The condition in which seizures are precipitated by bathing in hot water is referred to as “hot water” or “bathing” epilepsy. Isolated cases of hot water epilepsy (HWE) have been reported in diverse regions, including New Zealand, Australia, Japan, Canada, the United Kingdom, the United States of America, France, China, and Brazil. A small number have also been identified in Turkey. The largest case studies of HWE patients have been performed in India by Mani et al, Gururaj et al, and Satishchandra et al, respectively. Satishchandra et al reported that HWE accounts for 3.6–3.9% of all epilepsy cases. They speculated that genetic factors and the high temperature of bath water may underlie this finding. Although studies report that 7–32.4% of HWE cases are found in families in which more than one individuals are affected, the pathogenic and genetic mechanisms underlying the expression of HWE in humans remain to be demonstrated.

Neuroimaging data on patients with HWE have revealed largely normal findings. However, several studies have published neuroimaging data showing that HWE patients display structural cerebral lesions, such as hippocampal sclerosis, hippocampal/parahippocampal atrophy, pineal cysts, cavum septum pellucidi, cortical dysplasia, and arachnoid cysts.


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In this study, we examined a family containing several members diagnosed with both HWE and cerebral lesions.

**Patients and Methods**

Our index case was a 32-year-old man admitted to our outpatient clinic following a 24-year history of seizures while bathing. Family members with similar symptoms were identified in Tokat, a city in the Middle Black Sea region of Turkey, and a pedigree was prepared in the field. Data were collected after all subjects received a detailed explanation of the study and provided informed consent. This study was performed in accordance with the Helsinki Declaration.

We obtained a detailed history of seizures from each patient. Data on personal and family medical histories, age, age at onset of seizures, types of seizures, precipitating factors, and bathing habits were gathered. Ictal symptomatology was assessed from two perspectives: that of the patients via self-description, and that of their first degree relatives who had observed the seizures. Clinical histories served as essential criteria for diagnosis. Seizures were classified according to the standards of the Commission of the International League Against Epilepsy.

We performed detailed neurological examinations and routine laboratory tests, including hemograms, erythrocyte sedimentation rates, glucose levels, renal and liver function tests, thyroid function tests, creatine kinase levels, lipid profiles, protein electrophoresis, vitamin B₁₂ levels, and urine analyses.

Electroencephalography (EEG) was performed using the international 10-20 montage system on a 32-channel Nihon Kohden EEG device. All records included 3-min hyper-ventilation and intermittent photic stimulation in the selected stimulation range of 0.5–30 Hz.

Cranial magnetic resonance imaging (MRI) investigations were performed using a 1.5-T MRI unit (GE Signa Excite; GE Healthcare, Milwaukee, WI, USA) using an 8-channel dedicated neurovascular coil. All patients underwent routine sequences that included sagittal SE T₁W, transverse propeller T₂W, transverse T₂W FLAIR, and coronal thin section FSE T₂W. Three patients also had sagittal FSE T₂ FLAIR imaging and were administered a contrast medium; contrast T₁W images were obtained with transverse sequences serving as magnetization transfer sequences. In addition, each examination included diffusion imaging.

**Results**

The complete pedigree structure consisted of six generations, 75 individuals, one consanguineous parent, and eight patients diagnosed with epilepsy. Of these, seven suffered from HWE. Three males were diagnosed with HWE alone; one deceased male patient had features similar to those of the surviving patients with HWE alone; another deceased male patient showed both HWE and other types of epilepsy; two female patients were diagnosed with both HWE and other types of epilepsy; and the mother of the index case was diagnosed with complex partial seizures (CPS) and generalized tonic-clonic seizures (GTCS) in the absence of HWE.

Figure 1 shows the pedigree structure for this family. Clinical, electrophysiological, and neuroradiologic data were collected from the surviving three male and three female family members suffering from HWE (Table).

