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Case report

Caffeine intoxication as a result of excessive consumption of bottled coffee products: a case report

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Abstract

Objectives: Most cases of caffeine intoxication result from the excessive intake of over-the-counter drugs and energy drinks. However, few cases of caffeine intoxication due to the excessive consumption of bottled coffee products have been reported. Herein, we present a case report of caffeine intoxication.
Patient: A 39-year-old man experienced numbness and weakness in the extremities for three nights over five days.
Results: Blood tests revealed hypophosphatemia and low 25-OH vitamin D concentration. The symptoms disappeared the next day without any additional treatment. A lifestyle interview revealed that he regularly consumed bottled coffee like it was water and had approximately 1 L of it from evening to night. He was diagnosed with weakness in the extremities due to hypophosphatemia caused by caffeine intoxication. Upon investigating some bottled coffee products, we found that only a few of them had labels disclosing caffeine content and warnings of the risks of excessive caffeine intake.
Conclusion: We encountered a case of caffeine intoxication via coffee. Although rare in the past, caffeine intoxication might increase owing to the widespread use of bottled coffee products. The caffeine content of coffee products should be indicated on labels to warn consumers.

Key words: caffeine intoxication, coffee, hypophosphatemia, vitamin D

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Introduction

There have been reports of caffeine intoxication due to the excessive intake of energy drinks and over-the-counter drugs. The Ministry of Health, Labour and Welfare and the Ministry of Agriculture, Forestry, and Fisheries of Japan have issued warnings against excessive caffeine intake on their websites[1, 2]. The European Food Safety Authority (EFSA) states that caffeine intake of 3 mg/kg in adults is not associated with acute toxicity[3]. Over the past six years, Japan has shifted from canned coffee to marketing coffee in plastic bottles with larger capacities. However, the effects of these changes on coffee consumption and caffeine intoxication have not been reported yet. In this report, we present a case of a man who unintentionally overdosed with over 3 mg/kg of caffeine via excessive consumption of bottled coffee, showing signs of caffeine intoxication. Furthermore, we investigated the caffeine content of commercially available bottled coffee products.

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Patient and Methods

The patient was a 39-year-old man (height, 167 cm; weight, 77 kg; nonsmoker) with no relevant medical history. The first time, at around 23:40 h in his house, the patient became aware of numbness and weakness of the extremities and later began to hyperventilate. He was then brought to the emergency room. Upon arrival, he developed tetany due to hyperventilation. Physical examination revealed a normal state of consciousness, slight ankylosis of the limbs, tetany-like fingers, and no visible paralysis; however, the patient was unable to move his limbs voluntarily. The fingertips of the patient exhibited sensory disturbances. Pupil examination showed that both pupils had a diameter of 4 mm and exhibited prompt reflex to light. His vital signs were as follows: blood pressure, 143/104 mmHg; pulse, heart rate,

119 beats/min; body temperature, 38 °C; percutaneous arterial oxygen saturation, 98% (room air); Japan Coma Scale (JCS), 0 (restless). Laboratory findings revealed the following: white blood cells, 9,600/μL; hemoglobin, 15.7 g/dL; platelets, 362,000/μL; aspartate aminotransferase, 54 U/L; alanine aminotransferase, 48 U/L; lactate dehydrogenase, 240 U/L; alkaline phosphatase, 73 U/L; total bilirubin, 0.6 mg/dL; blood urea nitrogen, 13 mg/dL; serum creatinine, 0.81 mg/dL; uric acid, 7.5 mg/dL; glucose, 137 mg/dL; albumin, 4.6 g/dL; sodium, 139 nmol/L; potassium, 3.3 nmol/L; chlorine, 96 nmol/L; calcium, 10.5 mg/dL; phosphorus, 1.2 mg/dL; creatine phosphokinase, 269 U/L; C-reactive protein, 0.49 mg/dL; and negative for both COVID-19 and influenza antigens. A simple computed tomography scan was performed. No evidence of intracranial hemorrhage, clear pneumonitis, or clear compression lesions in the spinal canal was found; only fatty liver was observed. The patient also exhibited signs of hypophosphatemia. Suspecting tetany due to hyperventilation syndrome, he received 5 mg of diazepam intravenously and recovered; as a result, he went home.

