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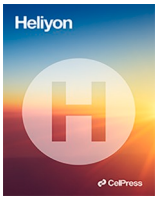

Case report

Rare electrocardiographic findings in a young woman with acute barium poisoning: A case report

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ABSTRACT

Background: Barium, as a heavy divalent alkaline earth metal, can be found in various products such as rodenticides, insecticides, depilatories, and fireworks. Barium can be highly toxic upon both acute and chronic exposure. The toxicity of barium compounds is dependent on their solubility. Both suicidal and accidental exposures to soluble barium can cause toxicity.

Case summary: We report a case characterized by two different wide QRS complex tachycardia in a patient with acute barium poisoning, one due to barium-induced ventricular tachycardia (VT) under hypokalemia and, subsequently, sino-ventricular conduction with intraventricular conduction delay due to hyperkalemia after aggressive potassium supplementation. The latter may be misdiagnosed as VT for the history of acute barium poisoning and the absence of peaked T wave in hyperkalemia. Of note, another hemodynamically unstable VT and profound hypokalemia occurred during the potassium-lowering therapy, which, in addition to barium poisoning, may also be due to the iatrogenic hypokalemia. We also observed the prominent T-U waves at serum potassium of 4.6 mM 12 hours after admission, which may indicate that barium had not been completely cleared from the plasma at that moment. There are some parallels to the Andersen-Tawil syndrome with prominent T-U waves and risk of ventricular tachycardias. To our knowledge, this is the first case report of conversion from hypokalemia to hyperkalemia, and in a short moment, from hyperkalemia to hypokalemia, in acute barium poisoning.

Conclusion: In addition to profound hypokalemia secondary to acute barium poisoning, hyperkalemia may also occur after aggressive potassium supplementation. A more careful rather than too aggressive potassium supplementation may be suitable in these cases of hypokalemia due to an intracellular shift of potassium. And a iatrogenic hypokalemia risk in the treatment of rebound hyperkalemia in barium poisoning must be considered.

1. Introduction

Barium, as a divalent alkaline earth metal, can block the potassium inward rectifier channel and inhibit potassium efflux in all muscle types [1]. Acute barium poisoning cases commonly result from incidental or suicidal soluble barium ingestion [1,2].

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Hypokalemia resulting from an intracellular shift of potassium and the direct barium's effect on the potassium channels explain the cardiac arrhythmias and muscle weakness that commonly occur in barium poisoning [1,3]. Here, we describe a case of acute barium poisoning characterized by two different wide QRS complex tachycardia, one due to barium-induced ventricular tachycardia (VT), and the other may be secondary to an entirely different mechanism.

2. Case report

A 21-year-old woman presented to the emergency department (ED) with nausea, vomiting, general paralysis, hypotension, and unconsciousness. Her parents reported that the patient ingested about 10 grams of barium chloride orally (bought from the Internet) 3.5 hours before ED presentation. The patient had a history of anxiety and was currently taking mirtazapine, oxazepam, and dexzopiclone. In the ED, her blood pressure was 51/23 mmHg, and heart rate was 118 beats per minute (bpm). Laboratory tests revealed profound hypokalemia (1.1 mM [millimole/L] potassium concentration; reference range, 3.5–5.5 mM), elevated levels of alanine aminotransferase (ALT) (2136 units per liter [U/L], reference range, 7–40 U/L) and aspartate aminotransferase (AST) (3049 U/L, reference range, 13–35 U/L). An arterial blood gas obtained on room air revealed severe acidosis (pH, 7.20) and PaO2 65.3 mmHg. An