**Clinical presentation of the family**

**Patient 1 (index case)**

Our index case is a 32-year-old man with consanguineous parents, who was admitted to our outpatient clinic reporting a history of seizures that occurred while bathing. These seizures began when the patient was six years old.
At first, he experienced simple partial seizures that were followed by nausea, dizziness and weird feelings when pouring hot water over his head. As his condition developed further, he experienced CPS characterized by the loss of contact accompanied by oral automatisms, staring gaze, and bimanual automatisms. At the age of 16, the patient began to experience CPS with secondary generalization while bathing. These CPS with secondary GTCS occurred once or twice over two to three years. The patient never experienced spontaneous seizures without bathing, and his bathing habits included the use of very hot water, which he would pour over his head. At the time of presentation, he had been taking 1200 mg oxcarbazepin daily for one year. According to his history, he was seizure-free over the course of a year in which he substituted warm water for hot water. Neurologic examination and interictal EEG were normal.

Magnetic resonance imaging revealed T2 hyperintense lesions in the periventricular white matter; the orientations of some of these lesions were perpendicular to the ventricular axis (Figure 2). However, the lesions showed no contrast enhancement after intravenous gadolinium administration. Diffusion imaging for this patient was unremarkable.

The patient did not consent to a lumbar puncture procedure. Routine laboratory tests, electrocardiogram, echocardiogram, and carotid and vertebral Doppler sonography were normal. Due to the patient’s age, additional laboratory tests were performed to rule out hypercoagulable disorder; all results were normal.

**Patient 2**

Patient 2, the 40-year-old sister of the index case, reported a history of CPS both with and without bathing. At the age of three, the patient had a febrile seizure. Between the ages of 7 and 23, she experienced loss of consciousness with oral automatisms, pallor of the face, and staring as soon as she poured hot water over her head. This patient also experienced CPS spontaneously, but the seizures completely stopped after a three-year course of treatment with carbamazepin, beginning at 20 years of age. Neurologic examination and interictal EEG were normal. Magnetic resonance imaging revealed small posterior parietal subcortical lesions, probably consistent with ischemic gliosis. She was not given intravenous gadolinium. Her diffusion MRI was within normal limits. Routine laboratory tests, electrocardiogram, echocardiogram, carotid and vertebral Doppler sonography were normal. Due to the patient’s age, additional laboratory tests were performed to rule out hypercoagulable disorder; all results were normal.

**Patient 3**

Patient 3, a 15-year-old male, experienced seizures only while bathing. Since the age of 7-8, he experienced CPS at the end of his bath. These seizures are characterized by nausea and
Patient 4

Patient 4, the 60-year-old father of the index case, died in 2007. He had suffered seizures from childhood until death. A clinical history was obtained from his wife and children, who had witnessed his seizures. According to their reports, the patient experienced three types of seizures. First, during baths, he experienced loss of contact with facial pallor and staring gaze, similar to his son. Second, he had seizures followed by oral automatisms, bimanual automatisms, slurred speech, and unusual body movements and postures (e.g., appearing hunchbacked) without bathing. Third, he experienced GTCS, usually while sleeping and occasionally occurring three or four times per night. His history revealed febrile seizures during childhood. His family reported that he was treated with phenytoin, which he took irregularly and at a possibly ineffective dose.

Patient 5

Patient 5, the 57-year-old mother of the index case, had experienced two or three GTCS per month, usually during sleep, since the age of 14. The patient underwent phenytoin treatment for approximately 5-6 years. With the help of the drug, the patient’s seizures were under control for approximately 7-8 years. However, at the age of 30 the patient began to experience one or two CPS per month. These seizures were characterized by an aura accompanied by abdominal sensations, an unpleasant odor, and anxiety; they were followed by loss of consciousness, oral automatisms, pallor, and staring. These seizures stopped spontaneously ten years ago.

The patient reported no history of HWS or febrile seizures. But the patient reported a history of systemic hypertension. Neurologic examination and interictal EEG were normal. Routine laboratory tests showed hypercholesterolemia.

