a known case of type 2 diabetes mellitus and hypertension. He is on aspirin for primary prophylaxis, presented with complaints of chest pain on exertion NYHA class III for ten days. The physical examination was unremarkable. ECG was showing normal sinus rhythm with no ST-T changes. The initial echocardiogram showed normal left ventricular function with no regional wall motion abnormality. There was no much change in the repeated Trop-T level. He underwent stress test under modified Bruce protocol. At second stage ECG showed ST-T depressions in anterior leads along with exertion on chest pain. Since stress test showed a high probability of coronary artery disease, it was decided to go with a coronary angiogram. The patient prepared for a coronary angiogram loaded with dual antiplatelet; the patient underwent for a coronary angiogram. CAG revealed that the single vessel disease with 90% discrete stenosis in distal dominant Left circumflex artery (LCx). Since dominant left circumflex artery supplying a considerable amount of myocardium had critical stenosis and presented with acute coronary syndrome, percutaneous coronary intervention (PCI) was planned to LCx artery with the drug-eluting stent, Procedure was completed with a TIMI 3 result.<sup>1</sup>

Since the patient was diabetic and on aspirin with unstable angina with critical stenosis in a dominant LCx artery, the decision was made to change ticagrelor for clopidogrel. 180 mg Ticagrelor Loaded to Patient. After an hour of administration of ticagrelor, the patient developed facial puffiness with periorbital edema. No history of any itching or breathing difficulty. The patient was hemodynamically stable.

Hold the next dose of ticagrelor, and the patient immediately treated with antihistamines and steroids. As the patient was put DES to LCX, clopidogrel was resumed immediately. As advised by the dermatologist, antihistamines were started and continued for ten days.

The next day patient was completely improved and discharged to home with aspirin and clopidogrel. About hypersensitivity reaction of ticagrelor explained to the patient and patient parties.

### DISCUSSION

Apart from the basic antiplatelet the aspirin, the 2 nd antiplatelet which makes the dual antiplatelet therapy are ADP P2Y12 receptor blockers are clopidogrel, prasugrel, ticagrelor. Ticagrelor is a reversible non-competitive inhibitor of the P2y12 receptor. The advantages of ticagrelor over clopidogrel are the rapid onset, greater and more consistent. In PLATO trial reveals that the ticagrelor is better than the Clopidogrel because it showed a significant reduction of death rate by principal causes and it decreases the bleeding risk. Subgroup analyses suggested that elderly patients may benefit more from Ticagrelor than from clopidogrel.<sup>2</sup> Studies also showed that Ticagrelor has better platelet inhibition compared to prasugrel in patients with high platelet reactivity after clopidogrel in post PCI patients.<sup>3</sup> Ticagrelor is well-tolerated drug and better pharmacological profile than clopidogrel.<sup>4,5</sup>

Allergic reactions are frequent with antiplatelet drugs with aspirin producing 1.5% in patients with cardiovascular disease.<sup>6</sup> Hypersensitivity reactions with pruritic rashes occur in 6% of patients with clopidogrel while 1.5% requires drug discontinuation.<sup>7</sup>



There are case reports which showed an allergic reaction with Ticagrelor but the exact incidence is not known.<sup>8</sup> In patients with Ticagrelor features of drug hypersensitivity with angioedema occurred within 72 hours of exposure. The mechanism of angina oedema is mainly due to mast cell activation or bradykinin release .but there is a time delay in contrary to that of an IgE-mediated immediate hypersensitivity mechanism. The antiplatelet also exhibit the cross sensitivity irrespective of their molecular structure.<sup>9</sup>

Here we are presenting the case with allergic response to Ticagrelor in the form of angioedema which started after a time delay to the intake. The condition was treated with the antihistamines and steroid and importantly stoppage of the drug ticagrelor. The recovery is prompt with no other complication and at the same time, the dual antiplatelet therapy was not interrupted it was continued with clopidogrel.

### Learning points

This case is important because it highlights one of the relatively rare side effects of ticagrelor.the early detection and treatment required. The situation it also occurs crucial were patient would have just undergone PCI with stenting. The potent dual antiplatelet therapy is necessary to prevent early stent thrombosis, so continuing DAPT with other P2Y12 receptor antagonist also paramount importance even though the cross reaction is a possibility.

### REFERENCES

1. Wallentin L, Becker RC, Budaj A, Cannon CP, Emanuelsson H, Held C, Horrow J, Husted S, James S, Katus H, Mahaffey KW. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. *New England Journal of Medicine*. 361(11):2009 Sep 10; 1045-57.
2. K. Reddy, A. Khaliq, and R. J. Henning, "Recent advances in the diagnosis and treatment of acute myocardial infarction," *World Journal of Cardiology*, vol. 7, no. 5, pp. 243–276, 2015.
3. Alexopoulos D, Galati A, Xanthopoulou I, Mavronasiou E, Kassimis G, Theodoropoulos KC, Makris G, Damelou A, Tsigkas G, Hahalis G, Davlouros P. Ticagrelor versus prasugrel in acute coronary syndrome patients with high-on-clopidogrel platelet reactivity following percutaneous coronary intervention: a pharmacodynamic study. *J Am Coll Cardiol*. 60(3):2012 Jul 17; 193-9.
4. Anderson SD, Shah NK, Yim J, Epstein BJ. Efficacy and safety of ticagrelor: a reversible P2Y12 receptor antagonist. *Annals of Pharmacotherapy*. 44(3):2010 Mar 1; 524-37.
5. Anderson SD, Shah NK, Yim J, Epstein BJ. Efficacy and safety of ticagrelor: a reversible P2Y12 receptor antagonist. *Annals of Pharmacotherapy*. 44(3):2010 Mar 1; 524-37.
6. Woessner KM. Aspirin desensitization for cardiovascular disease. *Current opinion in allergy and clinical immunology*. 15(4):2015 Aug 1; 314-22.
7. Lokhandwala J, Best PJ, Henry Y, Berger PB. Allergic reactions to clopidogrel and cross-reactivity to other agents. *Curr Allergy Asthma Rep*. 11 (1):2011Feb; 52-7.
8. Quinn KL, Connelly KA. First report of hypersensitivity to ticagrelor. *Can J Cardiol*. 30(8):2014 Aug; 957.e3-4.
9. Chin N, Rangamuwa K, Mariasoosai R, Carnes J, Thien F. Oral antiplatelet agent hypersensitivity and cross-reactivity managed by successful desensitisation. *AsiaPac Allergy*. 5 (1):2015 Jan; 51-4.

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