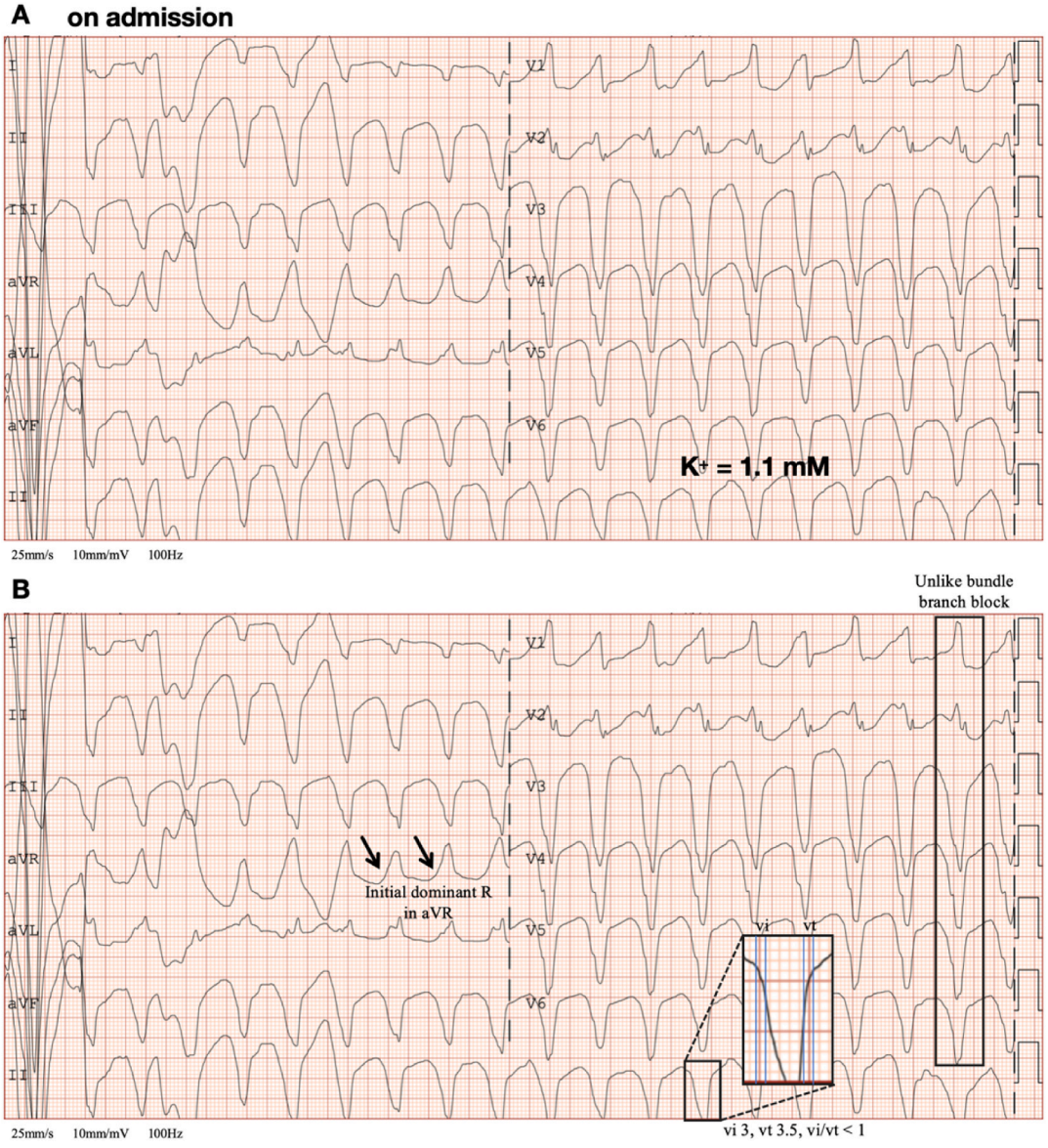

Fig. 1. A. A twelve-lead electrocardiogram (ECG) obtained on admission showed a WCT at 122 bpm at 1.1 mM potassium concentration. Fig. 1B. Annotated ECG of Fig. 1A revealed no AV dissociation, an initial dominant R wave in aVR, a QRS morphology unlike bundle branch block, and vi/vt less than 1, which, according to the Vereckei's algorithm, strongly suggested the diagnosis of VT.

electrocardiogram (ECG) obtained on admission showed a wide QRS complex tachycardia (WCT) (Fig. 1). The patient was intubated and admitted to the emergency intensive care unit immediately. The patient had recurrent episodes of WCT, which did not improve after repeated electrical cardioversion. Gastric lavage, sodium thiosulfate, rehydration, potassium supplementation (about 25 mmol per hour, routes of administration: oral, intervenous injection and intervenous drop infusion), and continuous venovenous hemodialysis-filtration were initiated promptly, combined with amiodarone, norepinephrine. The patient's blood pressure recovered gradually. A repeat ECG obtained 7 hours after admission revealed another different WCT (Fig. 2). The serum barium concentration was over 100 micrograms/L (μg/L) (over 13.73 μmol/L).

