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Central Pontine Myelinolysis in a Patient with Adrenal Insufficiency

John E. Brunner, MD*

Central pontine myelinolysis is a demyelinating process that has occurred in association with rapid correction of hyponatremia. Presented here is the case of a patient who had adrenal insufficiency and who experienced signs of central pontine myelinolysis after rapid correction of severe hyponatremia (28 mEq/L of sodium administered in the first 24 hours, initial serum sodium level 97 mEq/L). Sustained hyponatremia and the use of intravenous contrast material after hyponatremia correction are discussed as possible risk factors in the development of central pontine myelinolysis.

Central pontine myelinolysis (CPM) is a catastrophic neurologic process involving demyelination of nerve axons. When first described by Adams, Victor, and Mancall (1), CPM was thought to be related to a nutritional deficiency in alcoholic and malnourished patients. However, it is now evident that the disorder most often occurs clinically after the correction of hyponatremia (2,3). Experimentally, CPM has been produced in healthy dogs and rats after correction of vasopressin-induced hyponatremia (4,5). Histologically, lesions are characterized by the loss of myelin sheaths with relative sparing of nerve cell axons, preservation of blood vessels, and absence of inflammatory cells (1). The central pons is the major site of involvement, but extrapontine myelinolysis has been demonstrated in the thalamus, putamen, lateral geniculate body, cerebellum, and cortex (6).

CPM should be suspected in a patient whose neurologic condition deteriorates after correction of hyponatremia. This may be manifested by confusion that occurs clinically after the correction of hyponatremia (2,3). Experimentally, CPM has been produced in healthy dogs and rats after correction of vasopressin-induced hyponatremia (4,5). Histologically, lesions are characterized by the loss of myelin sheaths with relative sparing of nerve cell axons, preservation of blood vessels, and absence of inflammatory cells (1). The central pons is the major site of involvement, but extrapontine myelinolysis has been demonstrated in the thalamus, putamen, lateral geniculate body, cerebellum, and cortex (6).

Patients generally die of complications or underlying disease, and most reported cases have been described at autopsy. However, patients presumed to have CPM have survived with partial or complete recovery (7,8,12,13).

This report describes the second case of presumed CPM after correction of severe hyponatremia in a patient who had primary adrenal insufficiency (8).

Case Report

A 52-year-old, nonalcoholic woman was admitted suffering from cough, facial pain, and fever of nine days' duration. Three days before she was admitted, she experienced emesis, weakness, and postural dizziness. On admission, she received 5% dextrose in half-normal saline at 100 mL/hour and cefamandole for presumed maxillary sinusitis and dehydration. Sixteen hours after admission, laboratory studies indicated a sodium level of 102 mEq/L, a potassium level of 4.8 mEq/L, and a chloride level of 72 mEq/L. Her speech was slightly slurred, but she remained clinically stable and did not lose consciousness or have a seizure.

Thirty-six hours after admission, she was still awake and oriented, but her speech was slow. No focal neurologic findings were observed. Her temperature was 37°C; blood pressure was 90/60 mm Hg; and pulse was 100 beats per min. She had diffuse pigmentation of her skin, areola, and palmar creases. Her serum sodium level was 97 mEq/L. Findings of other laboratory tests included a creatinine level of 1.0 mg/dL, BUN level of 21 mg/dL, serum osmolality of 201 mosm/L, urine sodium value of 84 mEq/L, bilirubin value of 0.4 mg/dL, and glucose level of 120 mg/dL while she was receiving intravenous 5% dextrose solution. Hydrocortisone hemisuccinate 100 mg was administered every six hours for adrenal insufficiency.

Correction of hyponatremia was undertaken with a combination of 5% hypertonic saline and normal saline. Ten hours later, her serum sodium level was 114 mEq/L; at 24 hours, the serum sodium level was 125 mEq/L; the correction rate was 1.1 mEq/hour. During this period, she received 934 mEq of sodium and 3,000 mL of total fluids. Afterwards, the patient was alert, and her speech returned to normal. Thirty hours after therapy was started, contrast material was administered, and computed tomography of the head was undertaken to exclude an intracranial mass lesion, but no lesion was found. During this procedure, she received 300 mL of contrast material (30% iothalamate meglumine), an additional 246 mosm.

Forty-eight hours after therapy was started, the patient was disoriented as to time and place, which progressed until she became comatose. Examination revealed a flaccid quadriparesis, intermittent extensor plantar responses, weak gag
reflex, tonic left lateral gaze, and nystagmus. Her serum sodium level was 134 mEq/L. Lumbar puncture was performed, and findings of spinal fluid analysis were normal for glucose, protein, blood cell count, and pressure. Subsequent cultures and serology were negative for AFB, bacteria, and fungi. Toxicology studies for alcohol and drugs were negative, and an immediate repeat CT scan of the brain revealed no evidence of mass, hemorrhage, or infarction. Dexamethasone (10 mg) was administered intravenously followed by 4 mg every six hours.

