

# Severe hypernatremia and hyperchloremia in an elderly patient with IgG-kappa-type multiple myeloma

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**Abstract:** A 77-year-old male was admitted to hospital after suffering a pelvic bone fracture in a road traffic accident and was incidentally found to have IgG-kappa-type multiple myeloma with hypercalcemia. The patient was also noted to be hypokalemic and had low  $\text{HCO}_3^-$ , with possible damage to the distal tubules in the kidneys. When the treatment was begun with bortezomib/dexamethasone/elcatonin and sodium bicarbonate ( $\text{NaHCO}_3$ ) in normal saline (equivalent to a daily sodium dose of 200 millimoles per liter [mmol/L]), the patient was in a state of poor oral fluid intake. The patient developed hypernatremia and hyperchloremia, with a peak serum sodium and chloride levels of 183 mmol/L and 153 mmol/L, respectively, at the sixth day after the start of treatment. Following the switch of the intravenous infusions from normal saline to soldem 1 and soldem 3 solutions, these high-electrolyte levels gradually returned to normal over the next 7 days. Although the patient showed disturbed consciousness (Japan Coma Scale = JCS-I-3) during the period of electrolyte abnormality, he eventually fully recovered without sequelae. In this patient, we successfully managed the severe hypernatremia/hyperchloremia, caused by the combined effects of intravenous saline burden in a state of poor oral fluid intake, during the treatment for IgG-kappa type multiple myeloma.

**Keywords:** hypernatremia, hyperchloremia, multiple myeloma, IgG-kappa, metabolic acidosis, renal tubular damage

## Introduction

Hypernatremia (serum sodium concentration  $> 146$  millimoles per liter [mmol/L]) is a common electrolyte disorder that can occur in very young or elderly patients.<sup>1,2</sup> Severe hypernatremia is defined as a serum sodium concentration  $> 160$  mmol/L.<sup>3</sup> Hypernatremia may be caused by simple excess of sodium, often resulting from dehydration, due to excessive water loss or the ingestion of hypertonic fluids. Large losses of low-salt body fluids can occur during episodes of diarrhea or after the administration of diuretics or may result from renal tubular damage in patients with nephrogenic diabetes insipidus.<sup>1</sup>

Hypernatremia may occur with the use of certain drugs, such as lithium and valproate, which may lead to renal impairment.<sup>4,5</sup> Hypernatremia can also occur in patients treated with excess sodium bicarbonate ( $\text{NaHCO}_3$ ) to correct metabolic acidosis, which may increase the concentration of sodium in the serum.<sup>6</sup> Particular attention must be paid to hypernatremic episodes occurring in elderly patients, which are usually caused by high-salt loads due to poor oral fluid intake. Multiple myeloma is one of the common hematological diseases in elderly patients. In the past, reports are available on IgG-kappa-type multiple myeloma and proximal renal tubular acidosis

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(Fanconi syndrome),<sup>6–15</sup> but the occurrence of hypernatremia in such cases has rarely been described.<sup>16</sup>

Here, we report the case of an elderly patient presenting with multiple myeloma and underlying renal tubular damage, who developed extreme hypernatremia (peak serum sodium concentration, 183 mmol/L) and hyperchloremia (peak serum chloride concentration, 153 mmol/L) after intravenous treatment with bortezomib/dexamethasone/elcatonin and NaHCO<sub>3</sub> in normal saline.

