

# Episodic Spontaneous Hypothermia with Hyperhidrosis: Case Report

## Epizodik Spontan Hipotermili Hiperhidroz

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**ABSTRACT** Hypothermia can develop due to environmental or nonenvironmental factors. Episodic spontaneous hypothermia with hyperhidrosis (ESHH) is a rare cause of nonenvironmental hypothermia in which the core temperature is less than 35°C and is characterized by episodes of hypothermia and sweating without shivering. Although the episodes are usually short, cases with persisting episodes for months have been reported. The pathophysiology of episodic spontaneous hypothermia with hyperhidrosis is unknown. Patients with agenesis of corpus callosum have been described as the Shapiro's syndrome. There is no definitive treatment for episodic spontaneous hypothermia with hyperhidrosis. Antiepileptic, antiserotonergic agents have been reported to be effective to control episodes in some patients. We presented a patient with ESHH without corpus callosum agenesis who was treated with cyproheptadine.

**Key Words:** Hypothermia; hyperhidrosis; child; seizures

**ÖZET** Hipotermi çevresel veya diğer nedenlerle oluşabilir. Episodik spontan hipotermili hiperhidrozis (ESHH) vücut sıcaklığının 35 santigrat derecenin altına düştüğü, titremenin olmadığı hipotermi ve terleme epizotları ile seyreden, çevresel dış unsurların neden olduğu hipotermimin nadir görülen bir nedenidir. Epizotların genellikle kısa olmasına rağmen, aylarca devam eden epizotları olan vakalar da bildirilmiştir. Hiperhidrozisli epizodik spontan hipotermimin patofizyolojisi bilinmemektedir. Korpus kallosum agenezisi ile birlikte olan hastalar Shapiro sendromu olarak tarif edilmiştir. Hiperhidrozisli epizodik spontan hipotermi için kesin bir tedavi yöntemi yoktur. Antiepileptik ve antiserotonergik ilaçların bazı hastalarda epizotları kontrol etmek için etkili olduğu bildirilmiştir. Bu makalede, korpus kallosum agenezisi olmayan ve siproheptadin ile tedavi edilen bir ESHH olgusu sunulmuştur.

**Anahtar Kelimeler:** Hipotermi; hiperhidrozis; çocuk; nöbetler

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Hypothermia may develop due to environmental or nonenvironmental factors.<sup>1</sup> Episodic spontaneous hypothermia with hyperhidrosis (ESHH) is a rare cause of nonenvironmental hypothermia and is characterized by low core temperature less than 35°C that lasts from minutes to months. Although the pathophysiology of ESHH is unclear, congenital central nervous system anomalies and/or dysfunction of the hypothalamo-hypophyseal axis is suggested to play a role.<sup>2</sup> In this report, we presented a 5-year-old girl with ESHH.

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## CASE REPORT

A five-year-old girl presented to the outpatient clinic with a history of hypothermia attacks for the last two years. The episodes occurred approximately once a month two hours after the onset of sleep. The episodes were characterized by pallor, fear, disorientation and profuse sweating without shivering that lasted approximately one hour during sleep. The body temperature during the hypothermic episodes was lower than 35°C by ear electronic thermometer. The blood pressure and blood glucose levels were within normal ranges. There was no family history of ESHH, migraine and other periodic syndromes of childhood or history of environmental exposures, medication use, toxin ingestion or trauma.

Physical and neurological examination revealed that head circumference, height and weight were 52 cm, 112 cm (50<sup>th</sup> percentile), and 17 kg (25<sup>th</sup> percentile), respectively. Her developmental milestones were appropriate for her age. The cranial nerves were intact, and fundoscopic examination was normal. Her muscle tone was normal, and deep tendon reflexes were normoactive. She had no pathological reflexes.

Laboratory investigations revealed that complete blood count, blood urea nitrogen, serum creatinine, liver function tests, fasting blood sugar, serum electrolytes, serum uric acid, lactate, pyruvate, ammonia, erythrocyte sedimentation rate, C-reactive protein, thyroid function tests, adrenocorticotrophic hormone, and urinalysis were within normal limits. Video electroencephalography (EEG) could not be performed but interictal sleep EEG revealed normal electrophysiological results. Electrocardiography and echocardiography were also normal. Magnetic resonance imaging (MRI) of her brain and pituitary gland revealed normal anatomic findings (Figure 1).

She was prescribed cyproheptadine 2 mg/day, which was effective in preventing the episodes. She is still free of episodes under treatment for one year.

## DISCUSSION

Episodic spontaneous hypothermia with hyperhidrosis is a rare disorder that is characterized by



**FIGURE 1:** Normal brain magnetic resonance imaging findings with intact corpus callosum.

unprovoked episodes of hypothermia and profuse sweating without shivering.<sup>1</sup> Associated manifestations include pallor or flushing, a sensation of being cold or hot, bradycardia, generalized weakness, ataxia and confusion.<sup>2,3</sup> It has been reported in all age groups with the youngest case being a six-month-old girl.<sup>4</sup> The hypothermic episodes can occur at varying intervals, ranging from hours to months, and episodes can last from minutes to years.<sup>3</sup> In our patient, the attacks occurred monthly and lasted approximately one hour. She did not experience any shivering during the attacks.

