Shapiro’s Syndrome: A Case Report and Management Approach

Prashanth Venkataraman1, Mohammad Aziz2, Leo Chen3, Forshing Lui4

1Department of Clinical Neurology, California Northstate University College of Medicine, 9700 West Taron Dr. Elk Grove, California, 95757, USA, 2Department of Clinical Neurology, California Northstate University College of Medicine, 9700 West Taron Dr. Elk Grove, California, 95757, USA, 3Department of Clinical Neurology, Neurologist, Kaiser Permanente Sacramento/Roseville, California, USA, 4Department of Clinical Neurology, Neurologist, Neurology Clerkship Director, California Northstate University College of Medicine, 9700 West Taron Dr. Elk Grove, California, 95757, USA

ABSTRACT

Shapiro’s syndrome, first described in 1969, consists of the classic triad of spontaneous periods of hypothermia, hyperhidrosis, and agenesis/dysgenesis of the corpus callosum. In this article, we report a complex case of a patient with classic Shapiro syndrome and numerous other neurologic comorbidities and propose a management approach for hypothermic episodes. We suggest an approach of “masterly inactivity” during hypothermic episodes, as excessive rewarming will be combatted by homeostatic balances to lower the patient’s core temperature, ultimately causing more harm.

Key words: Corpus callosum, hypothalamus, hypothermia, masterly inactivity, shapiro’s syndrome

INTRODUCTION

Shapiro syndrome (SS), described a little under 100 times in the literature, consists of the classic triad of spontaneous periods hypothermia, hyperhidrosis, and agenesis/dysgenesis of the corpus callosum. Variations of the syndrome have been described, with spontaneous periods of hyperthermia termed as “Reverse SS”. Further cases without agenesis of the corpus callosum have also been described, termed Shapiro variants. Aberrations in thermoregulation seem to be the most ubiquitous entity among all clinical presentations and have been proposed as the defining hallmark of typical and variant SS.

Hypothermia is clinically classified as temperatures below 35°C and SS and variants are usually characterized by episodes lasting from minutes to hours associated with somnolence, delirium, labile hemodynamics, and potential polyuria. The pathophysiology of these paroxysmal episodes is not well understood but is likely a compilation of structural, biochemical, and electrical causes. It has been proposed that a complex interplay between neurons found in the hypothalamus, brainstem, and cervical spinal cord underlie the process of thermoregulation. Other than agenesis of the corpus callosum in classic SS, magnetic resonance imaging (MRI), single-photon emission computerized tomography, and positron emission tomography scans have failed to pinpoint a specific structural component responsible for triggering these episodes. The role of neurotransmitters derives from the medical therapies used in controlling symptoms which range from clonidine, anti-epileptics, serotonin and dopamine modulators, and more aggressive interventions like sympathectomy. These lend support to the effector mechanism at play but little insight into the underlying cause. Nonetheless, current management is centered around symptom management, and the following discussion will outline clinical experience with acute and chronic management in a patient with classic SS.

Address for correspondence:
Prashanth Venkataraman, California Northstate University College of Medicine, 9700 West Taron Dr. Elk Grove, California, 95757, USA. E-mail: Prashanth.Venkataraman6552@cnsu.edu

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CASE REPORT

A 37-year-old male with a medical history significant for classic SS, developmental delay, cerebral palsy, and Dandy-Walker malformation who presented to the Emergency Department on October 23, 2017 with characteristic episodes of hypothermia and hyperhidrosis. Mental status was tough to discern due to the patient’s history of developmental delay, but according to the family, he appeared more somnolent than usual. He is non-verbal at baseline but seems to respond to voices and makes eye contact. He did not appear to be in pain or any acute distress. Physical exam was remarkable for a temperature of 34.4°C and cool extremities without cyanosis. Labs were remarkable for a sodium of 120. Brain MRI showed no new structural abnormalities aside from agenesis of the corpus callosum and a Dandy-Walker malformation. Due to his hyponatremia, the patient was admitted to the hospital and given normal saline with serial improvements in his sodium level. The patient was stabilized and then sent home but returned later that evening with recurrence of hypothermic episodes.

