Shapiro’s Syndrome: A Renewed Appreciation for Vital Signs

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Vital signs are an invaluable diagnostic tool, but in this era of modern medicine and expensive tests, important information obtainable at the patient’s bedside is often overlooked. We report an unusual case, Shapiro’s syndrome, in which an appreciation of temperature recordings was essential to diagnosis. We review this disorder and the thermoregulatory system.

A previously healthy 49-year-old man from a small Midwestern town was admitted to the hospital in midautumn with complaint of bed-shaking chills and drenching sweats of up to 90 min duration, occurring every 4–6 h for the previous month. These episodes eventually exhausted the patient to the point of incapacitation. He was admitted to a local hospital 3 weeks into his illness, where an exhaustive laboratory and radiological work-up was unrevealing. He was subsequently transferred to our tertiary referral center for further evaluation and specifically placed under the care of the infectious diseases service because of the shaking chills.

The patient had no other complaints, except for a 33-kg weight loss over the past month. His medical, surgical, and family histories were unremarkable. He was receiving no medication before the onset of symptoms and had no allergies to any medication. He worked as a custodian in a food warehouse. Social and travel histories were otherwise unremarkable.

Examination revealed a fatigued, thin white man with a temperature of 35.7°C when he was asymptomatic (figure 1). All temperatures recorded on this patient were performed during each episode of sweating/chilling to 32°C–35°C at 34°C. Temperatures recorded during a sweating or chilling episode were typically <34°C, though much variation was seen throughout the patient’s hospital course. The patient’s temperature typically remained <34°C until resolution of symptoms and did not increase for ~1 h.

The following laboratory studies were performed, and the results were normal or negative: complete blood cell count, liver function tests, determination of erythrocyte sedimentation rate and C-reactive protein level, antinuclear antibody, rheumatoid factor, blood and urine cultures, Rapid Plasma Reagin, and detection of HIV antibody. Serological tests were negative for hepatitis A, B, and C virus; Lyme disease; Epstein-Barr virus; cytomegalovirus; Brucella species; West Nile virus; and Ehrlichia species. Analysis of fluid specimens obtained by lumbar puncture revealed nothing remarkable. The findings of endocrinologic studies were normal, including thyroid-stimulating hormone, free thyroxin, cosyntropin stimulation test, luteinizing hormone, follicle-stimulating hormone, prolactin, free and total testosterone, and urine porphyrins, normetanephrines, metanephrines, and 5-hydroxyindole acetic acid. The tuberculin skin test was nonreactive.

The following imaging and diagnostic studies were performed, and the findings were unremarkable: chest radiography; CT of the chest, abdomen, and pelvis; sinus radiography; tagged WBC scan; electroencephalography; and transesophageal echocardiography. The findings of an MRI of the brain were essentially normal, except for the neuroradiologist’s observation and notation of incidental agenesis of the corpus callosum.

The patient’s initial temperature of 35.7°C was initially presumed to be a nursing or technical error. However, during the next few days, we noted that the patient’s temperature decreased during each episode of sweating/chilling to 32°C–35°C and never increased to >36.7°C when he was asymptomatic (figure 1). All temperatures recorded on this patient were performed orally. Subsequent review of vital signs from the referring hospital revealed similar temperature fluctuations, with no recorded temperature of >35.5°C.

The triad of findings—hyperhidrosis, hypothermia, and agenesis of the corpus callosum—led us to the diagnosis of a rare disorder, Shapiro’s syndrome, and allowed us to review the infrequently reviewed thermoregulatory system.

“Shapiro’s syndrome,” a form of spontaneous periodic hypothermia, was coined after Shapiro and Plum described 2 cases of agenesis of the corpus callosum associated with episodic hyperhidrosis and hypothermia in 1969 [1]. No single area in the brain controls temperature; rather, thermoregulation in-
Centrally acting medications that mimic the neurotransmitters affecting the hypothalamus, including dopamine, acetylcholine, serotonin, prostaglandins, and catecholamines, have been described for therapy for this disorder, with only variable success [1, 3–6]. No definitive treatment for this disorder has ever been found. After 2 weeks of clonidine therapy, our patient’s core temperature and symptoms were unchanged. We then used a combination of other centrally acting agents, including gabapentin, chlorpromazine, levodopa-carbidopa, and venlafaxine, to try to “reset” this patient’s internal thermostat. With this combination, we observed an increase in the patient’s basal temperature to >36°C with improvement in temperature variations and symptoms.

In medical school, we are taught that the first important part of a physical examination should be obtaining accurate vital signs. However, how often do we glance at a hypothermic temperature recorded on the vitals chart and presume it to be a nursing or mechanical error? In our patient, this finding of hypothermia was not an error, but rather the key to his diagnosis of Shapiro’s syndrome. In this era of modern medicine and expensive tests, it is easy to overlook the valuable information obtained at the patient’s bedside.

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References