

## 症 例 短 報

## A case report of a patient with hidden caffeine intoxication

Yuji Fujita<sup>1)2)</sup>, Yoshifumi Onuma<sup>3)</sup>, Kiyotaka Usui<sup>4)</sup>, Tomoki Hanazawa<sup>5)</sup>,  
Yoshito Kamijo<sup>5)</sup>, Yasuhisa Fujino<sup>1)</sup>, Yoshihiro Inoue<sup>1)</sup>

<sup>1)</sup> Division of Emergency Medicine, Iwate Medical University School of Medicine

<sup>2)</sup> Poisoning and Drug Laboratory Division, Iwate Medical University Hospital

<sup>3)</sup> Department of Psychiatry, Kodama Hospital

<sup>4)</sup> Division of Forensic Medicine, Tohoku University Graduate School of Medicine

<sup>5)</sup> Emergency Medical Center and Poison Center, Saitama Medical University Hospital

原稿受付日 2019年9月13日, 原稿受領日 2020年2月4日

Caffeine, which is psychoactive, is found in coffee, chocolate, energy drinks, and over-the-counter medications. Caffeine is the most widely consumed psychoactive drug worldwide. Many cases of caffeine intoxication involving ingestion of excessive doses of caffeine have been reported recently<sup>1)</sup>. Although caffeine intoxication is a well-known type of intoxication, caffeine-induced symptoms could be difficult to notice in clinical environments. Here, we present a case of a patient with hidden caffeine intoxication. Written informed consent was obtained from the patient for the publication of this report (December 14, 2018).

A female patient in her 50s with a history of somatic symptom disorder was admitted to a hospital, presenting with anorexia and severe gastrointestinal symptoms including nausea and vomiting. She also experienced insomnia, anxiety, breathlessness, palpitations, and headache. Initial clinical examinations found the following : Glasgow Coma Scale score : 15 (E4V5M6) ; heart rate : 76 beats/min ; blood pres-

sure : 146/95 mmHg ; SpO<sub>2</sub> : 98% (room air) ; body temperature : 36.6 °C. The biochemistry test results were not extremely abnormal. An anti-nausea agent was administered, which somewhat improved the patient's nausea on hospital day (HD) 3 and completely improved it by HD 6. As insomnia persisted until HD 12, a sleep-inducing drug was administered, after which insomnia began to improve. Anxiety symptoms improved as gastrointestinal symptoms improved. However, the headache worsened on HD 6 and persisted until HD 14.

The symptoms experienced by the patient could not be attributed to somatic symptom disorder alone and could have been due to drug intoxication. Therefore, we performed a toxicological analysis using the patient's serum, which was collected during admission. Acetaminophen, ethenzamide, bromovalerylurea, caffeine, and N-desmethyldiazepam were detected in the patient's serum on arrival at the hospital ; except for that of caffeine, these concentrations were within or below optimal therapeutic ranges. The serum caffeine concentration (64 µg/mL) was within the toxic range (> 15–20 µg/mL)<sup>2)</sup>, indicating caffeine intoxication. During the hospitalization period, it was revealed that the patient had been

著者連絡先 : 藤田 友嗣  
岩手医科大学救急・災害・総合医学講座救急医学分野  
〒028-3694 岩手県紫波郡矢巾町医大通 1-1-1  
E-mail : yfujita@iwate-med.ac.jp

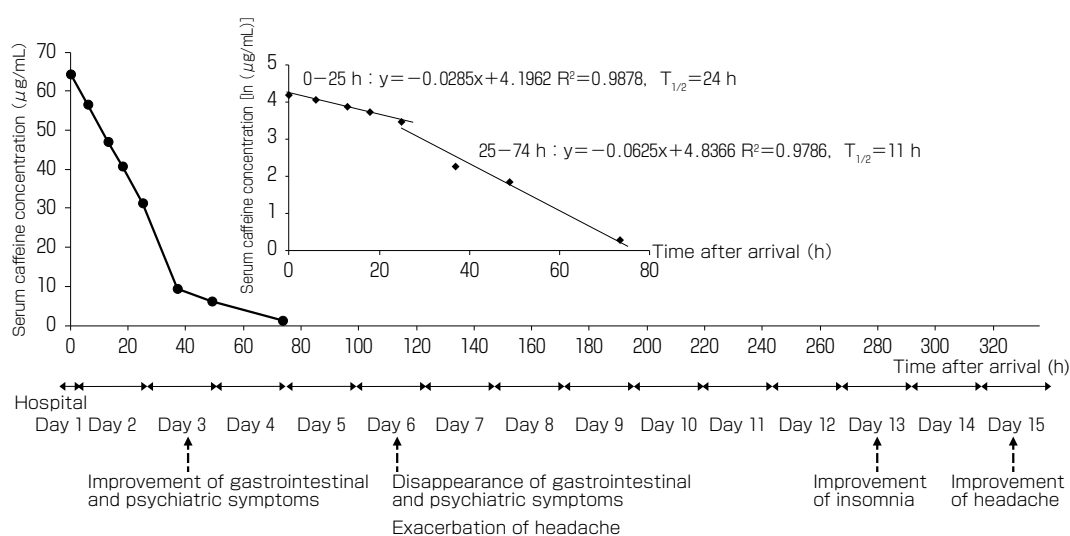
habitually ingesting a multi-ingredient common cold medication, composed of acetaminophen, ethenzamide, bromovalerylurea, and caffeine, for the past 4 years. The patient's serum elimination half-life ( $T_{1/2}$ ) of caffeine from 0 to 25 h after arrival was 24 h, and that from 25 to 74 h after arrival was 11 h (**Fig. 1**). The plasma  $T_{1/2}$  of caffeine in adults ranges from 3 to 7 h. Although she denied having ingested pure caffeine, the prolonged  $T_{1/2}$  of caffeine suggests that the patient consumed large amounts of pure caffeine, such as in the form of caffeine tablets, in addition to the common cold medication.

