Shimane J. Med. Sci., Vol.15 pp. 1-3, 1997

A CASE OF NONKETOTIC HYPEROSMOLAR COMA WITH PONTINE AND EXTRA-PONTINE MYELINOLYSIS ON MAGNETIC RESONANCE IMAGING

Kazunori OKADA, Shotai KOBAYASHI, Naoto KONO, Shingo YAMAGATA and Shuhei YAMAGUCHI

Department of Internal Medicine III, Shimane Medical University, Izumo 693, Japan

(Accepted May 13, 1997)

We present a patient with nonketotic hyperosmolar coma who exhibited extra-pontine myelinolysis as demonstrated by the findings including magnetic resonance imaging (MRI). The lesions appeared as widespread symmetrical hyperintensities that involved the subcortical white matter of the frontal, temporal, and parietal lobes. Thinning of the cerebral cortices was observed. The center of the pons was only slightly affected. The patient ultimately died of pneumonia. The abrupt changes in serum sodium concentration and/or osmolarity, induced not only by treatment of hyponatremia, but by alteration to the hypernatremic state, may have contributed to the development of pontine and extra-pontine myelinolysis. To our knowledge, this is the first case in which the MRI results corresponded to previously reported autopsy findings of extra-pontine form by Okeda *et al.* in pontine and extra-pontine myelinolysis.

Key words: Hyperglycemia / Hypernatremia / Central pontine myelinolysis

Pontine and extra-pontine myelinolysis (PEPM) is a well known osmotic demyelination syndrome that occurs usually after rapid correction of hyponatremia (1,2). Myelinolysis also occurs in the absence of hyponatremia and several reports have noted an association with hypernatremia and hyperosmolality (3-5). Although PEPM has become a more widely recognized entity owing to magnetic resonance imaging (MRI), there is few report concerning PEPM associated with hypernatremia and hyperosmolality. We describe a patient with nonketotic hyperosmolar coma who exhibited extra-pontine myelinolysis on MRI.

CASE REPORT

A 76-year-old Japanese woman was admitted to our hospital in a coma associated with hyperglycemia (977 mg/dl) and hypernatremia (192 mEq/l). She had a history of cerebral lacunar infarction detected by MRI. She had been treated at another hospital for atherosclerotic occlusive disease, and had received total parenteral nutrition since 7 days ago. She showed tremors on extremities and nystagmus for 3 days before admission and developed consciousness disturbance on the admission day. Physical examination revealed blood pressure of 70/50 mm Hg; her pulse was regular at 100 beats per minute. Skin turgor was diminished. Examination of the neck and chest revealed no abnormalities. Neurological examination revealed a state of deep coma with roving eye movements and tetraplegia. The deep tendon reflexes were diminished in the upper extremities but normal in the lower extremities. Plantar reflexes exhibited a normal response. Laboratory data (Table.1) showed no ketonuria, with the presence of hyperglycemia and hypernatremia. The blood urea nitrogen was elevated.

A computed tomogram (CT) of the brain on admission showed no abnormality except for "old" cerebral lacunae. Nonketotic hyperosmolar coma was diagnosed, and insulin and fluid therapy were instituted. The blood glucose level returned to normal within 3 days, but it took more than 7 days for the serum sodium level to return to normal (Fig. 1). Auditory brain stem responses (ABR) showed normal latencies on day 7. Despite a correction of the glucose and electrolyte imbalances, the patient remained comatose.

On hospital day 23, T2 weighted image on magnetic resonance imaging (MRI) showed widespread symmetrical hyperintensities involving subcortical white matter on the frontal, temporal and parietal lobes and

Table 1. Laboratory data on admission

Urinalysis	
Specific Gravity	1020
Sug	(4+)
Prot	(−)
Occ	(−)
Ketone	(−)
Hematology	
WBC	17800/μl
RBC	420X10⁴/μl
Hb	13.2 g/dl
Ht	40.5 %
Plt	11.7X10⁴/μl
PT	93.4 %
Fib	276 mg/dl
FDP	1.5 μg/ml
Chemistry	
TP	4.9 g/dl
Alb	2.2 g/dl
GOT	46 IU/l
GPT	54 IU/l
LDH	538 IU/l
ALP	68 IU/l
rGT	63 IU/l
ChE	142 IU/l
Amy	473 IU/l
TCHO	73 mg/dl
BUN	77 mg/dl
Cr	1.6 mg/dl
Na	192 mEq/l
K	3.4 mEq/l
Cl	146 mEq/l
Ca	9.2 mg/dl
UA	7.3 mg/dl
CK	124 IU/l
Posm	441.7 mOsm/l
BS	977 mg/dl
HbA1c	8.8 %
CRP	0.7 mg/dl
ESR	5 mm/hr
Blood gas analysis	
pH	7.386
pO2	67.2 mmHg
pCO2	35.1 mmHg
BE	−4.0 mmol/l

