Recurrent Episodes of Hypothermia With Psychiatric Medications: An Unsuspected Case of Primary Adrenal Insufficiency

To the Editor: Hypothermia is frequently seen in psychiatric patients.[1] In most cases, hypothermia is attributed to antipsychotic medications, which are known to predispose patients to hypothermia.[2] However, other etiologies of hypothermia are possible. The following is the case of a 64-year-old African American man with schizophrenia who presented repeatedly with life-threatening episodes of hypothermia. A diagnosis of primary adrenal insufficiency was confirmed, and appropriate therapy was instituted with resolution of hypothermia.

Case report. Mr A, a 64-year-old African American man with schizophrenia (*DSM-IV* criteria) and moderate mental retardation (total IQ: 59) residing in a personal care home and stable on treatment with mirtazapine, clonazepam, and divalproex sodium extended release (ER), exhibited significant behavioral changes in 2009. He was brought to the emergency department and found to be confused with a temperature of 94.1°F, pulse of 80 bpm, and blood pressure of 148/67 mm Hg. Laboratory findings were noncontributory. He was admitted to the intensive care unit (ICU), where his treatment included intravenous fluids and heating blankets, and his psychiatric medications were stopped. After stabilization, he was transferred to the psychiatric ward and psychiatric medications were reinstituted, and he was subsequently discharged back to the group home.

Six months later, Mr A again displayed confused behavior and was brought to the emergency department. His temperature was 90°F. Laboratory measures again were unremarkable. Both a computed tomography scan of the head and an magnetic resonance image without contrast were negative for acute intracranial pathology. After stabilization, he was transferred to the psychiatric unit. During his stay at the psychiatric unit, recurrent disorganized behavior and paranoid delusions emerged and required treatment. He received mirtazapine, clonazepam, divalproex, and, additionally, quetiapine. The day after quetiapine was added, Mr A was excessively somnolent with a temperature of 91.5°F and a blood pressure reading of 90/60 mm Hg. He was admitted to the ICU and aggressively warmed. Despite these interventions, he remained hypothermic and hypotensive. His cortisol level was checked in the morning and found to be unusually low at 7 µg/dL (normal > 20 µg/dL during acute stress). He was empirically started on oral hydrocortisone administered at 25 mg 3 times daily and gradually tapered to physiologic doses. Mr A's temperature improved, and he became hemodynamically stable. However, he did become aggressive with the discontinuation of his regular antipsychotic medications.

Upon stabilization, Mr A returned to the psychiatric unit receiving clonazepam and mirtazapine. Morning cortisol and adrenocorticotropic hormone (ACTH) levels were checked to determine a primary versus secondary cause of the adrenal insufficiency. His morning cortisol level was low at 9 µg/dL (normal range: 10–20 µg/dL). He underwent an ACTH stimulation test, which showed an inadequate increase in cortisol levels from 16 to 23 to 20 µg/dL at 0, 30, and 60 minutes after ACTH administration, respectively, with an elevated ACTH level of 86 pg/mL (normal range: 10–60 pg/mL) that is consistent with primary adrenal insufficiency. For unclear reasons, his hydrocortisone was not restarted, and, additionally, Mr A was started on benztropine, haloperidol, and divalproex sodium ER treatment and continued on mirtazapine treatment.

In the spring of 2010, Mr A developed a bradycardic pulseless electrical activity. The patient was profoundly hypothermic (91°F). A condition "C" was called, and cardiopulmonary resuscitation was undertaken twice before he was transferred to the ICU. An ACTH stimulation test was administered and reconfirmed primary adrenal insufficiency. Hydrocortisone was resumed, and, after stabilization, he was returned to the psychiatric unit. Thereafter, he tolerated oral haloperidol and haloperidol decanoate at prior doses. Mr A was subsequently discharged to the group home. A 6-month follow-up indicated no further episodes of hypothermia. His medications include hydrocortisone 15 mg in the morning and 10 mg in the evening, oral haloperidol, clonazepam, and haloperidol decanoate.

Primary adrenal insufficiency, known as Addison's disease, is a rare disorder defined as failure of both adrenal glands, occurring in up to 144 people per million population.[3,4] The disease is diagnosed by failure of the adrenal glands to produce cortisol upon stimulation with ACTH. Symptoms may include fatigue, anorexia, and hypothermia.[5] In our subject, the etiology of the adrenal insufficiency is uncertain. There was no history of prior steroid usage causing hypothalamic-pituitary-adrenal suppression, and given the elevated ACTH levels with low cortisol levels, a diagnosis of primary adrenal insufficiency was made. An autoimmune etiology was unlikely in view of the negative adrenal antibody titers. The chronic use of psychotropic medications was considered as a possible cause, and these relationships are worthy of further study.

The significance of this case is to alert physicians to consider adrenal insufficiency in their differential diagnosis of hypothermia among patients receiving psychotropic drugs. In our patient, antipsychotic drugs were initially implicated as the cause of his hypothermia, resulting in withholding of antipsychotics with psychiatric decompensation. Determination of the etiology of hypothermia followed by appropriate treatment prevented the recurrence of this life-threatening condition and eliminated further readmissions and also permitted the resumption of psychotropic medications.

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