The ECG in Fig. 1 revealed a monomorphic WCT at 122 bpm, a QRS duration of 220 ms, 1) no atrioventricular (AV) dissociation observed, 2) an initial dominant R wave in aVR, 3) a QRS morphology unlike bundle branch block, and 4) the ratio between the initial and terminal 40 ms of ventricular activation velocity (vi/vt) less than 1. According to the Vereckei algorithm (an algorithm designed for distinguishing between SVT and VT in ECG) [4], there was no doubt that the patient presented with a sustained VT. The ECG in Fig. 2 obtained after recovery of hemodynamics revealed another different WCT at 118 bpm. The initial diagnosis was still VT, as barium-induced hypokalemia can lead to VTs with different morphologies [5]. However, though 1) no P-wave was observed, 2) a qR pattern in aVR, 3) left bundle branch block pattern, 4) and vi/vt more than 1, according to the Vereckei algorithm [4], suggested a

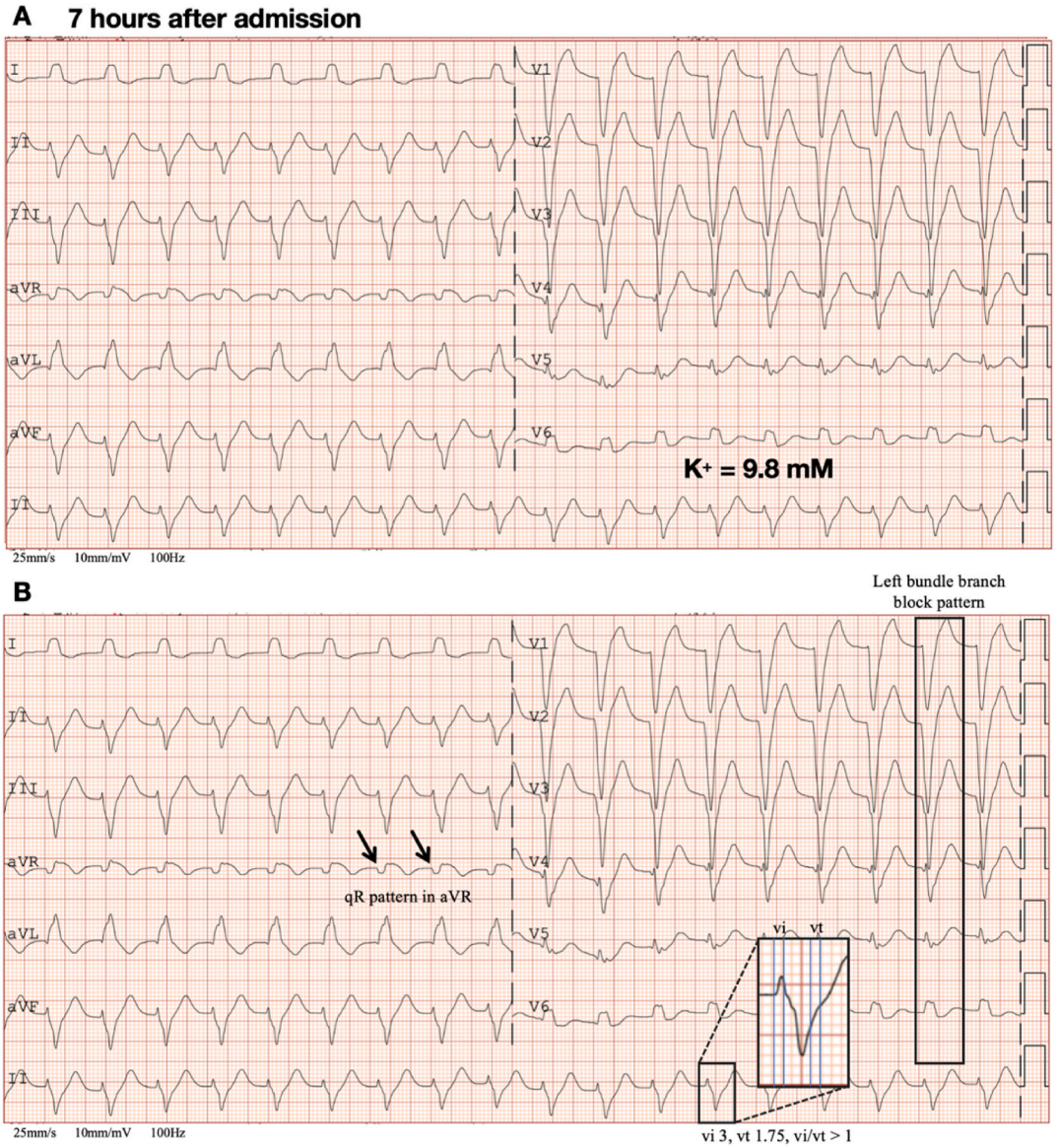

Fig. 2. A. A twelve-lead ECG obtained after hemodynamic recovery at 9.8 mM potassium concentration showed another WCT at 118 bpm; Fig. 2B. Annotated ECG of Fig. 2A revealed no P wave, a qR pattern in aVR, left bundle branch block pattern, and vi/vt more than 1, which, according to the Vereckei's algorithm, suggested SVT rather than VT and alerted clinicians to the possibility of rebound hyperkalemia.

