Near-fatal cardiac arrhythmia during intravenous calcium administration for symptomatic neonatal hypocalcemia: A case report

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ABSTRACT

A seven-day-old male neonate presented with symptomatic hypocalcemia in the form of generalized seizure activity for three minutes. He arrived at the pediatric emergency department in a postictal state. His clinical examination was unremarkable, but his initial laboratory evaluation revealed marked hypocalcemia and hypomagnesemia. The patient received intravenous boluses of calcium gluconate for correction. The patient had bradycardia during the first calcium gluconate infusion, and on the second infusion, he developed frequent premature ventricular contractions, which progressed into polymorphic ventricular tachycardia. Arrhythmia reverted to sinus rhythm after discontinuation of the calcium gluconate infusion without the need for chemical/electrical cardioversion. Subsequently, two extra doses of intravenous calcium gluconate for persistent hypocalcemia were administered safely. The patient was discharged home successfully in a good general condition after stabilization. The emergence of bradycardia during calcium gluconate infusion should be considered a red flag since it can trigger serious cardiac arrhythmia, especially in the presence of electrolyte abnormalities such as hypocalcemia and hypomagnesemia. We report this case to stress the need for continuous cardiac monitoring of children on calcium gluconate infusion even if proper dose, dilution, and rate of infusion are used, as serious cardiac arrhythmia can be unpredictable and may develop at any time.

Keywords: Intravenous calcium, ventricular tachycardia, hypocalcemia, neonate
INTRODUCTION

Hypocalcemia is not an uncommon disorder in the neonatal period, and can be a life-threatening emergency. Treatment of symptomatic hypocalcemia using intravenous calcium infusion is a common practice. Intravenous calcium gluconate administration, especially if given rapidly, may be associated with cardiovascular adverse effects like bradycardia, hypotension, arrhythmia, syncope, and cardiac arrest.

We report a case with polymorphic ventricular tachycardia (VT) that developed during the second dose of intravenous calcium gluconate administration for the treatment of symptomatic neonatal hypocalcemia that reverted after calcium gluconate infusion discontinuation.

CASE PRESENTATION

A previously healthy seven-day-old boy presented to the emergency department (ED) with a history of generalized tonic-clonic convulsions lasting for three minutes, which aborted spontaneously prior to arrival. He was born at 36 weeks of gestation with a birth weight of 2.7 kg to a healthy 30-year-old mother through a normal spontaneous vaginal delivery. On arrival, the patient was awake, afebrile, hemodynamically stable, and feeding well. Physical examination of the heart and lungs did not reveal any abnormalities. He had a normal neurological examination and his musculoskeletal assessment was within normal limits.

His laboratory evaluation demonstrated severe hypocalcemia and hypomagnesaemia (Table 1). The chest X-ray was reported to be normal.

A bolus of 200 mg/kg of calcium gluconate 10% diluted 1:10 to a concentration of 10 mg/mL with 0.9% saline was administered through a peripheral intravenous line over a 30-minute period, with cardiorespiratory monitoring.

Shortly after starting infusion of the first dose, the patient developed two brief episodes of bradycardia, 80 beats per minute. The calcium gluconate infusion rate slowed down over 60 minutes and then the heart rate rose up to >100 beats per minute. A 12-lead EKG after completing the first calcium infusion showed normal sinus rhythm with mild bradycardia of 90 beats per minute (Figure 1).

Six hours after the first dose, a second bolus of 200 mg/kg of calcium gluconate 10% was diluted 1:10 to a concentration of 10 mg/mL with 0.9% saline and given over one hour. Ten minutes after starting the infusion, the patient developed frequent premature ventricular contractions and a few minutes later, it progressed into polymorphic VT (Figure 2A and B). The patient continued to be hemodynamically stable throughout, with palpable pulses, a heart rate of 240/min, blood pressure of 86/60 mm Hg, and oxygen saturation of 99% on room air. The calcium gluconate infusion was stopped and two minutes later, VT terminated on its own and reverted to sinus rhythm (Figure 3).

Hypomagnesemia was treated with 75 mg/kg of elemental magnesium sulfate 50%, administered intravenously over 30 minutes and repeated every eight hours for a total of three doses.

Twelve hours after the first calcium gluconate infusion, serum calcium was still low (ionized calcium 0.75 mmol/L), and the patient was still having brief episodes of tonic-clonic convulsions that required two more doses (200 mg/kg/dose) of intravenous calcium gluconate diluted 1:10 to a concentration of 10 mg/mL with 0.9% saline, which were administered safely. Both doses were given over a one-hour period.

Table 1. Summary of the initial laboratory work-up for the patient on presentation to the ED.

