

A Case of Ticagrelor Resistance

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Ethics statement: This study was conducted according to the principles of the Declaration of Helsinki. The patient provided informed written consent for the publication of this report. Ethical approval was obtained prior to submission from the Research and Ethics Committee (ID#RERC/20/DCA/51).

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ABSTRACT

Ticagrelor is a directly acting cyclopentyltriazolo-pyrimidine which does not require conversion into an active metabolite. It inhibits the P2Y₁₂ receptors on platelets reversibly. Unlike clopidogrel and prasugrel, resistance to ticagrelor is rarely reported. Various mechanisms have been proposed for this resistance. The case of a 62-year-old man with diabetes who had undergone index percutaneous coronary intervention (PCI) 22 days previously is described. The patient presented to us with stent thrombosis. His primary PCI was successfully carried out with a drug-eluting stent. He showed resistance to ticagrelor on thromboelastography platelet mapping. He responded well to prasugrel (another P2Y₁₂ inhibitor) in combination with aspirin.

LEARNING POINTS

- Ticagrelor is a pro-drug and directly inhibits P2Y₁₂ receptors.
- This makes ticagrelor less susceptible to drug–drug interactions or pharmacogenetic influences.
- Thromboelastography platelet mapping measures the physical properties of clot formation and can reveals platelet resistance to various P2Y₁₂ inhibitors, including ticagrelor.

KEYWORDS

Ticagrelor, coronary artery disease, stent thrombosis, dual anti-platelet therapy

INTRODUCTION

Platelet inhibition is pivotal to reduce cardiovascular events in patients with coronary artery disease. Aspirin is the cornerstone treatment, but in this era of dual anti-platelet therapy (DAPT), the addition of a P2Y₁₂ inhibitor is recommended in acute coronary syndromes^[1]. Large scale trials have seen a shift from clopidogrel to prasugrel for P2Y₁₂ inhibition in patients with ST-elevation myocardial infarction (STEMI) and to ticagrelor in non-ST-elevation MI (NSTEMI)^[2]. However, despite DAPT, some patients experience recurrent cardiovascular events. Apart from non-compliance, a lack of response to anti-platelet therapy has been documented in many studies. A case of a sub-acute stent thrombosis (ST) in a patient after drug-eluting stent (DES) implantation and demonstrated resistance to ticagrelor on platelet mapping is described.

CASE DESCRIPTION

A 62-year-old man with type 2 diabetes and previous inferior STEMI, was treated with DES in the right coronary artery. He presented with ST 22 days after his index primary percutaneous coronary intervention while on aspirin 75 mg once daily and ticagrelor 90 mg twice daily. He was successfully treated with plain old balloon angioplasty with a drug-eluting balloon (SeQuent Neo, B. Braun, Melsungen, Germany). The mechanism of ST was not known, so intravascular abnormality was assessed via optical coherence tomography. The stent was well-approximated with no edge dissection or strut mal-apposition. History taking did not reveal any non-compliance with DAPT. The patient was haemodynamically stable after the procedure and his baseline haematology and biochemistry findings were within normal limits. After consultation with a haematologist, a platelet mapping study was advised with thromboelastography platelet mapping (TEG) (Haemoscope Corporation, Niles, IL, USA), which showed resistance to ticagrelor with a maximum amplitude (MA) of 66 mm with ADP. After a 1-week hospital stay, the patient was discharged on aspirin 150 mg/day and prasugrel 10 mg/day.

DISCUSSION

A number of studies have explained the reasons for platelet reactivity to clopidogrel, and include various genetic polymorphisms, hyporeactivity and drug interactions^[3]. However, little information is available on the causes of ticagrelor resistance. Ticagrelor is a pro-drug and directly inhibits P2Y₁₂ receptors. This makes it less susceptible to drug–drug interactions or pharmacogenetic influences. A large-scale trial implicated a reduced effect of ticagrelor when given in combination with morphine, but the results were not statistically significant^[4]. Similarly, smoking is also proposed as a substrate for increased platelet reactivity. The Platelet Inhibition and Patient Outcomes (PLATO) trial demonstrated the rate of ST with ticagrelor was 2.94%^[5]. It was seen that ticagrelor decreased sub-acute (24 h to 30 days) and late (>30 days) ST. However, the ST was not sub-acute in our case. We used TEG to look for P2Y₁₂ resistance. It measures the physical properties of clot formation. The MA demonstrates the clot strength which can test the effectiveness of P2Y₁₂ inhibitors and aspirin by platelet activation with ADP. A study found that an MA of > 47 mm was a strong predictor of platelet resistance and adverse events after coronary stenting^[6].

CONCLUSION

The prevalence of platelet resistance is greater with clopidogrel therapy as compared with ticagrelor or prasugrel. The differences are likely due to a different array of pharmacokinetics where ticagrelor produces effective platelet inhibition compared with clopidogrel. However, drug resistance is present in rare instances and TEG can play a pivotal role in detecting hypo-responsiveness. Changing to a more potent P2Y₁₂ inhibitor is the treatment of choice for ticagrelor resistance.

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