diagnosis of supraventricular tachycardia (SVT) rather than VT, which alerted clinicians to the possibility of rebound hyperkalemia.

Repeat testing after Fig. 2 showed 9.8 mM potassium concentration and confirmed rebound hyperkalemia after the aggressive potassium supplementation. During the potassium-lowering therapy (including norepinephrine 0.49 μg/kg/min, epinephrine 0.07 μg/kg/min, and 8 units insulin i.v. in 30 minutes), a repeat ECG revealed another wide QRS rhythm similar to that in Fig. 2 at 6.3 mM potassium concentration, in which each QRS complex was preceded by a P wave and was followed by slurred type T-U wave (a prolonged terminal portion of the T-wave descending [6]) (Fig. 3A). These ECG findings made us inclined to diagnose hyperkalemia-induced sino-ventricular conduction in Fig. 2, a rare occurrence typically associated with severe hyperkalemia.

Nine hours after admission, the patient experienced another hemodynamically unstable VT and profound hypokalemia (2.2 mM potassium concentration, Fig. 4A), which may be secondary to an intracellular shift of potassium not only via barium poisoning but also the combined action of catecholamines and insulins [7]. The symptomatic and supportive therapies were applied continuously, combined with potassium and barium level monitoring. The patient's serum potassium concentration returned to 4.6 mM 12 hours after admission, accompanied by sinus tachycardia with narrow QRS morphology and fused U type T-U waves (the fusion of positive T- and U-waves forming T-U complex [6]) (Fig. 3B).

The next day, the patient regained consciousness with stable vital signs, but was in a state of depression. A repeat ECG showed accelerated idioatrial rhythm with relatively wider QRS complexes and fused U type T-U waves (Fig. 3C) at 4.8 mM potassium concentration. Though the excretion of barium in 3 days was about 75 %, the remaining 10–20 % of barium would be excreted during the following 7–42 days, and the release of the rest barium may lead to new events of hypokalemia and arrhythmias [1,2]. The serum potassium concentration was maintained at 3.1–4.8 mM over the following days (Fig. 4B), and the serum barium concentration decreased to 9.33 μg/L (1.28 μmol/L) on day 8 and 2.24 μg/L (0.31 μmol/L) on day 13. The patient was transferred to the observation ward with continuous venovenous hemodialysis-filtration stop after ALT and AST levels returned to normal range on day 20. On day 22, the patient's serum potassium suddenly decreased to 2.6 mM, with no complaints of discomfort (Fig. 4B). In the following days, the patient's mood was stable, and potassium concentration was maintained in the normal range. The patient's blood and urinary barium concentrations decreased to normal limits after 27 days of hospitalization, and she was discharged the next day. The timeline of key points throughout the treatment process is shown in Table 1.

3. Discussion

Barium, a divalent alkali metal, can inhibit the potassium inward rectifier channel (K_{IR}) encoded by the *KCNJx* gene family in all muscle types [1]. Barium can be found in rodenticides, insecticides, depilatories and fireworks, and both suicidal and accidental exposures to soluble barium can cause toxicity [1,2]. With the accessibility to the Internet becoming more and more convenient and diverse, barium poisoning cases may become more common, especially among teens and young adults [5], as seen in this case. Gastrointestinal symptoms in barium poisoning usually appear early and are followed by cardiac arrhythmias and skeletomuscular symptoms such as ventricular arrhythmias and general paralysis, which may deteriorate to hemodynamically unstable VT and fatal respiratory paralysis [1,2,5].

Hypokalemia can occur in approximately 1/4 of acute barium poisoning cases [1]. As a common electrolyte disturbance, hypokalemia is often due to potassium deficiency secondary to inadequate intake, diarrhea, vomiting, and diuretic therapy [8]. However, hypokalemia in barium poisoning cases is not due to potassium deficiency but the result of an intracellular shift of potassium via barium inhibiting the passive efflux of potassium [1]. Of note, the barium-induced hypokalemia and barium's direct K_{IR} blockade result in cardiac arrhythmias and muscle weakness, which are common in barium poisoning [1,3].

