# Cinacalcet-associated torsades de pointes in a haemodialysis patient: a case report

Shakir Aiman bin Sema Onsha, Fahimatul Imtiaz binti Mohd Rahiman, Marilyn Aday, Curtis Walker, Ankur Gupta

Cinacalcet is a calcimimetic agent used primarily to manage secondary and tertiary hyperparathyroidism in patients with chronic kidney disease (CKD) undergoing dialysis.[1,2] We herein report the case of a 64-year-old male undergoing haemodialysis (HD) who developed life-threatening torsades de pointes (TdP) likely induced by cinacalcet.

## Case report

A 64-year-old male with stage 5 CKD on intermittent HD, atrial fibrillation, hypertension and type 2 diabetes mellitus experienced sudden central chest pain during dialysis, followed by unresponsiveness. He had no history of ischaemic heart disease and his baseline electrocardiogram (ECG) few months prior was normal (Figure 1). There was no recent alteration in dialysate concentration (3.0mmol/l of potassium and 1.25mmol/l of calcium). Haemodynamics are shown in Table 1. Telemetry at the time of event showed ventricular tachycardia (VT), which prompted cardiopulmonary resuscitation (CPR), calcium gluconate administration and three defibrillation shocks, successfully achieving return of spontaneous circulation (ROSC). Shortly after, he developed TdP (Figure 2a), requiring another round of CPR and defibrillation, which achieved ROSC. Laboratory investigations showed normal levels of calcium, magnesium, sodium, potassium, bicarbonate and phosphate (Table 2). ECG showed prolonged corrected "ventricular depolarisation and repolarisation interval" (QT; corrected QT interval [QTc]) Bazett interval ranging from 545 to 587 milliseconds (Figure 2b). Echocardiography demonstrated normal systolic function with mild calcification of the aortic valve. His medications included oral cinacalcet 30mg daily (initiated 10 days prior), bumetanide, felodipine, doxazosin, clonidine, erythropoietin and calcitriol. He denied intake of any herbal or alternative medications. Given the suspected drug-induced QT prolongation, cinacalcet was discontinued. Serial follow-up ECG within 9 months showed QTc reduction to 420–461 milliseconds (Figure 3).

## Discussion

Our case underscores the potential for cinacalcet, even in the absence of dyselectrolytaemia, to precipitate life-threatening arrhythmias such as TdP. On the Naranjo algorithm, cinacalcet is the "probable" aetiology for this reaction.[3] The QT interval represents the duration of ventricular depolarisation and repolarisation, and its prolongation is a well-recognised risk factor for TdP, particularly in patients with pre-existing metabolic imbalances and CKD. Furthermore, the QT interval and QT dispersion in HD patients are higher than in the general population.[4] Cinacalcet has been shown to potentially prolong QT intervals in the HD population.[5,6]

Historically, the first case of cinacalcet-induced TdP was reported in 2015, where hypocalcaemia was a contributing factor.[7] However, our case is significant as it represents the first documented instance of cinacalcet-induced TdP in Australasia without hypocalcemia. Cinacalcet lowers parathyroid hormone secretion and subsequently reduces serum calcium levels. Evidence has implicated that early afterdepolarisation (EAD) and QT-interval–prolonging drugs are those associated with re-entrant arrhythmias like TdP.[8] While hypocalcaemia is known to prolong action potential duration and increase the risk of EAD, our patient did not present with hypocalcaemia, suggesting that cinacalcet may contribute to QT prolongation through calcium-independent mechanisms.

Interferences with potassium channels, such as the rapid delayed rectifier potassium (IKr) channel responsible for the repolarisation phase, is probable, thus prolonging the QT interval

regardless of calcium levels.[8] A pattern of short-cycle QT interval followed by a long one, followed by a short one, which also occurs in our patient, is typical for drug-associated TdP. Short-long-short sequences create a pause-dependent setup for TdP by facilitating the generation of EADs during the extended beat, followed by an unstable repolarisation phase, which can heighten TdP susceptibility.[8] Alterations in IKr function may contribute to the development of TdP, especially when long-short or short-long-short sequences are present. This highlights how QT prolongation—through IKr suppression—interacts with specific ECG patterns to create a high-risk arrhythmogenic environment.

In addition, a study showed that cinacalcet, particularly in higher doses, may cause dose-related calcium-independent direct effects on cardiac electrophysiology.[5] However, our patient in this case was prescribed the lowest recommended dose of cinacalcet.

