Amelioration of Extrapontine Myelinolysis and Reversible Parkinsonism in a Patient with Asymptomatic Hypopituitarism

Kyoko OKADA*, Masatoshi NOMURA**, Norihiro FURUSYO*, ***, Shigeru OTAGURO*, Shigeki NABESHIMA* ***, and Jun HAYASHI* ***

Abstract

A 37-year-old woman with a history of transphenoidal surgery and gamma knife treatment for prolactinoma was admitted because of pneumoniae with hyponatremia (Na 109 mmol/l). After the careful correction of the serum sodium level within 15 mmol/l/day, the patient developed parkinsonism. MRI of the brain disclosed a signal increase in the bilateral basal ganglia on T2-weighted images, a finding consistent with extrapontine myelinolysis (EPM). Interestingly, the parkinsonism fully disappeared after the replacement therapy of hydrocortisone for adrenal insufficiency due to hypopituitarism, and MRI 5 months later showed complete disappearance of the lesions, indicating the patient had ameliorated from the EPM.

Key words: extrapontine myelinolysis, basal ganglia, reversible parkinsonism, hypopituitarism

Case Report

On March 30, 2001, a 37-year-old woman was admitted to the nearest hospital because of a continuous cough and high fever. Her past history revealed that she had transphenoidal surgery for a prolactinoma at 29 years of age and medication with bromocriptine mesylate for residual adenoma and galactorrhea had been done in the gynecology department of our hospital for three years until gamma knife treatment was done at the age of 34 (a dose of 20 Gy). During the follow-up period, her anterior pituitary function had not been analyzed. Acute pneumoniae was diagnosed and she was treated with antibiotics (sulbactam sodium/cefoxeraz sodium), but her condition did not improve. From March 30 to April 11, 2,000 ml per day of Lactec (containing Na 130 mmol/l) was injected because of appetite loss and diarrhea. An analysis of blood chemistry including sodium had not been done since the admission day until April 11 when she became lethargic and developed adynamia. On April 11, laboratory studies showed hyponatremia [sodium (Na') 109 mmol/l]. She was referred to our hospital because of lethargy and adynamia due to hyponatremia (Na 109 mmol/l) on April 11, 2001.

She was drowsy, and the Glasgow coma scale for the level of consciousness was eleven. Physical examination revealed a normal heart rate of 80 beats per minute. Body temperature was 38.4°C and blood pressure was 88/44 mmHg. Deep tendon reflex was depressed, and no Babinski sign was noted. Laboratory data showed electrolyte abnormalities, with Na' 109 mmol/l, chloride (Cl') 73 mmol/l, and potassium (K') 2.7 mmol/l, an osmotic abnormality of 229 mOsm/kg, and a high concentration of C-reactive protein. Chest X-ray showed abnormal infiltration of the right lower lung. After the initiation of Clarithromycin, the respiratory symptoms immediately disappeared and body temperature became normal. No hypoxic event or other identifiable cause for the neurological symptoms was noted during the time while the patient was being followed. MRI scanning of the brain on hospital day 2 (Fig. 1) was done to search for abnormalities that might explain the lethargy and adynamia. It showed a pituitary tumor on the sella turcica, but this tumor had not changed since the previous MRI in October 1997. There were no other abnormal findings.

From *the Department of General Medicine, Kyushu University Hospital, Fukuoka, **the Department of Medicine and Bioregulatory Science, Graduate School of Medical Sciences and ***, the Department of Environmental Medicine and Infectious Disease, Faculty of Medical Sciences, Kyushu University, Fukuoka

Received for publication July 23, 2004; Accepted for publication February 21, 2005

Reprint requests should be addressed to Dr. Kyoko Okada, the Department of General Medicine, Kyushu University Hospital, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582

Internal Medicine Vol. 44, No. 7 (July 2005) 739
Treatment for hyponatremia was initiated with a fluid containing 0.9% percent sodium chloride, supplemented with K⁺ at a rate of 150 ml per hour. In order to avoid myeloneuropathy, the correction of the hyponatremia was aimed at a rate of 1 mmol/l/h. The serum sodium level was 115 mmol/l after 6 hours, at which time the intravenous fluid was changed to 0.45% sodium chloride. After 16 hours, the serum sodium concentration increased to 120 mmol/l. Infusion of the same fluid was continued, and 28 hours after the start of administration the serum sodium level was 124 mmol/l. In three days, her general condition seemed to improve; she became cooperative, and was able to talk.