Blocking the potassium inward rectifier channel current I_{K1}, the major ionic current for atrial and ventricular resting membrane potential, is an underlying cause of cardiac arrhythmias and associated ECG changes in barium poisoning cases. Ventricular arrhythmias, including frequent ventricular extrasystoles and VT, were observed in almost half of barium poisoning cases, which are mainly determined jointly by 1) diastolic depolarization of resting membrane potential through barium's direct K_{IR} blockade (enhancing ventricular automaticity) and 2) early afterdepolarization due to the barium-induced hypokalemia [1,5]. In addition, prominent T-U waves were present in more than 3/4 of barium poisoning cases, which, apart from hypokalemia, may also be related to the prolonged action potential through barium's direct K_{IR} blockade [1]. There are some parallels to Andersen-Tawil syndrome (ATS), with prominent T-U waves and risk of ventricular tachycardias [9,10], as I_{K1} channels mutated in ATS are the same type of channels inhibited by barium [11]. The prominent T-U waves at a normal serum potassium concentration in Fig. 3B and C may suggest that barium had not been completely cleared from the plasma at that moment. Other ECG features of barium poisoning included ST-T changes, QT prolongation, and, more rarely, atrial fibrillation, atrioventricular block, and ventricular fibrillation [1]. [5].

It is the intracellular shift of potassium, rather than potassium insufficiency, that leads to the profound hypokalemia in barium poisoning. Therefore, the risk of rebound hyperkalemia after an aggressive potassium supplementation should be considered [1]. The alternation in conduction velocity (CV) due to hyperkalemia is biphasic [3]. Generally, when a potassium concentration is over 8 mM, the effect of hyperkalemia on the reduction of CV by decreasing Na + channel availability would be greater than that on the acceleration of CV by hyperkalemia-induced depolarization of the resting membrane potential and then results in intraventricular conduction delay, and can be accompanied by P-wave disappearing (sino-ventricular conduction, a rare occurrence due to severe hyperkalemia-induced disruption to atrial transmembrane potential) [3,12]. The peaked T wave that is common with hyperkalemia was not observed in Figs. 2 and 3, which was probably the result of the antagonism between 1) the hyperkalemia shortening action potential duration (APD) and 2) the barium's K_{IR} blockade prolonging APD [1,3]. Of note, another hemodynamically unstable VT and profound hypokalemia occurred during the potassium-lowering therapy in our case, which, in addition to barium poisoning, may also be due to the iatrogenic hypokalemia (both catecholamines and insulins can cause an intracellular shift of potassium) [7].