## Case report

A 77-year-old man (height, 170 cm; body weight, 55 kg; blood pressure, 172/66 mmHg; and heart rate, 84 beats per minute) was transferred to our care after being injured in a road traffic accident. On admission, he had an Eastern Cooperative Oncology Group performance score of 4. His medical history prior to admission was not significant. A computed tomography scan revealed a fracture of the left pelvic bone (Figure 1). The laboratory findings were: white blood count, 5600/μL; hemoglobin, 9.9 g/dL; platelet count, 142,000/μL; aspartate transaminase, 42 (normal range; 13–37) units/L; alanine aminotransferase, 21 (8–45) units/L; lactate dehydrogenase, 402

(122–228) units/L; ammonium, 61 (<100) μg/dL; total protein, 9.1 (6.7–8.3) g/dL; albumin, 3.1 (4.1–5.2) g/dL; blood urea nitrogen, 18.1 (7.8–18.9) mg/dL; creatinine, 1.73 (0.64–1.11) mg/dL; uric acid, 9.3 (3.0–7.0) mg/dL; estimated glomerular filtration rate, 41.5 (>90) mL/min/L; Ca, 11.9 (8.7–10.3) mg/dL; inorganic phosphate (IP), 2.6 (2.9–4.9) mg/dL; Na, 140 (138–146) mmol/L; K, 2.8 (3.6–5.1) mmol/L; Cl, 102 (99–108) mmol/L; and serum beta 2-microglobulin, 3.1 (0.9–1.9) mg/L.

Urinalysis revealed a pH of 5.0 with occult blood (2+) and protein (2+) but glucose (–). Because the patient showed high levels of total protein in the serum, we considered a differential diagnosis of multiple myeloma. Further tests revealed serum IgG levels of 4389 (870–1700) mg/dL, with IgG-kappa-type M protein. Bence–Jones protein was also detected in the urine. The bone marrow comprised 60% myeloma cells. Based on these findings, the patient was diagnosed with multiple myeloma (Durie–Salmon stage 2A). Clinically, the patient showed the complete range of multiple myeloma symptoms (hypercalcemia, renal dysfunction, anemia, and bone disease, such as osteolytic pelvic bones and ribs), which had been unrecognized until hospital admission.



**Figure 1** CT scan showing a fracture of the left ilium (arrow), which caused a large hematoma.

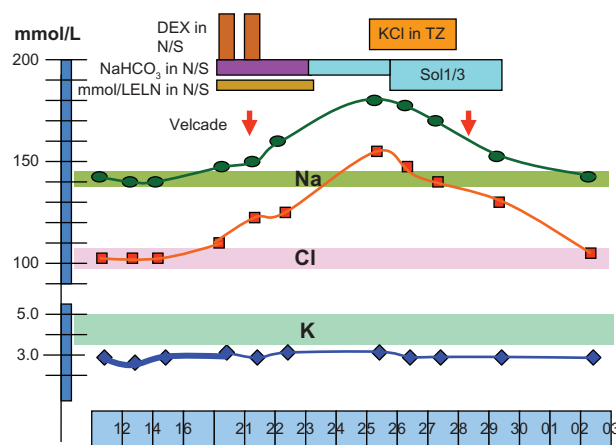
During the first week after admission, the patient was able to communicate but was somehow in a state of a mild disturbance of consciousness (Japan Coma Scale; JCS-I-2; disoriented) and had difficulty imbibing oral fluids; thus, he was hydrated with 1000–1500 mL of peripheral parenteral nutrition solution (soldem 3: sodium [Na] concentration, 35 mmol/L; chloride [Cl] concentration, 35 mmol/L).

After the diagnosis of multiple myeloma with hypercalcemia, specific treatment was instigated, according to the following protocol (Figure 2): intravenous normal saline (Na, 154 mmol/L; Cl, 154 mmol/L; 500 mL  $\times$  2/day; daily), dexamethasone (8 mg per day  $\times$  2 consecutive days), NaHCO<sub>3</sub> (80 mmol/L per day; daily), bortezomib (1.3 mg/m<sup>2</sup> per dose, weekly), elcatonin (40 units per day for 5 consecutive days), and zoledronic acid hydrate (4 mg per dose, monthly). All drugs were intravenously administered in normal saline (N/S); thus, the patient received 200 mmol/L of sodium per 24 hours over a period of 6 days.

As shown in Figure 2, the patient experienced a gradual increase in serum sodium and chloride levels, which peaked at 183 mmol/L and 153 mmol/L, respectively.