The second time, two days later, at around 23:40 h in his house, he experienced the same symptoms again. He was brought to the emergency room again. Physical examination revealed a normal state of consciousness, numbness in the extremities, ability to shake hands, no skin rash, no goiter, and slight obesity. Biceps brachii, triceps brachii, iliopsoas, quadriceps femoris muscle, and hamstring were graded "4" in the manual muscle test. Pupil examination revealed that both pupils had a diameter of 4 mm and exhibited prompt reflex to light. His vital signs were as follows: blood pressure, 135/80 mmHg; pulse, heart rate, 109 beats/min; body temperature, 38 °C; percutaneous arterial oxygen saturation, 97% (room air); and JCS, 0 (restless). Laboratory findings were as follows: white blood cells, 9,200/μL; hemoglobin, 15.4 g/dL; platelets, 321,000/μL; aspartate aminotransferase, 41 U/L; alanine aminotransferase, 43 U/L; lactate dehydrogenase, 287 U/L; alkaline phosphatase, 72 U/L; total bilirubin, 0.3 mg/dL; blood urea nitrogen, 16 mg/dL; serum creatinine, 0.75 mg/dL; uric acid, 6.5 mg/dL; glucose, 248 mg/dL; albumin, 4.4 g/dL; sodium, 137 nmol/L; potassium, 3.9 nmol/L; chlorine, 97 nmol/L; calcium, 9.6 mg/dL; phosphorus, 1.5 mg/dL; creatine phosphokinase, 186 U/L; C-reactive protein, 0.42 mg/dL, and negative for both COVID-19 and influenza antigens. The subjective symptoms included weakness, lack of strength from the neck down, and numbness in the limbs. The patient was diagnosed with hypophosphatemia and hospitalized. He was administered glucose-added acetic acid maintenance infusion solution (500 mL). His blood tests at midnight revealed a low serum phosphorus level of 1.5 mg/dL; however, the following day, his serum phosphorus level was within normal limits (3.8 mg/dL), and the symptoms were improving without further treatment. As a result, the patient was discharged from the hospital; however, similar symptoms appeared for the third time, late at night on the same day. He visited the hospital the next day and was readmitted. Laboratory findings were as follows: white blood cells, 8,700/μL; hemoglobin, 15.8 g/dL; platelets, 371,000/μL; aspartate aminotransferase, 41 U/L; alanine aminotransferase, 41 U/L; lactate dehydrogenase, 206 U/L; alkaline phosphatase, 66 U/L; total bilirubin, 0.6 mg/dL; blood urea nitrogen, 12 mg/dL; serum creatinine, 0.72 mg/dL; uric acid, 7.0 mg/dL; glucose, 212 mg/dL; albumin, 4.7 g/dL; sodium, 136 nmol/L; potassium, 3.3 nmol/L; chlorine, 97 nmol/L; calcium, 9.9 mg/dL; phosphorus, 2.1 mg/dL, and C-reactive protein, 0.82 mg/dL. No abnormalities were detected on contrast-enhanced magnetic resonance imaging of the head. Additional laboratory tests indicated the following: fibroblast growth factor 23, 32.5 pg/mL; parathyroid hormone-related peptide, 1.0 pmol/L; intact parathyroid hormone, 38.4 pg/mL; and 25-OH vitamin D, 14.0 ng/mL. Using dual-energy X-ray absorptiometry, his bone mineral density was found to be 105–113% that of a young adult. Bone scintigraphy findings were not suggestive of a tumor. The patient had no abnormal hormone levels.