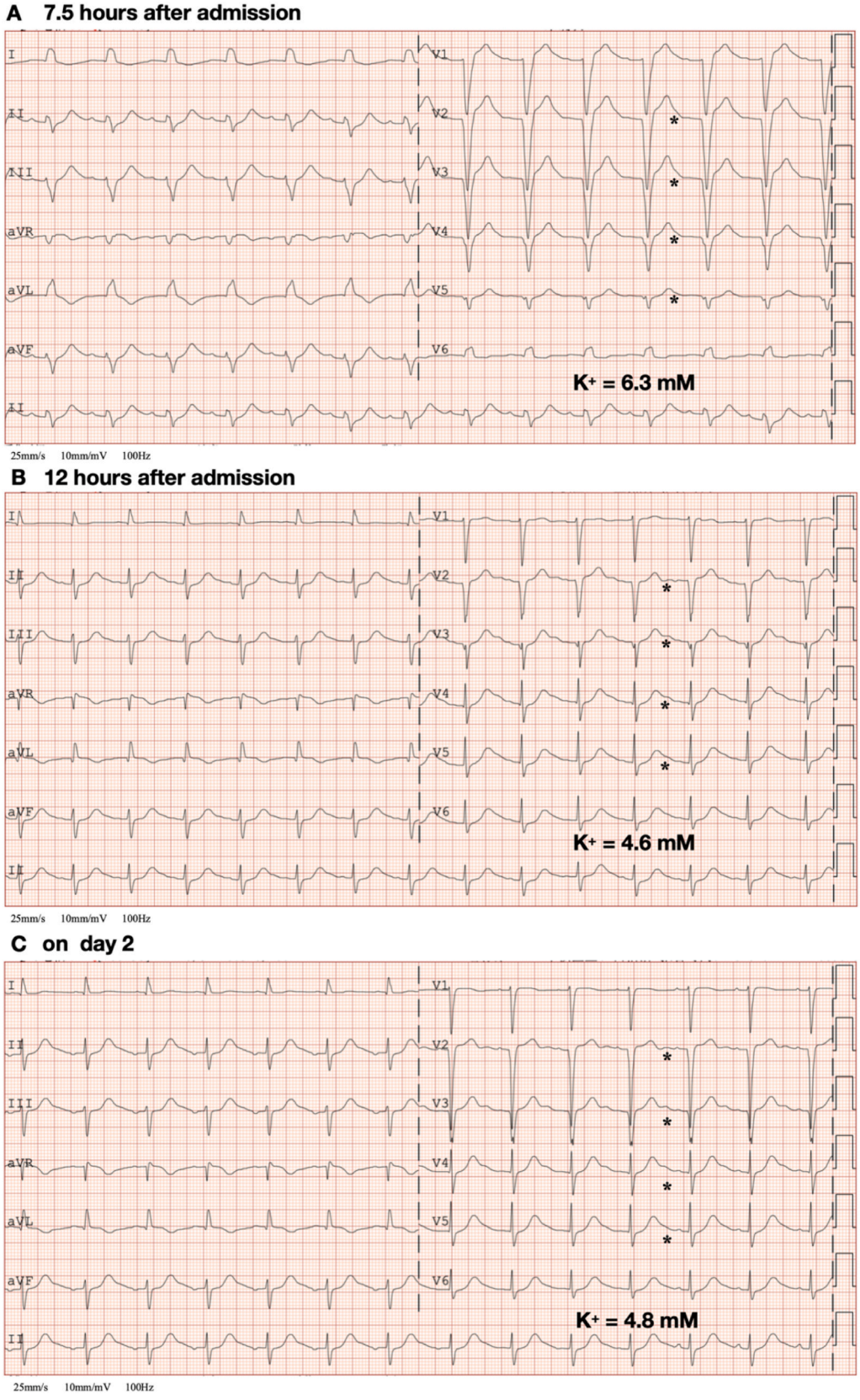

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Fig. 3. A. A twelve-lead ECG obtained 7 hours after admission at 6.3 mM potassium concentration revealed another wide QRS rhythm similar to that in Fig. 2, in which each QRS complex was preceded by a P wave and was followed by slurred type T-U waves (a prolonged terminal portion of the T-wave descending) (asterisks). Fig. 3B. Twelve hours after admission, a twelve-lead ECG was obtained at serum potassium of 4.6 mM,. The ECG revealed sinus tachycardia with narrow QRS morphology and fused U type T-U waves (the fusion of positive T- and U-waves forming T-U complex) (asterisks). Fig. 3C. A twelve-lead ECG obtained on day 2 at 4.8 mM potassium concentration showed accelerated idioatrial rhythm with relatively wider QRS complexes and fused U type T-U waves (asterisks). From Fig. 3A–**C**, the amplitude of positive deflection in T-U waves gradually decreased from slurred type to fused U type, which may be associated with a decrease in serum Barium concentration. The T-U waves at a normal serum potassium concentration in this case may suggest that barium had not been completely cleared from the plasma at that moment.

In cases of acute barium poisoning, the primary goal is to decrease barium absorption and increase its excretion [1]. Considering barium has long biological half-lives and continuously releases after accumulating in the skeleton that creates the substrate for long-term new events of profound hypokalemia and arrhythmias, the symptomatic and supportive therapies should be applied continuously, combined with potassium and barium level monitoring [1,2,13]. In addition, serum barium concentrations as low as 2.5 μmol/L were associated with hypokalemia [1], which may explain the sudden hypokalemia on day 22 (even though serum barium concentrations on day 8 were already 1.28 μmol/L).

In conclusion, this case highlights ECG features of acute barium toxicity, one due to barium-induced VT and, subsequently, sino-ventricular conduction with intraventricular conduction delay due to hyperkalemia after aggressive potassium supplementation. Differentiating whether WCT is ventricular or supraventricular is crucial for therapy in this patient; otherwise, if sino-ventricular conduction, as seen in Fig. 2, is mistaken for VT, it may lead to continuous potassium supplementation under high serum potassium concentration, which may further aggravate electrolyte disorders. Hypokalemia or hyperkalemia not corrected in time may result in arrhythmias and cardiac arrest [3,14]. A better understanding of the underlying mechanism(s) for ECG changes needs further investigation. In addition to symptomatic and supportive treatments, a more careful rather than too aggressive potassium supplementation may be suitable in these cases of hypokalemia due to an intracellular shift of potassium. In turn, we must consider iatrogenic hypokalemia and arrhythmia risk in the treatment of rebound hyperkalemia in barium poisoning.

