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## Case report

# Hot water epilepsy and McCune–Albright syndrome: A case report

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## ABSTRACT

We observed a 15-year-old Caucasian boy with a rare form of reflex epilepsy, known as hot water epilepsy (HWE), associated to McCune–Albright syndrome (MAS). This is a rare disease due to post-zygotic and somatic mutations of the Gs-alpha gene, that results in cellular mosaicism. Predominant features of MAS occur in the bony skeleton, the skin, the endocrine system, and, in atypical presentations, in other non-endocrine tissues. It is unknown whether or not an expression of the GNAS1 product in the brain does exist. Although the association of MAS with HWE in our patient may be merely casual, it brings up the possibility that the striking phenotypic variability of MAS might also include epilepsy.

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## 1. Case report

A 15-year-old Caucasian boy was admitted to hospital because of a secondarily generalized tonic–clonic seizure that had occurred while having a hot shower. The seizure started with a sense of fear followed by elevation of the left arm and the deviation of the head to the right, followed by a loss of consciousness with cyanosis and massive jerking. Previously, the boy had experienced epileptic seizures on three different occasions, twice at the age of 8 years and once at 11 years, all with the same characteristics. These epileptic seizures were precipitated by the stimulus of bathing with the pouring of hot water over the head. The phenomenology of the seizures, described by the boy's mother, included a sense of fear, irrelevant speech and dazed look lasting approximately 1–2 min. No history of febrile seizures and/or birth distress was reported by his relatives. Facial acne, pubic hair with enlargement of the penis, deepening of the voice, all indicative of precocious puberty, were present since the age of 7 years. At the same age, a fibrous cortical lesion on the distal femur (Fig. 1) was evidenced following a radiograph of the right leg which was carried out because of bone pain.

On admission, physical examination showed: an asymmetric bulge on the frontal area of the skull, pectus excavatum, cifoscoliosis and five large café-au-lait spots with irregular margins, three of which were located on the neck. No axillary

freckling, skin tumours or Lisch nodules were evidenced. Vision, gross visual field, extra-ocular movements, and optic fundi were found to be normal, while no neurologic deficits were evidenced. An anteroposterior radiograph of the left hand suggested a bone age of 18 years, advanced more than 2 S.D. above the mean. Ultrasound examination of the thyroid gland revealed cysts several centimetres wide in the left lobe. Brain MRI, CT, a radiograph of the skull and an interictal scalp EEG were normal. The medical familiar history was unremarkable and, in particular, no history of epilepsy, febrile seizure or neurocutaneous syndrome was reported. Laboratory investigations included complete blood count, creatinine, calcium, proteins, albumin, electrolytes, serum aspartate aminotransferase, thyroxine, thyroid-stimulating hormone, cortisol and luteinizing hormone, which all were within the physiological range. Total triiodothyronine (T<sub>3</sub>) was 4.5 pg/ml (normal: 2.3–4.2); follicle-stimulating hormone (FSH) was 1.16 mIU/mL (normal: 1.4–18.1); phosphorus was 2.2 mg/dL (normal: 4–7).

On the basis of the clinical presentation, the diagnosis of McCune–Albright syndrome (MAS) was advanced and DNA PCR sequencing of Gs-alpha gene (GNAS1α) was performed on a skin biopsy sample. No mutation was found.

## 2. Discussion

Seizures precipitated by the stimulus of bathing with hot water poured over the head are known as hot water epilepsy (HWE), a rare and self-limited reflex form of epilepsy.<sup>1–3</sup> Although this form of epilepsy is quite common among the South Indian population and in Turkey, HWE has been reported only in isolated cases in the

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**Fig. 1.** Frontal view of distal femur showing a right fibrous cortical lesion homogeneously transparent (white arrow).

Caucasian population.<sup>3,4</sup> HWE has been associated to mesial temporal sclerosis and dysplasia and most patient showed an abnormal interictal EEG.<sup>4,5</sup> However, our patient, in agreement with previous reports,<sup>1–3</sup> showed a normal interictal scalp EEG and an unremarkable brain MRI. Although spontaneous non-reflex epilepsy has been reported to occur in 16–38% of patients a few years after onset,<sup>1–3</sup> our patient experienced only four epileptic seizures exclusively while showering, specifically when hot water was poured over his head. This is known to be a typical triggering stimulus that could involve a combination of factors such as (1) the contact of scalp with water, (2) a high water temperature and (3) the involvement of a specific cortical area of stimulation.<sup>2</sup> HWE is regarded as a geographically specific Epilepsy Syndrome of India. It was first described in 1945 in New Zealand<sup>6</sup> and, subsequently, there were isolated case reports from all round the world.<sup>3,4</sup> Familial HWE cases with more than one affected member have been reported in 7–15% of Indian patients and a percentage of 11–27% of these patients had reported a previous history of febrile convulsions.<sup>3</sup>

Although clinical manifestations such as pectus excavatum, cifoscoliosis, the presence of café-au-lait skin spots and epilepsy had initially suggested a neurocutaneous syndrome, the patient's clinical presentation (sexual precocity, large café-au-lait spots and fibrous dysplasia) and the laboratory findings (slightly elevated T<sub>3</sub>

level, low levels of phosphorus and FSH) fulfilled the diagnostic criteria for a MAS, a rare disease associated to a mutation of *GNAS1* gene.<sup>7,8</sup> To the best of our knowledge epilepsy associated to MAS has not been reported. The percentage of MAS patient exhibiting a mutation of *GNAS1* gene on skin biopsy, however, is quite small, being approximately 25–30%.<sup>8</sup> MAS was for the first time described 71 years ago by McCune.<sup>9</sup> Previously, this disorder was misdiagnosed as either primary hyperparathyroidism due to osseous abnormalities, or as neurofibromatosis because of osseous and cutaneous findings. The predominant features of MAS occur in three areas: the bony skeleton, the skin and the endocrine system. Somatic mosaicism of *GNAS1* gene could also account for the great variations in the site and degree of involvement of different tissues among patients; with some patients having only gonadal involvement and others having severe multisystem disease.<sup>10</sup> These same *GNAS1* activating mutations have also been found in several non-endocrine tissues of patients with the MAS, including liver, heart and the gastrointestinal tract. As consequence, chronic hepatitis, intestinal polyps, and cardiac arrhythmias, have been described as clinical manifestations.<sup>10</sup> Although gene mutations have been identified in some human growth hormone secreting pituitary tumours, the exact expression of *GNAS1* gene product in the brain is still not known. Moreover, in our patient genetic analysis failed to identify any pathogenetic mutation in this gene. Thus, any possible discussion about gene function as well as about how it can lead to seizure remains speculative in this case.

The case here described is a rare example of coexistence of two very rare genetic disorders. Although this coexistence might be merely casual, it brings up the possibility that epilepsy might be part of the clinical picture of MAS and that the two disorders share, at least in part, some common unidentified genetic mechanism.

### Conflict of interest

The authors report no conflicts of interest.

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