The MRI revealed multiple T2 hyperintense white matter lesions localized bilaterally in the periventricular white matter, and in the right external capsule and right parietal subcortical white matter. No contrast enhancement was noted. Her diffusion MRI findings were normal.

Patient 6

Patient 6, the 53-year-old maternal uncle of the index case, had a history of GTCS that occurred while bathing in hot water. Before seizure onset, the patient would feel nauseated and hear vomiting with an aura accompanied by an unpleasant odor (valonia oak). These experiences were followed by cyanosis on the lips, loss of consciousness. Each seizure lasted approximately two to three minutes, and was followed by confusion, fatigue, weakness, and sleep. The patient had no history of anti-epileptic therapy. Over the two years prior to this study, the patient decreased the duration of his bathing sessions and used warm, rather than hot, water; subsequently, the frequency of his seizures decreased.

The patient had no childhood history of febrile seizure. Neurologic examination was normal. Interictal EEG revealed slow-wave activity within the theta range in both frontal regions, and sharp waves in the predominantly F4 electrode position. The patient did not consent to cranial MRI.

Figure 3: Transverse T2 weighted FLAIR images (a-b) for Patient 6 showing subcortical distribution of small T2 hyperintense lesions (arrows).
frontotemporal area. Routine laboratory tests and carotid and vertebral Doppler sonography were normal. An electrocardiogram revealed atrial fibrillation.

Cranial MRI revealed mild to moderate cerebral atrophy and ischemic gliotic white matter lesions localized in the posterior periventricular white matter (Figure 4). Contrast scans showed no pathologic enhancement. Her diffusion MRI results were normal.

DISCUSSION

We evaluated six generations of a Turkish family, which included one set of consanguineous parents and eight family members diagnosed with epilepsy. Of these, seven suffered from HWE. Moreover, cranial MRI performed on five of the six surviving patients revealed cerebral lesions.

The patients described here are similar to those described in other studies, particularly in terms of age at onset, seizure type, precipitating factors, and interictal EEG findings. Consistent with nearly all previous studies, we observed that males are affected more frequently than females (i.e. five male versus two female patients). The pathophysiological mechanisms underlying this finding or pattern of sex linkage inheritance have not yet been explained.

Our data concerning age at HWE onset (i.e. a range during childhood) and seizure semiology (i.e. the relative frequency of CPS) are consistent with previous studies, which reported the ratio of CPS in HWE as high as 67–80%. Furthermore, the ratio of concomitant spontaneous non-reflex seizures has been reported in 16–100% of patients. In this family, seven members were diagnosed with HWE. Consistent with the literature, spontaneous seizures (in addition to reflex seizures) were observed in three family members.

Interictal EEG revealed abnormalities which were sharp waves and slow waves in Patient 3 and Patient 8, respectively. Patient 3 had HWE alone, but the other patient had HWE as well as other types of epilepsy. All of the our patients had no video monitoring. Interictal EEG results were usually normal, although 15-20% might show diffuse abnormalities. Interictal EEG results were consistent with the literature in our cases. Interestingly, two studies conducted in Turkey reported the incidence of EEG abnormalities in HWE to be as high as 60% and 40.9%.

Several studies on HWE support the possible aetiological contribution of aberrant thermoregulation, within the context of coexisting enviromental influences and the genetically susceptible population. However, the exact pathogenic and genetic mechanisms underlying the expression of HWE in humans have not been clearly demonstrated thus far.

Familial HWE cases with more than one affected member have been noted in 7-15% of Indian probands. Among the 279 HWE patients reported in South India, there were three dizygotic twins, each with one member affected. Hot water epilepsy was intra-familial in 18% of the cases in a descriptive epidemiological study conducted in rural parts of Bangalore, South India. This study included one family in which all seven members were diagnosed with HWE.