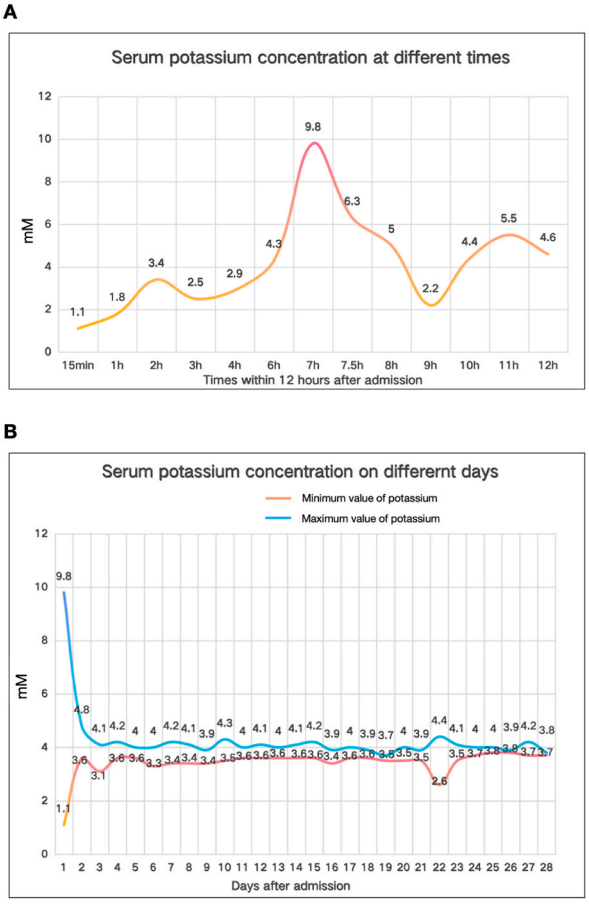

Fig. 4. A. The serum potassium concentration at different times within 12 hours after admisson. Fig. 4B. The serum potassium concentration on different days from admission to discharge.

Table 1
Timeline of key points throughout the treatment process.

Day 1, on admission	Overdosed on barium chloride orally 3.5 hours ago with unstable hemodynamics and symptoms (nausea, vomiting, general paralysis, hypotension, and unconsciousness).
15 minutes after admission	Laboratory tests revealed profound hypokalemia ($K^+ = 1.1$ mM), elevated ALT (2136 U/L) and AST (3049 U/L, r) levels. ECG on admission showed WCT tachycardia with a diagnosis of ventricular tachycardia (Fig. 1). The start of the symptomatic and supportive therapies. The blood pressure recovered gradually. The serum barium concentration was over 100 μg/L (over 13.73 μmol/L).
7 hours after admission	A ECG showed another WCT with an initial diagnosis of VT. However, ECG analysis supported the diagnosis of SVT, which suggested the possibility of rebound hyperkalmeia (Fig. 2). A repeat testing revealed hyperkalemia ($K^+ = 9.8$ mM). The start of the potassium-lowering therapy.
7.5 hours after admission	A ECG obtained at 6.3 mM potassium concentration (Fig. 3A) confirmed the diagnosis of sino-ventricular conduction in Fig. 2.
9 hours after admission	The patient experienced another hemodynamically unstable VT and profound hypokalemia ($K^+ = 2.2$ mM).
12 hours after admission	A ECG obtained at 4.6 mM potassium concentration revealed sinus tachycardia with narrow QRS morphology and prominent T-U waves (Fig. 3B).
Day 2	The patient regained consciousness with stable vital signs, but was in a state of depression. A ECG obtained at 4.8 mM potassium concentration showed accelerated idioatrial rhythm with relatively wider QRS complexes and prominent T-U waves (Fig. 3C).
Day 8	The serum barium concentration was 9.33 μg/L (1.28 μmol/L).
Day 13	The serum barium concentration was 2.24 μg/L.(0.31 μmol/L)
Day 20	The patient was transferred to the observation ward after ALT and AST levels returning to normal range.
Day 22	The patient's serum potassium suddenly decreased to 2.6 mM, with no complaints of discomfort.
Day 27	The patient's blood potassium remained stable, and blood and urinary barium concentrations decreased to normal limits.
Day 28	The patient discharged.