Correspondence : Kazunori Okada, M. D., Department of Internal Medicine III, Shimane Medical University, 89-1 Enya-cho, Izumo 693, Japan. Tel 0853-23-2111 Fax 0853-21-8483

a thinning of the cerebral cortices. High-intensity lesions were also distributed on the corpus callosum, anterior cerebral commissure, the external and internal capsules, the fornix cerebri, and the cerebellum. The high-intensity lesions observed in the center of pons were a trivial changes compared with those seen in the white matter (Fig.2). T1 weighted image showed only the pre-existing lacunae. Single photon emission tomography (SPECT) using hexamethyl propylene amine oxide (99mTc-HMPAO) revealed areas of hypoperfusion throughout, except in the cerebellum and occipital lobe (Fig.3). Follow-up MRI after three months revealed persistent high-intensities on subcortical white matter, ventricular dilatation, and an increase in the periventricular high-intensities. The patient did not recover from the coma, and died of pneumonia 6 months later. An autopsy was not performed.

COMMENTS

The diabetic nonketotic hyperosmolar state is characterized by severe hyperglycemia, hyperosmolarity and dehydration in the absence of ketoacidosis. Etiologic factors include infectious disease, cerebrovascular hemorrhage, myocardial infarction, pancreatitis, uremia with nausea and vomiting, and iatrogenic causes such as the administration of total parenteral nutrition (6). The disorder is associated with a high mortality rate (7). Pinies *et al*. (8) reported that mortality was correlated with a history of cardiovascular disease, older age, low blood pressure, low plasma levels of sodium and bicarbonate, elevated plasma pH and uremia. While we were able to sustain the patient's life, she failed to regain consciousness. Despite a normalization of the metabolic findings, she remained comatose because of severe cortical and subcortical damage. Her brainstem functions were relatively preserved as shown by ABR findings.

Involvement of the white matter is characteristic of infection, neoplasm and multiple sclerosis. MRI findings in patients with infection or neoplasm differ from those in our case. Multiple sclerosis (MS) produces patchy demyelinations (plaques) on the corpus callosum and periventricular white matter, but such extensive demyelination as seen in our case would be unusual in MS. MRI findings in our patient suggested pontine and extra-pontine myelinolysis (PEPM); this combination was reported by Wright *et al*. (1). Okeda *et al*. (3) reported extra-pontine lesions with a characteristic localization in three autopsied cases; the lesions occurred mainly in the bundles of myelinated fibers in the gray matter and in the white matter surrounded by massive gray matter. They referred to one case, which was devoid of central pontine myelinolysis (CPM), as the "extra-pontine form." Gocht and Colmant (4) reported 58 autopsied cases of PEPM, and classified this condition into three subtypes: CPM, in which the lesion was confined to the pons (27 cases), CPM combined with extra-pontine myelinolysis (18 cases), and exclusively extra-pontine myelinolysis (13 cases). These investigators emphasized that the incidence of extra-pontine lesions in their study was more frequent and widespread than had been previously reported in the literature.

Since the advent of MRI, numerous cases of CPM and PEPM have been reported (9-13). Some of these patients manifested a combination of CPM and extra-pontine myelinolysis with involvement of the basal ganglia and thalamus(9,10). Ikeda *et al*. (13) reported a patient with CPM and occipital subcortical involvement. All of these cases showed a rapid improvement of hyponatremia. Case reports of MRI findings of hyperglycemic patients are rare, but autopsied cases with hypernatremia and hyperglycemia have been reported (3-5). Investigators have suggested that, in both hyponatremic and hypernatremic states, the significant event may be a marked, rapid increase in serum sodium or in serum osmolarity (2,5). This theory is supported by results of animal experiments (14).