The symptoms experienced by the patient during admission are those induced by caffeine intoxication<sup>1)</sup>. Improvement of gastrointestinal and psychiatric symptoms were correlated with a decrease in serum caffeine concentration during the patient's hospital stay (Fig. 1). However, her headache had intensified on HD 6, which was the day after caffeine was no longer detected in the serum, and it persisted for 8 days (Fig. 1). Headache is a common caffeine-withdrawal symptom, which typically emerges 12–24 hours after abrupt caffeine use cessation and may emerge later ( $> 24$  h) with abstinence from higher

doses; the duration of caffeine withdrawal is 2–9 days<sup>3)</sup>. This suggests that the symptoms experienced by the patient were related to caffeine intoxication and withdrawal.

Approximately 1 month after discharge, the patient returned to the hospital complaining of gastrointestinal symptoms. Further, including the present case, she had been hospitalized 11 times over 21 months, for similar symptoms and clinical courses. Noteworthy, a consistent clinical course was observed during all cases of hospitalization. Although there was no record of the patient's previous serum caffeine levels, the information obtained in the present case suggests that her repeated hospitalization was associated with repeated excessive caffeine consumption, which can be attributed to a persistent desire to consume caffeine.

Caffeine is added to many products such as energy drinks and over-the-counter drugs. An environment wherein caffeine is likely to be unintentionally and regularly consumed in large quantities might have been one of the causes of the patient's intoxication. Caffeine-induced symptoms could be difficult to notice in clinical environments, as laboratory data



**Fig. 1** Chronological change of serum caffeine concentrations and caffeine-induced symptoms

Quantification analysis of caffeine was performed using liquid chromatography instrument with UV detector (JASCO, Tokyo, Japan). Detection wavelength for caffeine was set at 274 nm. Extraction of caffeine from serum was performed using the QuEChERS method. Quantification limit of serum caffeine concentrations was 1.0 µg/mL.

might not show any abnormality, as described in this case. Therefore, it is recommended that clinicians ask patients with complaints of cryptogenic gastrointestinal and psychiatric symptoms about their history of intake of caffeine. Drug screening, including screening for caffeine, should also be performed if possible.

The authors report no conflict of interest.

## References

- 1) Kamijo Y, Takai M, Fujita Y, et al : A retrospective study on the epidemiological and clinical features of emergency patients with large or massive consumption of caffeinated supplements or energy drinks in Japan. *Intern Med* 2018 ; 57 : 2141–6.
- 2) Schulz M, Iwersen-Bergmann S, Andresen H, et al : Therapeutic and toxic blood concentrations of nearly 1,000 drugs and other xenobiotics. *Crit Care* 2012 ; 16 : R136.
- 3) Juliano LM, Griffiths RR : A critical review of caffeine withdrawal : Empirical validation of symptoms and signs, incidence, severity, and associated features. *Psychopharmacology (Berl)* 2004 ; 176 : 1–29.

## Summary

A female patient in her 50s with a history of somatic symptom disorder was admitted to hospital, presenting with anxiety and severe gastrointestinal symptoms ; she had been hospitalized 11 times in 21 months, with similar symptoms. The patient's symptoms were not attributable to somatic symptom disorder alone and could have resulted from drug intoxication. Acetaminophen, ethenzamide, bromovalerylurea, and caffeine were detected in the patient's serum on arrival at the hospital ; with the exception of that

of caffeine, concentrations were within or below optimal therapeutic ranges. The caffeine concentration ( $64 \mu\text{g/mL}$ ) was within the toxic range, indicating caffeine intoxication. It may be difficult to notice caffeine-induced symptoms in clinical environments. Therefore, it is recommended that clinicians inquire patients with complaints of cryptogenic gastrointestinal and psychiatric symptoms about their history of caffeine intake. Drug screening, including screening for caffeine, should also be performed if possible.