The pathogenesis of ESHH is unclear. Skin temperature is mainly regulated by the central nervous system (CNS). The most important thermoregulatory region of the CNS is the medial pre-optic/anterior area of the hypothalamus.<sup>4</sup> Sheth et al.<sup>2</sup> have suggested that ESHH is caused by episodic dysfunction of the shivering mechanism, in which it fails to respond to normal fluctuations in body temperature. Shivering is believed to be under control of the pre-optic nucleus in the anterior hypothalamus (POAH) and its connections to the extrapyramidal system. Serotonergic neurons from the raphe nuclei project fibers to the POAH. Experimental microinjections of serotonin in the

POAH decrease the threshold temperature for shivering. Post-mortem pathological studies of patients with ESHH have revealed severe neuronal loss and fibrillary gliosis of the hypothalamus, and infundibular nucleus as well as severe spongiosis of the white matter.<sup>5</sup> Hyperhidrosis is an important component of ESHH. In general, children sweat less than adults, regardless of the surrounding environmental conditions.<sup>5</sup> Sweating causes heat loss via evaporative cooling. Thus, the excessive sweating that occurs in ESHH might be an important factor in enhancing the severity of the hypothermia that occurs in these patients.

Similar to our patient, no CNS anomalies have been reported in ESHH.<sup>4</sup> In the differential diagnosis, Shapiro's syndrome, which is characterized by agenesis of the corpus callosum and ESHH should be ruled out.<sup>3</sup>

The episodic nature of this disorder has led some authors to believe that the episodes represented "diencephalic epilepsy". Although ESHH can occasionally be accompanied with epilepsy, it does not appear to be a manifestation of a seizure disorder. The EEG performed during episodes shows diffuse slowing rather than epileptiform discharges.<sup>4</sup> Additionally, antiepileptics have been relatively ineffective in treating this disorder.<sup>2</sup> Although video EEG was not performed, interictal EEG findings and clinical manifestations of our patient during these episodes were not compatible with seizure. The serum levels of ammonia, lactate and pyruvate were normal and she did not have any clinical findings suggestive of mitochondrial disease or potential causes of hypothermia.

The main group of disorders that should be considered in the differential diagnosis is the periodic syndromes of childhood, which are characterized by periodic and paroxysmal occurrence like ESHH; benign paroxysmal torticollis, benign paroxysmal vertigo, abdominal migraine and cyclic vomiting are the most common ones. The clinical features of the periodic syndromes of childhood are well documented (Table 1).<sup>6</sup>

Torticollis, vertigo, ataxia, vomiting, abdominal pain and nausea were not the main characteristics of the episodes in our case while pallor, fear, disorientation and profuse sweating represented the main features of attacks of ESHH.

No definitive treatment has been reported for ESHH. Anticonvulsants, clonidine, bromocriptine, and chlorpromazine are all used in the treatment of ESHH, with varying degrees of success.<sup>3</sup> Cyproheptadine, an antiserotonergic agent is the most commonly recommended with variable therapeutic success rates.<sup>1,2</sup> Our patient has been on cyproheptadine treatment for a year and she is still episode-free. Since ESHH is a rare disorder, the duration of cyproheptadine therapy is uncertain. Sheth et al reported that ESHH did not occur after 6 months of treatment with cyproheptadine in a patient.<sup>2</sup> However, after discontinuation of therapy the episodes recurred. Thus, to continue treatment unless side effects occur may be a rational approach.

In conclusion, ESHH is a heterogeneous and rare condition. It should be considered in the differential diagnosis of confusion and hypothermia episodes in order to avoid unnecessary clinical evaluations.

**TABLE 1:** Main clinical features of childhood periodic syndromes.

Periodic syndrome	Mean Age at Onset (Extremes)	Signs	Duration of Episodes	Age at Resolution
Benign paroxysmal torticollis	5 mo (0.25-30)	Torticollis Dystonia	4.5 days (<1-30 days)	3 yr (3 mo- 5 yr)
Benign paroxysmal vertigo	3 yr (5 mo to 8 yr)	Vertigo Ataxia	10 min (a few seconds to 72 hr)	5 yr (2-16 yr)
Abdominal migraine	7 yr (infancy to adulthood)	Abdominal pain Pallor	4 hr (1-72 hr)	Adolescence to adulthood
Cyclic vomiting	5 yr (6 days to 73 yr)	Vomiting nausea	24 hr (2hr to 10 days)	10 yr ( may persist in adulthood)

Hr: Hours; Min: minutes; Mo: months; Yr, years.

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