Subsequent CT scans of the brain 19 days, 65 days, and 90 days after the onset of coma revealed no definite evidence for CPM but remained negative for infarction, mass, or hemorrhage. Brain stem auditory evoked potentials were normal; somatosensory evoked potentials demonstrated delay of the intralatency periods between high cervical to cortex potentials, consistent with brain stem dysfunction. A test for determination of myelin basic protein (MBP) was negative four weeks after onset of coma.

Primary adrenal insufficiency was substantiated by a low serum cortisol level of 1.3 g/dl and a high ACTH level of 237 pg/ml in blood obtained just before sodium correction. A three-day ACTH stimulation test was performed; the patient received dexamethasone 2 mg every 12 hours during the procedure. Final serum and urine data were: serum cortisol value, 2.5 g/dl; total 24-hour urinary 17-hydroxysteroids value, 1.8 mg; and total 24-hour urinary cortisol value, 9.5 g. Random analysis of aldosterone showed a level of less than 1.0 mg/dl. Further endocrine studies revealed normal TSH, FSH, LH, and prolactin levels, and normal sella turcica size.

The patient remained comatose for one month, and her condition was complicated by repeated aspiration of oropharyngeal contents. Thirty-six days after her admission, she began to follow objects with her eyes and made attempts to swallow. Voluntary hand and leg movements were noted after 60 days, but were severely ataxic. Her speech returned, but it was dysarthric. She has had repeated episodes of respiratory failure from aspiration pneumonitis that have required extended hospitalization.

Discussion

This is the second reported case of presumed CPM in a patient who had primary adrenal insufficiency and who underwent rapid correction of severe hyponatremia (8). Antemortem diagnosis of CPM is difficult, and the disorder cannot be absolutely differentiated from a pontine infarct. The diagnosis in this patient is based upon clinical evidence of progressive neurologic deterioration occurring after rapid correction of hyponatremia (a 28 mEq/L rise of serum sodium concentration within 24 hours). Unlike a pontine infarct, which would most likely be a sudden event, this patient had a progression of events starting with an organic brain syndrome, progressing to a flaccid quadriplegia, followed by loss of gag reflex, nystagmus, and coma without evidence of mass, infarction, or inflammatory process on CT scan of the brain or cerebral spinal fluid analysis. The abnormal somatosensory evoked potentials between the high cervical to cortex potentials are supporting evidence of brain stem dysfunction, probably involving the medial lemniscus in the pons. Normal brain stem auditory evoked potentials have been demonstrated in documented cases of CPM (14) and may be related to the variable extent of myelinolysis with some lacking extension into the more dorsilaterally located lateral lemniscus through which the brain stem auditory pathway passes. Elevations of MBP have been reported in two cases of CPM (8,15). In this case the MBP level was normal four weeks after the onset of the clinical event and probably was measured long after demyelination occurred. Failure to demonstrate a definite pontine lesion by CT does not absolutely preclude a pontine lesion. Imaging of the pons is difficult because of its deep location and the surrounding bone of the skull.

A debate exists over the appropriate, safe rate of serum sodium correction. Most authors feel that rapid correction is a precipitating factor in CPM, and this view is supported by data of dog and rat experiments (3-5). Many suggest correction rates of less than 10 mEq/L of serum sodium concentration per day; although, Ayus et al (16) advocated rapid correction within 24 hours at a rate greater than 2.4 mEq/L per hour. The latter authors were unable to demonstrate clinical CPM in seven cases of rapidly corrected hyponatremia. The overall correction rate in this patient was approximately 1.1 mEq/L per hour, with an initial 24-hour rise of 28 mEq/L in serum sodium concentration.

In addition to the rate of sodium correction, the total osmotic load from sodium chloride and contrast material must be considered. This patient received 1,680 mosm of sodium chloride within the first 24 hours, and intravenous contrast material in the immediate post-correction period added another 250 mosm. The osmotic load should not be overlooked when hyponatremia is corrected, and perhaps intravenous contrast material should not be used in the immediate post-correctional period of hyponatremia.

It is not known if patients who have adrenal insufficiency are at increased risk for the development of CPM. Sustained hyponatremia has been mentioned as a possible factor after hyponatremia correction (5). This concept is supported by the empiric observation that alcoholics, who are known to be at risk to experience CPM, also are susceptible to prolonged hyponatremia (3,17). Even the experimental models of CPM in dogs and rats had hyponatremia induced for three days before correction (4,5). Thus, patients who have adrenal insufficiency may be at increased risk to experience CPM because they are susceptible to prolonged hyponatremia (18).
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References


