



## Ketoprofen-induced photoallergic dermatitis

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**Key words** anti-inflammatory agent, dermatitis, emergency medicine, ketoprofen, non-steroidal, pediatrics.

An 11-year-old girl presented to the emergency department with a 9 day history of bilateral foot rash, swelling, and tenderness. Nine days earlier, she had used ketoprofen-containing compresses on both feet to ease ankle pain. On the next day, she noticed slight erythema beneath the compresses and stopped using at the time. Although the rash continued even after she stopped using the compresses, she went about her daily activities wearing sandals. The erythema gradually expanded and was accompanied by small blisters and exudate within a rectangular area on both feet corresponding to the shape of the compresses. After a wet dressing was applied in the emergency department for 3 days, the exudate and tenderness resolved but the borders of the lesions became more distinct (Fig. 1). These characteristic findings led to the diagnosis of photoallergic contact dermatitis. To prevent a relapse of the dermatitis, we referred the patient to a dermatologist.

Drug-induced photosensitivity is a cutaneous reaction to a medication triggered by exposure to ultraviolet light. Any drug reaching to skin can be a cause of this type dermatitis.<sup>1</sup> Drug-induced photosensitivity comprises up to 8% of drug adverse effects involving the skin and appendages,<sup>2</sup> with non-steroidal anti-inflammatory drugs (NSAID), angiotensin II receptor blocker, thiazide diuretic, and antibiotics often provoking the condition.<sup>1</sup>

Drug-induced photosensitivity is classified into phototoxic and photoallergic reactions. Phototoxic reactions are common and stem from DNA damage due to reactive oxygen species. Thus, this type of reaction can develop minutes to hours after exposure to ultraviolet light. Photoallergic reactions are a type IV hypersensitivity reaction typically requiring several exposures to the medication, with the interval from exposure to onset being 1–3 days. Treatment includes discontinuing use of the medication, avoiding sunlight, and applying topical corticosteroid. Typically, approximately 2 weeks are required for clinical improvement.<sup>3</sup> Recurrence, however, is possible, and one-third of patients report prolonged photosensitivity 1–14 years after discontinuing the medication.<sup>4</sup>

Of the topical NSAID implicated in photoallergic dermatitis, ketoprofen is responsible in 82% of cases.<sup>1</sup> The median time to onset of ketoprofen-induced photoallergic dermatitis is



**Fig. 1** Erythema accompanied by small blisters and exudate in a rectangular area on both feet, corresponding to the shape of the compresses.

8 days. Physicians are therefore advised to explain the risk of ketoprofen-induced photoallergic dermatitis to their patients when prescribing the drug.<sup>5</sup>

Although drug-induced photoallergic dermatitis is not common in pediatric patients, the present case demonstrates typical features and furnishes a useful clinical image. We should be aware that pediatric patients can sometimes have an adverse reaction to drugs normally prescribed to adults. For diagnosis, it is important to obtain a thorough drug history.

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### Disclosure

The authors declare no conflict of interest.

### Author contributions

T.N. treated the patient and wrote the paper; Y.H. supervised the writing of the manuscript. Both authors read and approved the final version of the manuscript.

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## Early juvenile Tay–Sachs disease with atypical symptoms

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**Key words** cerebral atrophy, epilepsy, juvenile GM2 gangliosidosis, perampanel, Tay–Sachs disease.

Tay–Sachs disease (TSD) is caused by a deficiency of  $\beta$ -hexosaminidase A (HEXA). The classical infantile form of TSD is characterized by the onset of symptoms before the age of 6 months and progresses rapidly to death by 3–5 years of age, while juvenile TSD is known to be clinically heterogeneous, develop later in childhood, and progress more slowly.<sup>1</sup> We report a case of early juvenile TSD with atypical symptoms including rapid neurological regression after onset, refractory epilepsy, and cerebral atrophy. We suggest that these symptoms should also be considered as clinical symptoms of juvenile TSD. Furthermore, it is noteworthy that perampanel was effective for treating the refractory epilepsy in the present case.

A 2-year-old girl had mild developmental delay. She was born at 36 weeks 6 days, after an uncomplicated pregnancy, weighing 2,706 g (+0.30 SD). The clinical course is summarized in Figure 1. She presented with hypoglycemic seizure (blood glucose, 20 mg/dL) without fever, and had repeated morning hypoglycemic seizures four times from 18 to 32 months old. On hypoglycemic attacks, total ketone body concentration was moderately elevated (4,015  $\mu$ mol/L), while growth hormone, adrenocorticotrophic hormone, thyroid-stimulating hormone, cortisol, and insulin (2.29  $\mu$ U/mL), urinary organic acid, and serum acylcarnitine were all normal. Brain and abdominal magnetic resonance imaging (MRI) were normal. Glycogen storage disease was ruled out on glucagon-loading and oral glucose tolerance tests on morning fasting, which led to a diagnosis of repeated episodes of age-related ketotic hypoglycemia. Hypoglycemic attacks disappeared after corn starch therapy. She had

mild developmental delay, refractory seizures, and regression of motor and speech functions, and began hand-wringing from the age of 5 years. She rapidly lost her ability to walk, speak, and swallow within several months, and we became aware of her hypersensitivity to loud sounds, but her mother had been conscious of that since infancy. She had refractory tonic, clonic, and absence seizures, which continued even with combination therapy of several anti-epileptic drugs. Electroencephalogram (EEG) showed sporadic spike and slow waves dominantly in the frontal region at 5 years 4 months old. Brain MRI at 5 years 8 months old showed global cerebral atrophy (Fig. 1). On considering neurological regression and auditory hypersensitivity, we analyzed the activity of lysosome enzymes and noted the reduced activity of HEX A (2 nmol/h/mg protein; normal control, 114 nmol/h/mg protein). After we got informed consent from the parents, we performed genetic testing and she had a compound heterozygous mutation in HEXA gene: c.32T>C, p.L11P/c.571-1G>T. This genetic test is approved by the ethical board in Osaka University School of Medicine. On the basis of these data, we diagnosed her with juvenile TSD. On ophthalmological examination, cherry red spots were absent. At the age of 6, she could not walk or speak, while her seizure frequency significantly decreased after starting perampanel (2 mg/day). EEG showed improvements of spike and slow waves.

Infantile TSD is characterized by specific features including cherry red spots, hyperacusis, progressive head expansion, and rapid neurological regression, while the juvenile type often lacks these symptoms.<sup>1</sup> In addition, the present patient had various distinctive symptoms such as repeated hypoglycemic attacks, and hand-wringing. To the best of our knowledge, these symptoms have not been reported in juvenile TSD. We diagnosed her hypoglycemic attacks as age-related ketotic hypoglycemia, and she did not fulfill the diagnostic criteria of Rett syndrome.<sup>2</sup>

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