To our knowledge, the family described in this study has the second largest number of members diagnosed with HWE identified so far. Satishchandra et al. reviewed their case series for intra-familial HWE, and found five families with two to three members manifesting HWE. Savitha et al. recently reported family histories of HWE among 32.4% of 71 patients with HWE. Bebek et al. reported that 10% of their cases had a history of HWE. However, neither Bebek et al nor Savitha et al reported how many members of the same family were also affected. None of the patients in a study by Yalçın et al had a family history of HWE. A single case of HWE in a Japanese monozygotic co-twin was reported by Itoh et al.

Using a mouse model of HWE, Ullal et al. suggested that patients with HWE may have a genetically determined aberrant thermoregulatory system that causes extreme sensitivity to rapid increases in temperature, which occurs while bathing in hot water; this aberration may precipitate seizures. Other studies in rats showed that repeated hot water stimuli had a kindling-like effect, most notably on the amygdala; this produced a progressive increase in convulsive responses to stimulation.
Although primarily precipitating factors for seizures were pouring water over the head and temperature of water in reported series and in our family, the importance of water temperature in precipitating seizures has yet to be elucidated. In Indian patients, seizures were precipitated by water temperatures ranging from 40–50°C. However, Iooos et al16,17 described French patients who experienced seizures in water with temperatures around 37°C. The authors pointed out that patients of Caucasian descent may differ from those described in studies conducted in southern India10,16,17. Auvin S, Lamblin MD, Pandit F, Bastos M, Derambure P, Vallée L. 1. Satishchandra P. Hot water epilepsy. Epilepsia. 2003;44:29−32.

In this context, Satishchandra et al21 performed an existence of structural lesions in the temporal lobe of these patients, indicating the presence of structural cerebral lesions (e.g., hippocampal sclerosis, hippocampal/parahippocampal atrophy, hypothalamus on the left in three patients, and on the right in two patients).

In summary, descriptions of HWE-affected families with different ethnic backgrounds, and investigations using innovative neuroimaging methods, may yield more definite conclusions regarding the mechanisms of epileptogenesis, as well as the varying clinical presentations and nature of the genetic defects underpinning this disease. These data may provide increased insight into the treatment of HWE.

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5. Ioos et al. 6. Seneviratne at al. 7. Auvin et al. 8. Sommer’s sector in the hippocampus, neural layers 4 and 5 of the cerebral cortex, and reticular neurons in the brain stem, in response to such stimulation. These phenomena produced a kindling-like effect, primarily in the amygdala8,22,23.

Moreover, Iibay et al24 investigated the status of the blood-brain barrier and the roles of blood pressure and body temperature during the induction of HWE in rats. They found that hot water-induced seizures increased cerebrovascular permeability. Although high blood pressure and hyperthermia contributed to permeability, seizure activity was the major factor in this change.

In a pathological study of four confirmed human patients with HWE, distinct hippocampal involvement, with gliosis and ischemic changes in the reticular nuclei of the brain stem, were observed in two cases. In the remaining two cases, a right thalamic glioma was observed in one patient, and cerebral atrophy with neuronal loss and gliosis in both sides of the hippocampus were observed in the other1,25.

We suggest the possibility that the cerebral lesions found in Patients 1, 2, and 6 may be related to the etiopathogenetic mechanisms of HWE. We further suggest that the probability of the co-occurrence of these lesions and HWE may extend beyond chance, even if there is a no more than chance association between the presence of cerebral lesions and the epileptogenesis of HWE in Patient 8. In our opinion, these lesions in Patients 1, 2, and 6 may represent permanent effects of hot water seizures. However, lacking neuropathologic data, it is difficult to establish whether the lesions derive from acquired impairments (e.g., infarcts of the white matter) or genetic determinants based on neuroradiological and clinical data alone.

In summary, descriptions of HWE-affected families with different ethnic backgrounds, and investigations using innovative neuroimaging methods, may yield more definite conclusions regarding the mechanisms of epileptogenesis, as well as the varying clinical presentations and nature of the genetic defects underpinning this disease. These data may provide increased insight into the treatment of HWE.

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