The patient was first diagnosed in 2005 when he presented with his first hypothermic episode with a temperature above 29°C. He was managed in the ICU where hypervigilance of his presentation prompted warming with electric blankets and warm saline infusions. As a result of these interventions, he would lose up to 5–10 L of fluid through sweating alone. These hypothermic episodes were followed by intense shivering that would return his body temperature to normal or near normal. The neurologist managing his care at the time figured that aggressive intervention was likely causing more profound electrolyte disturbances due to the compensatory hyperhidrosis his body used to combat the iatrogenic rise in temperature. Therefore, the patient was allowed to subsist at the mercy of his hypothalamus to eventually readjust his thermostat to physiological levels. This resulted in less dramatic electrolyte disturbances and lessened the duration and frequency of his episodes.

Meanwhile, various medications were tried to manage recurrence. Medications that were tried included trazodone, carbamazepine, modafinil, promethazine, ondansetron, memantine, melatonin, cyproheptadine, clonazepam, amitriptyline, and amantadine. After a lengthy ICU stay, he was discharged on topiramate, clonidine, cyproheptadine, and oxcarbazepine with less frequent and much more brief hypothermic episodes till late 2017.

DISCUSSION

Temperature regulation is a complex process that has been localized to the anterior and posterior hypothalamus with the former coordinating the neural pathways that lead to the shivering/sweating response. The anterior hypothalamus has been shown to be the main entity that regulates the body temperature at a set point. The basal forebrain probably provides input to the anterior hypothalamus from both sides. Any basal forebrain malformation or agenesis of the anterior corpus callosum will lead to dysregulation of the anterior hypothalamus.[7]

There have been multiple attempts at uncovering and describing the pathophysiology behind spontaneous period hypothermic episodes. Fluorodeoxyglucose - positron emission tomography imaging has demonstrated hypermetabolism in multiple areas of the brainstem and cerebellar regions during these episodes.[4] These spontaneous hypothermic episodes are a characteristic of the syndrome described by Shapiro et al. in which the hallmark anatomic finding is agenesis of the corpus callosum or dysgenesis of the anterior corpus callosum.[1] Since reverse SSs (episodes of spontaneous hyperthermia) and Shapiro variants without the characteristic anatomic findings have been described, the true pathophysiology behind the homeostatic imbalance in temperature regulation of these diseases has not been elucidated.[6,7]

These episodes have also been described as the epileptiform activity of the anterior hypothalamus-corpus callosum connections; however, no electroencephalogram activity has been documented.[8] The increased perfusion to these areas during the hypothermic/diaphoretic episodes more likely reflect neurotransmitter release secondary to poor homeostatic control of the thermoregulatory center. These are described as “diencephalic discharges” of neurotransmitters - specifically serotonin and dopamine.[6]

Our case is a complex case of SS as the patient has multiple neurological comorbidities and the overall clinical picture is muddled with multiple medical issues related to lengthy hospital stays. Our patient was able to have a sufficient period of remittance before recurrence of symptoms and did not have an indolent progression toward an increasing frequency of episodes. Therefore, the disease course seems to mimic a pattern of punctuated equilibrium rather than gradual deterioration. We observed improved clinical outcomes with minimal intervention during acute episodes resulting in less dramatic perturbations in homeostasis when compared to aggressive symptom control. Medical management was achieved on a trial basis with multiple medications.

Management approach

Our management approach, in this case, was to NOT try to elevate body temperatures during his hypothermic episodes. In fact, keeping him cool helped him more than drastic measures to keep him warm. Any attempt to raise body temperatures during the hypothalamic episode will be met with
the body trying to lower the core temperature with increased diaphoresis and fluid/electrolyte loss, ultimately, leading to more harm. We observed him closely on bed rest and just monitored his vital signs closely - his pulse decreased, and his sensorium deteriorated during each episode. An approach we termed “masterly inactivity.”

In between spells, medications were utilized to decrease the frequency, severity, and duration of these spells. He is currently on topiramate, cyproheptadine, and oxcarbazepine.

REFERENCES