He had no flare-up of symptoms after hospitalization; therefore, we again inquired about his lifestyle. He mentioned that he had consumed 1 L coffee daily instead of water for the last two months and had concentrated his intake, especially in the evening and at night. Before these two months, he had consumed coffee only at convenience stores. Two months before the appearance of these symptoms, he had purchased boxes of bottled coffee and kept them at home, leading to a drastic increase in his daily coffee intake. Based on the assumed value of approximately 60 mg of caffeine per 100 mL of regular coffee[1, 2], 1 L of coffee would entail a total daily caffeine consumption of approximately 600 mg. Therefore, we suspected caffeine intoxication. When coffee consumption was prohibited, and the patient recovered. He was subsequently discharged. At his outpatient consultation, 11 days after being discharged, the patient reported no coffee consumption and no recurrence of symptoms. Laboratory findings were as follows: white blood cells, 8,700/μL; hemoglobin, 15.8 g/dL; platelets, 371,000/μL; aspartate aminotransferase, 41 U/L; alanine aminotransferase, 41 U/L; lactate dehydrogenase, 206 U/L; alkaline phosphatase, 66 U/L; total bilirubin, 0.6 mg/dL; blood urea nitrogen, 12 mg/dL; serum creatinine, 0.72 mg/dL; uric acid, 7.0 mg/dL; glucose, 212 mg/dL; albumin, 4.7 g/dL; sodium, 136 nmol/L; potassium, 3.3 nmol/L; chlorine, 97 nmol/L; calcium, 9.9 mg/dL; phosphorus, 2.1 mg/dL, and C-reactive protein, 0.82 mg/dL. No decrease was observed in the serum phosphorus levels. The patient was diagnosed with caffeine intoxication (weakness in the extremities due to hypophosphatemia).

Thus, we sought to investigate the caffeine labels and

caffeine content of common coffee products produced by Japanese beverage companies (Tables 1 and 2).

Discussion

A patient with weakness and numbness in the extremities was diagnosed with hypophosphatemia, and its cause was investigated. The maximal tubular reabsorption of phosphate per glomerular filtration rate (Tmp/GFR) was 1.1, indicating a decreased renal phosphorus reabsorption. The most important regulator of Tmp/GFR is fibroblast growth factor 23, followed by parathyroid hormone[4], both of which were within normal ranges. In addition, bone scintigraphy was performed to investigate tumorigenesis; however, no findings were suggestive of a tumor. Therefore, upon enquiring about the patient's unbalanced diet again, he admitted to excessive coffee intake, which led to the suspicion that hypophosphatemia was caused by caffeine intoxication. Coffee consumption was prohibited, and the patient was discharged. During the outpatient consultation after discharge, his symptoms did not recur, but his serum phosphorus levels did not decrease. The patient was diagnosed with caffeine intoxication.

The symptoms of weakness in the extremities included hypophosphatemia and vitamin D deficiency caused by caffeine intoxication. He enjoyed drinking coffee, and his coffee intake was excessive. The patient was unaware of the possibility of caffeine intoxication; therefore, he did not disclose excessive coffee intake to doctors or medical staff during the initial lifestyle check. After returning home, he drank large amounts of coffee, leading to a flare-up of his symptoms of caffeine intoxication. Upon readmission, he admitted to eating less in the morning and afternoon and having a larger dinner when asked about his unbalanced diet. He regularly consumed large amounts of coffee, and his coffee intake was concentrated from the evening to midnight after returning home. The EFSA states that caffeine intake of 3 mg/kg is not associated with acute toxicity in adults[3]. However, 500 mg caffeine led to increased tension, nervousness, anxiety, excitement, irritability, nausea, paresthesia, tremors, perspiration, palpitations, restlessness, and dizziness. High sublethal doses (approximately 7–10 mg/kg) in normal adults may also cause symptoms such as chills, flushing, nausea, headache, palpitations, and tremors, although individual responses vary significantly[5].