At this point, his consciousness deteriorated further (JCS-I-3; confused). The patient was then switched to an intravenous infusion (1500 mL) of soldem 1 (Na, 90 mmol/L; Cl, 70 mmol/L), soldem 3, and potassium chloride (KCl) in 5% glucose, which helped gradually resolve the hyponatremia/hyperchloremia over the next 7 days, but the patient continued to have difficulty in swallowing and a

low oral fluid intake. The patient's disturbed consciousness persisted for almost a month, then the situation improved significantly thereafter. During the entire period of hyponatremia/hyperchloremia, low serum potassium and IP levels also persisted. The former was associated with the excretion of high levels of potassium (38 mmol/L; normal levels, <20 mmol/L), although IP excretion was normal (1.14 grams per day; normal range, 0.5 grams–2.0 grams per day). There was no evidence of glucosuria, hypouricemia, or generalized aminoaciduria. While examining other factors that might contribute to the electrolyte disorders in this patient, we observed that, although the levels of adrenocorticotrophic hormone (19.9 pg/mL), plasma renin (2.4 ng/mL per hour), and aldosterone (56 pg/mL) were all within the normal range, his serum cortisol levels (22.4  $\mu$ g/dL) were slightly elevated. Arterial blood gas analysis, which was performed not in the critical period, but in the convalescent phase of the disease, revealed the following: pH, 7.481; PaO<sub>2</sub>, 84.0 mmHg; PaCO<sub>2</sub>, 28.2 mmHg; HCO<sub>3</sub><sup>-</sup>, 20.8 (normal; 23–31) mmol/L base excess, -1.0 mmol/L; and anion gap, 8.9 (normal; <12) mmol/L. These data were suggestive of metabolic acidosis. However, the urine anion gap was 48 mmol/L. We later confirmed that the patient's low-serum potassium and plasma HCO<sub>3</sub><sup>-</sup> levels eventually normalized after a month. Taken together, these data suggested that the patient was probably suffering from distal renal tubular damage<sup>17</sup> during the period of severe hyponatremia/hyperchloremia. Thereafter, the patient has fully recovered with no further disturbances of consciousness and with normal oral fluid intake, and continues to receive treatment for multiple myeloma.



**Figure 2** Clinical course of electrolyte disturbances (hypokalemia and hyponatremia/hyperchloremia) in association with treatment for multiple myeloma.

**Notes:** The numbers in the blue boxes running along the bottom of Figure 2 represent dates between November 12–16 and November 21–30, 2012, and December 1–3, 2012. The horizontal colored bars represent the normal ranges for sodium (green), chloride (pink), and potassium (pale blue).

**Abbreviations:** DEX, dexamethasone (8 mg per dose); ELN, elcatonin; KCl, potassium chloride; Na, sodium; NaHCO<sub>3</sub>, sodium bicarbonate; N/S, normal saline; TZ, 5% glucose; Sol1/3, soldem 1 and soldem 3 infusion fluids; Velcade, bortezomib (1.5 mg per dose).

## Discussion

Severe hyponatremia (defined as a serum sodium concentration > 160 mmol/L)<sup>3</sup> has been described in various case reports, as high as a serum Na concentration of 196 mmol/L, 201 mmol/L, 202 mmol/L, or 211 mmol/L.<sup>3,5,18,19</sup> In addition, in a reported case of fatal ingestion of sodium hypochlorite bleach, the patient showed hyponatremia (serum Na, 169 mmol/L) and hyperchloremia (Cl, 143 mmol/L) in association with metabolic acidosis,<sup>20</sup> and a patient with acute salt poisoning, due to an overdose of sodium chloride, showed a Na load of 400 mmol/L over 12 hours.<sup>21</sup> Here, we report a case of severe hyponatremia (Na, 183 mmol/L) in a patient with multiple myeloma. To date, however, few cases of hyponatremia in association with multiple myeloma have been described.<sup>16</sup> In the present case, hyponatremia occurred after the patient was hydrated intravenously mainly with N/S

