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CASE REPORT

Unmasking of sinoatrial disease with ticagrelor post percutaneous coronary intervention

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Introduction

Antiplatelet agents are core treatments for patients with acute coronary syndromes. In recent years, use of agents such as ticagrelor and prasugrel has been established in clinical practice. Ticagrelor is a reversible P2Y12 receptor antagonist which acts on the platelet surface. Common side effects include bruising, bleeding and, more specific to ticagrelor, dyspnoea. A lesser known side effect is its ability to alter metabolic pathways of endogenous adenosine resulting in conduction abnormalities; hence caution is needed in patients with high grade atrioventricular conduction disease, evidence of sick sinus syndrome or a prior history of unexplained syncope. Specific questioning about contraindications to such therapies is often overlooked in the history taking.

This article presents the case of a 54-year-old woman who was diagnosed with a non-ST elevation myocardial infarction. Following the loading dose of ticagrelor she developed asystole and compromising bradycardia, necessitating emergency transvenous pacing and implantation of a permanent pacing system.

Case report

A 54-year-old woman with diabetes mellitus and an extensive smoking history was admitted to the coronary care unit with a non-ST elevation myocardial infarction (Figure 1). Her peak troponin was measured at 557 ng/litre (normal range <40 ng/litre). Coronary angiography undertaken the next day documented a significant lesion within the left circumflex artery and she received intravascular ultrasound-guided percutaneous coronary intervention. The procedure was uneventful and she was loaded with ticagrelor 180 mg peri-procedurally.

Approximately 2 hours post-loading of ticagrelor, the patient was found unresponsive with no cardiac output. She received a single cycle of cardiopulmonary resuscitation and gained spontaneous return of circulation without the use of DC cardioversion or emergency drugs.

Post arrest she was alert, self-ventilating and her observations were blood pressure 130/80 mmHg, pulse 70 bpm, and oxygen saturations 95% on room air. Arterial blood gas showed a normal acid–base status including glucose and electrolytes. The 12-lead electrocardiogram did not show evolving changes from admission and specifically no conduction abnormalities. An urgent echocardiogram showed preserved left ventricular function without a pericardial effusion. Telemetry documented a junctional rhythm which degenerated to asystole (Figure 2).

The initial episode was managed conservatively, but following further significant episodes of bradycardia and haemodynamic compromise the patient underwent an emergency externalised generator via a right internal jugular approach. This provided temporary backup VVI pacing, set at 40 beats per minute.

Serial interrogation of the externalised generator over the next 48 hours confirmed no ventricular pacing with normal sinus rhythm. It was decided to remove the external generator and perform continuous telemetry; this showed several nocturnal pauses with the longest recorded pause of 8 seconds.

Clinical history was reviewed and the patient volunteered a prior history of presyncopal and syncopal episodes that had not fully been investigated. The addition of ticagrelor was deemed to be the unmasking factor for acute deterioration. She was reloaded on prasugrel on the basis of European Society of Cardiology guidelines (Valgimigli et al, 2018).

After discussions with the patient, she was formally put forward for a permanent dual chamber pacemaker. This was implanted without complication and she was discharged well without further sequelae.

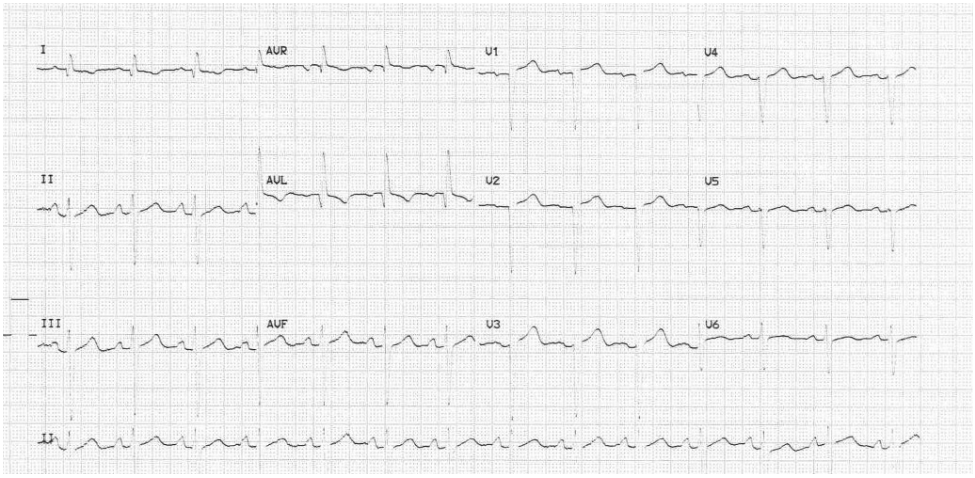

Figure 1. Electrocardiogram on admission to coronary care.