The patient weighed 77 kg, and his estimated caffeine intake from coffee was 600 mg or 7.8 mg/kg daily, which led to symptoms of acute caffeine intoxication. Caffeine intoxication symptoms typically occur at doses of 1 g, with a lethal dose of 3–50 g[5]. The mechanisms of action of caffeine intoxication include (I) gastrointestinal and central nervous system symptoms due to competitive adenosine-receptor blockade; (II) beta-receptor stimulation and hypokalemia due to stimulation of catecholamine release from

Table 1 Disclosure of caffeine content of coffee products

Corporate name	Disclosure status of the label of the product[1]	Disclosure status on website	Disclosure status by inquiry
ASAHI SOFT DRINKS CO., LTD.	non-disclosure	disclosure	NA
Coca-Cola (Japan) Company, Limited	non-disclosure	non-disclosure	non-disclosure
DyDo DRINCO, INC.	non-disclosure	disclosure	NA
ITO EN, LTD.	disclosure	disclosure	NA
Kirin Holdings Company, Limited	non-disclosure	disclosure	NA
Nestlé Japan Ltd.	non-disclosure	non-disclosure	disclosure
Suntory Holdings Limited	non-disclosure	disclosure	NA

[1]Excluding decaffeinated coffee.
NA: not applicable.

Table 2 Caffeine contents of the coffee products

Product name[1]	Caffeine content per container	Container size	Caffeine content (per 100 mL or 100 g)
Wanda Kiwami black bottled can	ca. 240 mg	400 g	ca. 60 mg
Georgia Caffe bottle coffee black sugarless	not disclosed	950 mL	not disclosed
DyDo Blend CRAFT Black, supervised by the world's best barista	250 mg	500 mL	50 mg
TULLY'S COFFEE BARISTA'S BLACK bottled can 390 mL	234 mg	390 mL	60 mg
KIRIN FIRE ONE DAY Latte low in sugar 600 ml plastic bottle	258 mg	600 mL	43 mg
Nescafe gold blend, bottle coffee sugarless	453.6 mg	720 mL	63 mg
Premium boss black 390 g bottled can	ca. 234 mg	390 g	ca. 60 mg

[1]Product names were in Japanese and translated into English.

the adrenal medulla; (III) myocardial stimulation and vasodilation due to cAMP elevation caused by phosphodiesterase inhibition; (IV) central nervous system symptoms due to gamma-aminobutyric acid receptor suppression; and (V) ryanodine-receptor stimulation of the skeletal muscle. Clinical symptoms of intoxication resulting from these effects include gastrointestinal symptoms such as nausea and vomiting; central nervous system symptoms such as headaches, dizziness, insomnia, anxiety, and convulsions; and cardiovascular symptoms such as sinus tachycardia, atrial fibrillation, ventricular fibrillation, hypokalemia, metabolic acidosis, and rhabdomyolysis[6].

However, our patient did not present with gastrointestinal symptoms. Although the patient presented with sinus tachycardia and hypokalemia, the symptoms were mild. The primary symptom was paroxysmal weakness of the extremities. Blood tests revealed hypophosphatemia and low 25-OH vitamin D levels. Hypophosphatemia can be caused by (I) intracellular or bone phosphorus transfer due to excess catecholamines, (II) reduced phosphorus absorption from the intestinal tract, or (III) loss of phosphorus from the kidneys due to vitamin D deficiency or inadequate vitamin D action[4]. Rapuri *et al.*[7] reported the effects of caffeine on vitamin D receptors and 25-OH vitamin D. Excessive coffee intake for over two months caused vitamin D deficiency and the onset of hypophosphatemia.

Most caffeine is metabolized by CYP1A2. The half-life of caffeine averages 4–5 h[8]. Caffeine metabolism is concentration-dependent and exponential; the saturation of metabolic enzyme activity has been reported to occur at intake levels of 500 mg (approximately 7 mg/kg) or higher[8, 9]. The patient experienced metabolic retardation and symptoms of intoxication after consuming an estimated 600 mg of caffeine. Because he did not consume any coffee after being admitted to the hospital, the excessive caffeine was metabolized; therefore, his serum phosphorus level recovered. His symptoms improved the next day, and he was discharged from the hospital. After returning home, he consumed a large amount of coffee and experienced a relapse. Purchasing a box of bottled coffee triggered his abnormal coffee consumption at home and the occurrence of caffeine intoxication symptoms. He liked coffee; however, before purchasing the box of bottled liquid coffee, he consumed a normal amount of coffee, that is, <3 mg/kg caffeine, bought from a convenience store. Preparing coffee without bottled coffee at home would have required time and effort. Therefore, he would not have consumed large quantities of coffee. Warning people about caffeine intoxication is necessary given that bottled coffee has become a part of their daily lives[10].