<table>
<thead>
<tr>
<th>Laboratory findings</th>
<th>Results</th>
<th>Normal values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum total calcium (corrected) (mmol/L)</td>
<td>1.18</td>
<td>2.12–2.64</td>
</tr>
<tr>
<td>Serum ionized calcium (mmol/L)</td>
<td>0.62</td>
<td>1.0–1.5</td>
</tr>
<tr>
<td>Serum magnesium (mmol/L)</td>
<td>0.58</td>
<td>0.65–1.05</td>
</tr>
<tr>
<td>Serum phosphorous (mmol/L)</td>
<td>2.6</td>
<td>1.25–2.6</td>
</tr>
<tr>
<td>Serum alkaline phosphatase (U/L)</td>
<td>161</td>
<td>75–316</td>
</tr>
<tr>
<td>Blood sugar (mmol/L)</td>
<td>4</td>
<td>3.3–5.6</td>
</tr>
<tr>
<td>Blood gases (venous): pH</td>
<td>7.21</td>
<td>7.35–7.45</td>
</tr>
<tr>
<td>pCO2 mm Hg</td>
<td>52.4</td>
<td>46</td>
</tr>
<tr>
<td>Base excess (mmol/L)</td>
<td>−7.0</td>
<td>−15–3</td>
</tr>
<tr>
<td>Serum sodium (mmol/L)</td>
<td>143</td>
<td>135–145</td>
</tr>
<tr>
<td>Serum potassium (mmol/L)</td>
<td>5.7</td>
<td>3.7–5.9</td>
</tr>
</tbody>
</table>
Figure 1. Twelve-lead EKG of the patient after the first dose of intravenous calcium infusion showing normal sinus rhythm with bradycardia relative to age (heart rate 90/min). The QTc intervals are within normal limits for the age (QTc = 406 milliseconds).

Figure 2. (A) and (B) EKG rhythm strips of the patient showing occurrence of polymorphic ventricular tachycardia during the infusion of the second intravenous calcium bolus.

Figure 3. Twelve-lead EKG of the patient showing termination of VT to sinus rhythm shortly after discontinuation of calcium infusion.
Assessment of the serum 25-hydroxyvitamin D status of the baby and mother showed severe deficiency of 5 ng/mL and 13 ng/mL (30–80 ng/mL), respectively. Parathyroid hormone serum level (PTH) assay was similar in both mother and baby at 38 pg/mL (15–65 pg/mL). The baby's thyroid function tests were normal.

Normalization and stabilization of serum calcium and magnesium were achieved within 24 hours. On the second day, the baby was switched to oral calcium 50 mg/kg/day and oral 1α-hydroxyvitamin D₃ (alfacalcidol), and the mother was treated with oral vitamin D₂ (ergocalciferol). After four days of observation, the patient was discharged from the hospital in good general condition. The patient was followed up in our tertiary care outpatient clinic for six months and was doing well.

**DISCUSSION**

The frequency of bradycardia and cardiovascular adverse effects of intravenous calcium gluconate administration is reported to be <1:1000.5 Calcium is an ion that regulates the contraction of cardiomyocytes. The entry of extracellular calcium ions triggers the release of further calcium from the sarcoplasmic reticulum (calcium-induced calcium release) into the cytoplasm. Excess intracellular calcium induces delays in the after-depolarization, which may precipitate cardiac contractile dysfunction or arrhythmias.6

The initial EKG showed a QTc interval of 406 milliseconds (normal range 370–440 milliseconds), with the absence of fingerprints for cardiac channelopathies; thus, this was less likely to be the cause of arrhythmia. Echocardiography did not show any underlying structural heart disease which could explain our patient’s arrhythmia.

As per the manufacturer’s recommendation, the calcium infusion should be administered at a rate not exceeding 200 mg/kg/min, with a maximum concentration of 50 mg/ml.7 In newborn infants, the recommended dose of intravenous calcium is 200 mg/kg and may be repeated three or four times as necessary, and the infusion duration should be longer than 10 minutes,8 which was followed in our case. Although the recommendations for proper dosing, concentration, and rate of intravenous calcium infusion were followed,7,8 the patient developed bradycardia followed by runs of ventricular tachycardia. The rhythm strips demonstrated a polymorphic VT, suggestive of possible torsade de points. With the patient’s hypomagnesemia, this may have been exacerbated by competitive inhibition from the infusion of another divalent cation (calcium). We cannot eliminate the impact of hypomagnesemia and hypocalcemia in the development of arrhythmia here,9,10 especially with the absence of calcium and magnesium levels before the occurrence of arrhythmia, which makes it difficult to prove the role of both of these on the patient’s arrhythmia. The occurrence of arrhythmia during calcium gluconate infusion and its resolution on stopping is likely to have made calcium gluconate infusion a major contributor to developing cardiac arrhythmia.

The development of cardiac arrhythmia related to calcium infusion may be unpredictable. The patient was healthy otherwise without the need for other medications. Decreasing the rate of infusion appeared to resolve the dysrhythmia. Since calcium infusion interacts with many other medications, which can lead to serious side effects,11,12 careful assessment of the patient’s medical history including drug history is needed before intravenous calcium administration. Hypocalcemic seizure in our patient was likely due to vitamin D deficiency secondary to maternal hypovitaminosis D. The baby was breastfed and supplemented with formula. Vitamin D deficiency was the attributed cause of symptomatic neonatal hypocalcemia in a previous retrospective study.2

**CONCLUSION**

The occurrence of bradycardia during intravenous calcium correction is a warning sign that warrants close monitoring for the development of unpredictable life-threatening cardiac arrhythmia, especially in the presence of electrolyte disturbance.

**Abbreviations**

VT – ventricular tachycardia, ED – emergency department, EKG – electrocardiogram, PTH – parathyroid hormone

**Conflicts of interest**

The authors had no conflict of interest.
Financial disclosure
The authors have no financial relationships relevant to this article to disclose.

Authors' contributions
The authors contributed to the conception and design of the study, critically revised the content, and gave final approval to the manuscript.

REFERENCES