as well as all necessary drugs (bortezomib, dexamethasone, elcatonin, and  $\text{NaHCO}_3$ ) were given in N/S, as he was unable to take fluids orally. Besides the high-saline burden,  $\text{NaHCO}_3$ <sup>16</sup> and dexamethasone administration might have accelerated the hypernatremia. In calculation, he received a salt load of 200 mmol/L over 24 hours, which was nearly comparable to one-fourth of the dose in a fatal case of household bleach ingestion reported by Ross et al.<sup>20</sup> The peak serum concentrations of sodium and chloride in the current patient reached 183 mmol/L and 153 mmol/L, respectively. Although the patient suffered some mild disturbances of consciousness, he made a full recovery within approximately 1 month, with no residual adverse effects.

In our case, the cause of the hypernatremia/hyperchloremia was likely to be linked to the renal tubular damage due to multiple myeloma, as the laboratory data showed a normal blood anion gap and a high urine anion gap, both of which are indicative of hyperchloremic acidosis (base excess  $< -2$  mmol/L; anion gap  $< 17$  mmol/L).<sup>22</sup> In general, decreases in plasma  $\text{HCO}_3^-$  levels are associated with hyperchloremic acidosis and lactic acidosis. Both type 1 (distal) and type 2 (proximal) renal tubular damage have been reported in patients with multiple myeloma and other related diseases.<sup>6–15</sup> In particular, distal renal tubular acidosis is characterized by hyperchloremic metabolic acidosis<sup>23</sup> and hypokalemia.<sup>24</sup> On the other hand, Sakaue et al and Uchida et al described IgG-kappa-induced proximal renal tubular acidosis, as observed in Fanconi syndrome, in patients with IgG-kappa type myeloma.<sup>14,15</sup> Although the patient in the present study showed persistently low levels of  $\text{HCO}_3^-$ , hypokalemia, and hypophosphatasia, he did not show evidence of glucosuria or generalized aminoaciduria, indicating that he did not have Fanconi syndrome. Therefore, we concluded that the extreme hypernatremia/hyperchloremia was due to a combination of excess saline and  $\text{NaHCO}_3$ , dexamethasone administration in association with poor oral fluid intake, on top of the distal renal tubular damage caused by multiple myeloma.

Considering the rarity of hypernatremia regardless of renal tubular damage in patients with multiple myeloma, it remains unclear how much myeloma-associated renal damage played a role in causing severe hypernatremia in this patient.

The outcome of myeloma-related renal tubular damage is not clear. Minemura et al<sup>8</sup> reported that renal tubular acidosis was not improved by treating the myeloma with chemotherapy agents; indeed, in their case, the patient died from an exacerbation of the disease. On the other hand, Uchida et al<sup>15</sup> reported a case in which renal tubular acidosis

was corrected after chemotherapy for multiple myeloma, and Sakaue et al<sup>14</sup> reported that serum IgG levels and urine sugar levels decreased, and serum potassium levels returned to normal, in a patient receiving chemotherapy for multiple myeloma. In the current case, the patient recovered from the electrolyte disturbances and acidosis within a month, responding to the myeloma therapy. The improvement in the electrolyte imbalance was associated with a return to normal levels of consciousness.

## Conclusion

In summary, there appears to be an increased risk of hypernatremia in elderly patients with renal tubular damage associated with multiple myeloma; therefore, clinicians must exercise caution and not prescribe excess salt, particularly in elderly patients who have difficulty taking oral fluids.

## Consent

Written, informed consent to publish this case report was obtained from the caregiver of the patient involved.

## Author contributions

SI, NK, and KK contributed equally to this work; SI, NK, and KK managed the patient; KK performed bone marrow studies; all authors prepared the manuscript; all authors read and approved the final manuscript.

## Disclosure

The authors report no conflicts of interest in this work.

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