The Japan Soft Drink Federation created guidelines for labeling soft drinks with high levels of caffeine, such as energy drinks. The guidelines state that soft drinks with added caffeine, containing 21 mg or more of caffeine per 100 mL, should indicate the caffeine amount per bottle on the label to prevent excessive caffeine intake[11]. However, many of the coffee-based products we examined did not list their caffeine content, perhaps because caffeine is not an additive, making it difficult for consumers to know the amount of caffeine in the product (Table 1).

Table 2 lists the caffeine content of the major beverage manufacturers' products. It has been reported that 3 mg/kg of caffeine is not addictive for adults[3]. We found that some bottled coffee had over 200 mg of caffeine per bottle, which could lead to a dose exceeding 3 mg/kg for a person weighing ≤66 kg. We recommend clear labeling of the caffeine content of coffee products to ensure safe consumption.

Conclusion

With the advent of bottled coffee products, consumption of large amounts of coffee has become easy. Here, we encountered a case of acute caffeine intoxication. To ensure safe enjoyment of coffee in appropriate quantities, it is necessary to warn consumers against excessive caffeine intake by stating the caffeine content on coffee product labels.

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Consent for publication: We obtained consent to publish.

Data availability statement: The anonymized patient data used in this study are all included in the text.

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References

1. Q&A about excessive caffeine in foods. Be careful not to consume too much caffeine. Ministry of Health, Labour and Welfare (in Japanese). https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/0000170477.html. Accessed December 18, 2022.
2. Excessive Caffeine Intake: Ministry of Agriculture, Forestry and Fisheries (in Japanese). https://www.maff.go.jp/j/syouan/seisaku/risk_analysis/priority/hazard_chem/caffeine.html. Accessed March 13, 2023.
3. Caffeine: European Food Safety Authority. https://www.efsa.europa.eu/en/topics/topic/caffeine. Accessed March 13, 2023.
4. Takeuchi Y. Hypophosphatemia and endocrine disorders. Nippon Naika Gakkai Zasshi 2020; 109: 746–751 (J Jpn Soc Int Med). [CrossRef]
5. Willson C. The clinical toxicology of caffeine: a review and case study. Toxicol Rep 2018; 5: 1140–1152. [Medline] [CrossRef]
6. Imai T. Caffeine intoxication resulting in convulsions and ventricular fibrillation. Gekkan Yakuji 2020; 62: 1079–1084.
7. Rapuri PB, Gallagher JC, Nawaz Z. Caffeine decreases vitamin D receptor protein expression and 1,25(OH)2D3 stimulated alkaline phosphatase activity in human osteoblast cells. J Steroid Biochem Mol Biol 2007; 103: 368–371. [Medline] [CrossRef]
8. Kaplan GB, Greenblatt DJ, Ehrenberg BL, *et al*. Dose-dependent pharmacokinetics and psychomotor effects of caffeine in humans. J Clin Pharmacol 1997; 37: 693–703. [Medline] [CrossRef]
9. Kuribara H. Caffeine Intake in the Daily Life: Mechanism of Action and Safety Assessment. Tokyo Fukushi Daigaku Daigakuin kiyou (Bulletin of Tokyo University and Graduate School of Social Welfare) 2016; 6: 109–125 (in Japanese, Abstract in English).
10. Japan Soft Drink Association. Japan soft drinks statistics 2021 (in Japanese). http://www.j-sda.or.jp/images_j/stories/con05_about_jsda/2021jsda_databook.pdf. Accessed April 22, 2023.
11. Japan Soft Drink Association. Guidelines for the labeling of soft drinks with high caffeine content, including so-called energy drinks. 2017 (in Japanese).