On hospital day 4 after the correction of the hyponatremia, she developed a mask-like face, bradykinesia, dysarthria, and an intermittent resting tremor. Neurological examination showed a marked reduction of voluntary movements as well as gait disturbance. Pseudobulbar palsy consisting of dysarthria and extrapyramidal signs consisting of resting tremor and cogwheel rigidity were also noted. No other neurological findings, such as pyramidal signs, were observed. These symptoms and physical examination suggested parkinsonism. EEG done on hospital day 7 showed moderate voltage and a diffuse δ, θ bursts, which suggested there was diffuse brain dysfunction. A second MRI done on hospital day 12 revealed increased symmetrical signals in the bilateral basal ganglia; however, no abnormal signals in the pons (Fig. 2A, 2B), which was compatible with extrapontine...
myelinolysis (EPM). The symptoms gradually improved without any anti-parkinsonian drugs.

After the sodium level rose up to the normal range, the endocrinological dynamic tests were performed. The basal levels of ACTH and cortisol were below the normal range. The response of ACTH was delayed and relatively hyper-reactive. ACTH tolerance test showed the induction of cortisol secretion was insufficient. CRH and TRH tolerance test revealed that the response of the LH, FSH and TSH was far below from the normal range. These data suggested not only pituitary insufficiency but hypothalamic dysfunction leading to hypopituitarism. Therefore, the replacement therapy of cortisol was begun. Interestingly, parkinsonism improved rapidly after the replacement of cortisol. All symptoms and EEG were almost completely normal within about one month. A third follow-up MRI 5 months later showed improvement of the lesion in the bilateral basal ganglia (Fig. 3). The patient is being followed as an outpatient and remained asymptomatic as of January 2004.

**Discussion**

Central pontine and extrapontine myelinolysis (CPM, EPM) are demyelinating diseases. CPM was first described by Adams et al (1) in 1959 in alcoholic patients shortly after intravenous medications began to be widely administered. EPM, which locates outside the pons, is later found in approximately 10–30% of patients with CPM (2). The introduction of CT and MRI has resulted in more cases of EPM being diagnosed, particularly mild or asymptomatic cases.

The initial manifestations of CPM are usually mutism and dysarthria. On the other hand, among the various clinical symptoms of EPM are ataxia and abnormal behavior. When CPM and EPM occur together, combined symptoms are exhibited (3). In the present case, parkinsonism was the clinical manifestation of EPM. To date, only two such patients with parkinsonism have been reported in the literature (4, 5). To our surprise, in all three, EPM occurred after transsphenoidal surgery for pituitary adenoma. Laws et al reported that the incidence of iatrogenic hypopituitarism occurring after transsphenoidal surgery in patients harboring pituitary adenoma is less than 3% (6). However, it seems reasonable to suppose that the neurosurgical treatment in these three cases could have caused subclinical hypopituitarism and in the case of severe infection, if might result in overt hypopituitarism and severe hypopituitarism.

The mechanism of CPM / EPM is not well understood. Increasing clinical and experimental evidence has shown it to be associated with changes in the serum sodium, especially after rapid correction of hyponatremia. It is not clear whether myelinolysis occurs because of the rapid change in osmolality or is related to the sodium ion itself (7). Hyperosmolality due to hyperglycemia can cause myelinolysis (8), indicating that this process may be related to the osmotic gradient rather than to the sodium ion itself.

Sterns et al (9) also demonstrated experimental findings that patients who had been hyponatremic for more than 48 hours before treatment were more likely to develop myelolytic lesions than were those whose hyponatremia had been of shorter duration. They have shown that the brain uses several mechanisms to avoid severe edema during hypotremia and that once the brain adapts to hypotremia, it is not well protected from the osmotic stress that accompanies correction of the condition (9, 10). This is the first case report of myelinolysis related to hypopituitarism. Chronic and mild hypotremia likely preexisted, and the hypopituitarism became aggravated following the pneumoniea that was a stress to such a patient.

It has been said that once myelinolysis occurs, there is no chance of recovery. However, in the subacute phases of myelinolysis, CPM/EPM may be less severe and better defined, which probably reflects the resolution of edema remyelination (11), and in those cases, successful treatment and decreased morbidity are still possible. With the assumption that undefined myelinotoxic compounds contribute to the demyelinating process in CPM/EPM and they are similar in this regard to patients with immune-mediated demyelination, some authors have reported complete recovery after steroid administration (12, 13). Because the present patient completely recovered from EPM just after the induction of the cortisol for hypopituitarism, it seems reasonable to assume that she had only the subacute phase of EPM which can be detected by MRI T2-weighted images and that

![Figure 3. About 5 months after the correction of hyponatremia, the lesion seen in the previous MRI (2B) had almost completely disappeared.](image-url)
cortisol could help to reduce myelin swelling.

We reported a case of EPM related to hypopituitarism. It seems feasible that preexisting adrenal insufficiency might have increased the risk of myelin damage. Before starting correction for hyponatremia, the duration and the degree of hyponatremia must be taken into account.

References