Emerging alternatives to cinacalcet, such as evocalcet, may have a more favorable safety profile concerning QT prolongation when compared with cinacalcet. Cinacalcet is a potent CYP2D6 inhibitor, which could cause serious drug interactions.[9] Evocalcet has reduced non-calcium receptor off-target effects and fewer issues of CYP-related interactions.[10] This could represent a vital development for patients with secondary hyperparathyroidism undergoing HD, as a safer calcimimetic could mitigate the risk of life-threatening cardiac events while effectively managing hyperparathyroidism.

## Conclusion

This case emphasises the importance of recognising both calcium-dependent and independent mechanisms of QT prolongation in patients treated with cinacalcet. The normalisation of the QT interval following drug discontinuation highlights the direct role of cinacalcet in inducing arrhythmias, even in the absence of hypocalcemia. Clinicians should be aware of QT prolongation in HD patients treated with cinacalcet, particularly those with underlying cardiac disease or electrolyte imbalances. Regular monitoring of serum electrolytes including mineral balance and ECG (both prior to cinacalcet initiation and follow-up) in a dialysis clinic is advisable to prevent potentially fatal outcomes.

**Figure 1:** Electrocardiogram prior to cinacalcet initiation showing QTc of 402–447msec and heart rate 75/minute.

**Figure 2a:** Torsades de pointes (TdP) on day of hospitalisation in telemetry strip, demonstrating short-long-short cycle followed by TdP.

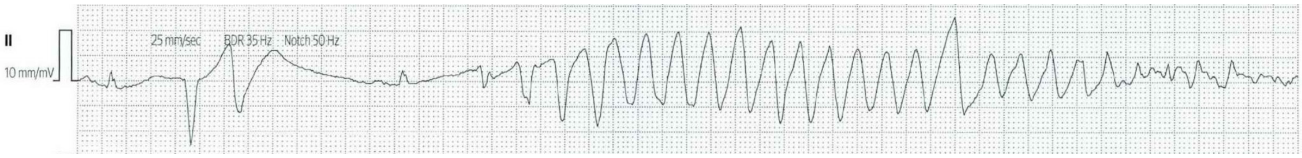


**Figure 2b:** Electrocardiogram on the same day after resuscitation showing QTc of 545–587ms.

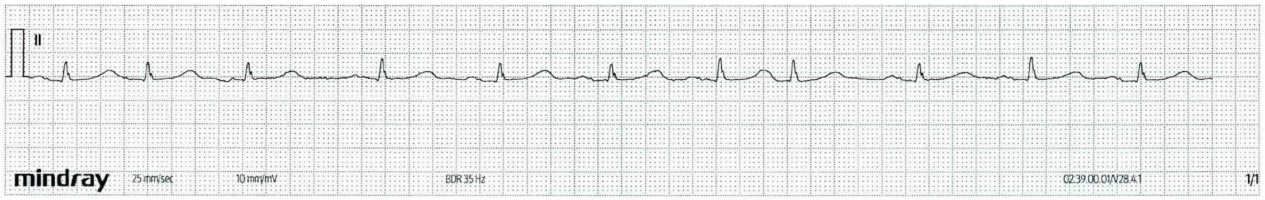

**Figure 3:** QTc (420–461ms) in a follow-up electrocardiogram 9 months after the event.

**Table 1:** Haemodynamic parameters.

| | Baseline | Pre-event | Post-event |
|---|---|---|---|
| Blood pressure (mmHg) | 191/67 | 171/94 | 187/72 |
| Heart rate (beats per minute) | 70 | 89 | 60 |

**Table 2:** Biochemical and haematological laboratory investigations.

| | Prior to cinacalcet | Pre-event | Post-event |
|---|---|---|---|
| White cell count (x10'9/L) (4.0–10) | 5.3 | 6.1 | 13.4 |
| Haemoglobin (g/L) (125–170) | 71 | 91 | 98 |
| Platelet (x10'9/L) (150–400) | 117 | 113 | 128 |
| Sodium (mmol/L) (135–145) | 134 | 141 | 138 |
| Potassium (mmol/L) (3.5–5.2) | 3.7 | 4.4 | 3.4 |
| Bicarbonate (mmol/L) (21–27) | 27 | 23 | 21 |
| Ionised calcium (mmol/L) (1.15–1.30) | 1.12 | 1.15 | 1.17 |
| Corrected calcium (mmol/L) (2.10–2.55) | 2.46 | 2.41 | 2.41 |
| Magnesium (mmol/L) (0.7–1.10) | 0.68 | 0.69 | 0.64 |
| Phosphate (mmol/L) (0.75–1.5) | 1.99 | 0.76 | 0.76 |
| Troponin T (ng/L) (0–13) | N/A | 185 | 178 |
| PTH (pmol/L) (1.8–7.9) | 116 | N/A | N/A |

**COMPETING INTERESTS**
Nil.

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