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Ethics statement

The informed consent was obtained from the patient for the publication of all the data and images.

CRediT authorship contribution statement

Yubin Zhang: Writing – review & editing, Writing – original draft. **Xi Huang:** Writing – review & editing. **Yiru Han:** Writing – review & editing. **Ren Yan:** Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] B.S. Bhoelan, C.H. Stevering, A.T. van der Boog, M.A. van der Heyden, Barium toxicity and the role of the potassium inward rectifier current, Clin. Toxicol. 52 (2014) 584–593, https://doi.org/10.3109/15563650.2014.923903.
[2] A. Oskarsson, Chapter 29 - barium, in: G.F. Nordberg, B.A. Fowler, M. Nordberg (Eds.), Handbook on the Toxicology of Metals, fourth ed., Academic Press, 2015, pp. 625–634, https://doi.org/10.1016/B978-0-444-59453-2.00029-9.
[3] J.N. Weiss, Z. Qu, K. Shivkumar, Electrophysiology of hypokalemia and hyperkalemia, Circ Arrhythm Electrophysiol 10 (2017), https://doi.org/10.1161/CIRCEP.116.004667.
[4] A. Vereckei, G. Duray, G. Szenasi, G.T. Altemose, J.M. Miller, Application of a new algorithm in the differential diagnosis of wide QRS complex tachycardia, Eur. Heart J. 28 (2007) 589–600, https://doi.org/10.1093/eurheartj/ehl473.
[5] N. Zhang, J. Liu, T. Liu, B. Chen, The heavy heart: an unusual cause of ventricular tachycardia, Am. J. Med. 136 (2023) e57–e60, https://doi.org/10.1016/j.amjmed.2022.10.022.
[6] S. Kurokawa, S. Niwano, M. Kiryu, M. Murakami, S. Ishikawa, Y. Yumoto, M. Moriguchi, H. Niwano, T. Kosukegawa, T. Izumi, Importance of morphological changes in T-U waves during bepridil therapy as a predictor of ventricular arrhythmic event, Circ. J. 74 (2010) 876–884, https://doi.org/10.1253/circj.cj-09-0937.
[7] M.D. Willard, Disorders of potassium homeostasis, Vet Clin North Am Small Anim Pract 19 (1989) 241–263, https://doi.org/10.1016/s0195-5616(89)50029-9.
[8] A. Mirijello, E. Rinninella, F. De Leva, A. Tosoni, G. Vassallo, M. Antonelli, G. Addolorato, R. Landolfi, Hypokalemia-induced pseudoischemic electrocardiographic changes and quadriplegia, Am. J. Emerg. Med. 32 (2014) 286 e281–e284, https://doi.org/10.1016/j.ajem.2013.09.033.
[9] J. Junker, W. Haverkamp, E. Schulze-Bahr, L. Eckardt, W. Paulus, R. Kiefer, Amiodarone and acetazolamide for the treatment of genetically confirmed severe Andersen syndrome, Neurology 59 (2002) 466, https://doi.org/10.1212/wnl.59.3.466.
[10] A.R. Perez-Riera, R. Barbosa-Barros, N. Samesina, C.A. Pastore, M. Scanavacca, R. Daminello-Raimundo, L.C. de Abreu, K. Nikus, P. Brugada, Andersen-tawil syndrome: a comprehensive review, Cardiol. Rev. 29 (2021) 165–177, https://doi.org/10.1097/CRD.0000000000000326.

[11] H.L. Nguyen, G.H. Pieper, R. Wilders, Andersen-Tawil syndrome: clinical and molecular aspects, Int. J. Cardiol. 170 (2013) 1–16, https://doi.org/10.1016/j.ijcard.2013.10.010.
[12] J. Maradey, P. Bhave, Sinoventricular conduction in the setting of severe hyperkalemia, JACC Clin Electrophysiol 4 (2018) 701–703, https://doi.org/10.1016/j.jacep.2017.12.011.
[13] D. Newton, G.E. Harrison, C. Kang, A.J. Warner, Metabolism of injected barium in six healthy men, Health Phys. 61 (1991) 191–201, https://doi.org/10.1097/00004032-199108000-00002.
[14] L.W. Andersen, M.J. Holmberg, K.M. Berg, M.W. Donnino, A. Granfeldt, In-hospital cardiac arrest: a review, JAMA 321 (2019) 1200–1210, https://doi.org/10.1001/jama.2019.1696.