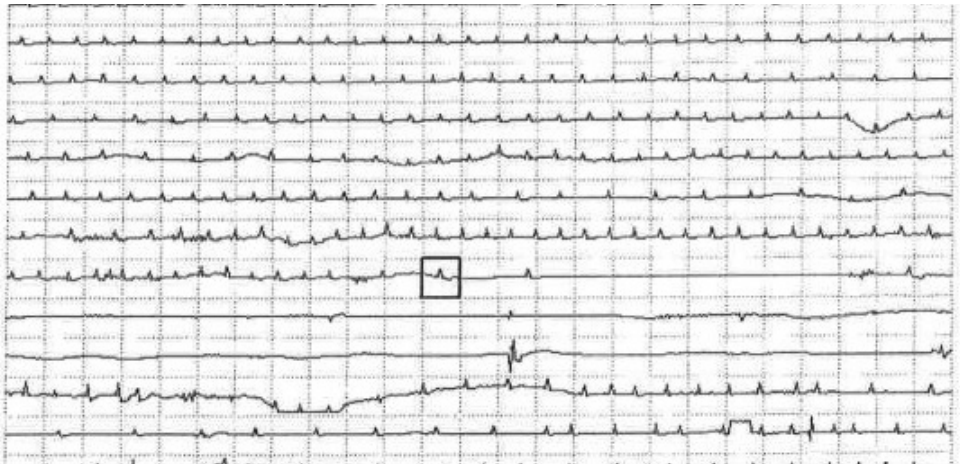

Figure 2. Coronary care unit telemetry showing a junctional rhythm deteriorating into asystole.

Discussion

As a result of molecular similarity, ticagrelor-mediated inhibition of the sodium independent equilibrative nucleoside transporter (ENT-1) has several systemic effects: increased concentration of circulating adenosine, increased coronary blood flow and greater ability to inhibit the sinus node as demonstrated in animal and healthy human subjects (Dobesh and Oestriech, 2014). Unique biochemical changes in the acute ischaemic phase leads to increased production of adenosine in local tissues during this phase and results in pauses frequently noted in the early commencement of ticagrelor therapy.

In a subgroup analysis of the Plato study an increasing trend toward bradycardia and syncope was noted in the ticagrelor group compared with those taking clopidogrel. Although this was not significant, there was a higher incidence of heart block and pacemaker insertion in patients treated with ticagrelor. More statistically significant results were seen in the rates of ventricular pauses at 3 seconds or more in the first week (Wallentin et al, 2009).

In the OFFSET/ONSET trial, Gurbel et al (2009) reported faster platelet inhibition at 30 minutes and near maximal platelet inhibition at 2 hours post ticagrelor loading. These data may explain the quick onset and persisting effects of ticagrelor in this patient who, although she had a normal documented electrocardiogram, likely had underlying sinoatrial disease.

Low et al (2019) present a summary of published case reports in which individuals shared a common theme with this case presentation of having undergone percutaneous coronary intervention, subsequently loaded on ticagrelor, then developed a bradyarrhythmia with an underlying conduction block. However, this case distinctly demonstrates the very acute and profound effects of ticagrelor requiring cardiopulmonary resuscitation and permanent pacing.

Learning points

- Ticagrelor must be used with caution in those individuals with prior syncope which has not been fully investigated.
- It is important to appreciate the natural history of acute biochemical changes that occur during the acute phase of ischaemia, with increased levels of endogenous adenosine.
- Cardiac monitoring is important in high risk groups, especially as increasing evidence suggests a trend towards ventricular pauses with ticagrelor.

The current European Society of Cardiology guidelines recommend ticagrelor or prasugrel as a class 1a recommendation post percutaneous coronary intervention with drug-eluting stent, bare-metal stent or drug-coated balloon. With this recommendation unlikely to change in the near future, this case report aims to inform health professionals of the biochemical changes occurring during a myocardial infarct and how a lack of appreciation can exacerbate underlying conduction abnormalities with well-intended treatments.

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