In our patient the hypernatremia was gradually

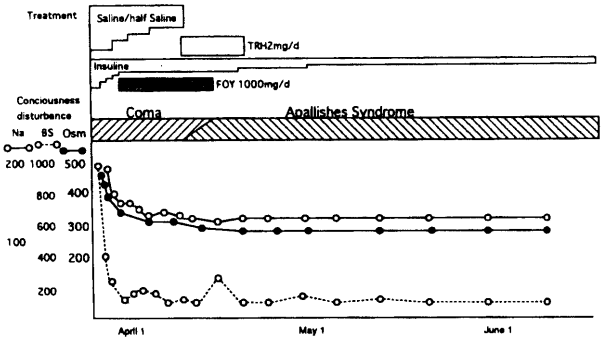

Fig. 1. Clinical course.

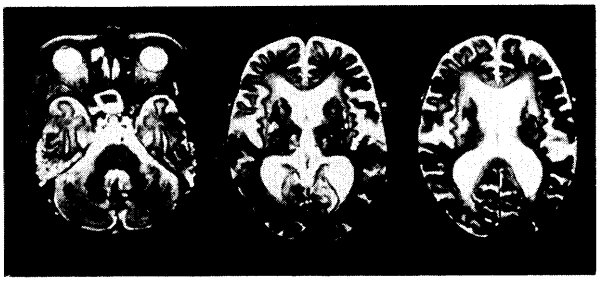

Fig. 2. T2 weighted image (TR 3500 msec, TE 120 msec) of 1.5 Tesla MRI on day 23 shows widespread symmetrical hyperintensities involving the subcortical white matter of all but the occipital lobe, with thinning of the cerebral cortices. High-intensity lesions also were distributed on the white matter in the cerebellum. High-intensities on the center of pons were trivial compared with those seen in white matter. Pre-existing lacunar lesions on the basal ganglia and periventricular high-intensity areas that were seen on an earlier MRI study were detected.

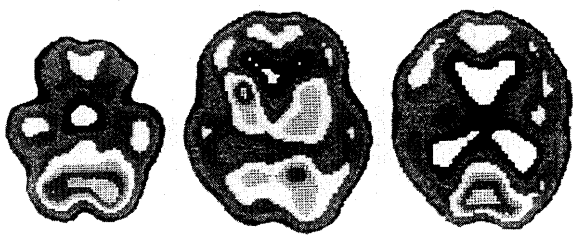

Fig. 3. 99mTc-HMPAO SPECT on day 25 revealed areas of hypoperfusion throughout the whole brain except the cerebellum and occipital lobe.

improved over 7 days, but the consciousness disturbance persisted despite the metabolic correction. A delayed restoration of consciousness may be common in patients with nonketotic hyperosmolar coma because of the presence of demyelinated white matter lesions.

REFERENCES

1) Wright DG, Laureno R and Victor M (1979) Pontine and extra-pontine myelinolysis. *Brain* 102:361-385.
2) Norenberg MD, Leslie KO and Robertson AS (1982) Association between rise in serum sodium and central pontine myelinolysis. *Ann Neurol* 11:128-138.
3) Okeda R, Kitano M, Sawabe M, Yamada I and Yamada M (1986) Distribution of demyelinating lesions in pontine and extra-pontine myelinolysis - three autopsy cases including one case devoid of central pontine myelinolysis. *Acta Neuropathol (Berl)* 69:259-266.
4) Gocht A and Colmant HJ (1987) Central pontine and extra-pontine myelinolysis: a report of 58 cases. *Clin Neuropathol* 6:262-270.
5) McComb RD, Pfeiffer RF, Casey JH, Wolcott G and Till DJ (1989) Lateral pontine and extra-pontine myelinolysis associated with hypernatremia and hyperglycemia. *Clin Neuropathol* 8:284-288.
6) Lorber D (1995) Nonketotic hypertonicity in diabetes mellitus. *Med Clin North Am* 79:39-52.
7) Wachtel TJ, Tetu-Mourddjian LM and Goldman DL (1991) Hyperosmolarity and acidosis in diabetes mellitus: a three year experience in Rhode Island. *J Gen Intern Med* 6:495-502.
8) Pinies JA, Cairo G, Gaztambide S and Vazquez JA (1994) Course and prognosis of 132 patients with diabetic nonketotic hyperosmolar state. *Diabete Metab* 20:43-48.
9) Rippe DJ, Edwards MK, D'Amour PG, Holden RW and Roos KL (1987) MR imaging of central pontine myelinolysis. *J Comput Assist Tomogr* 11: 724-726.
10) Dickoff DJ, Raps M and Yhar MD (1988) Striatal syndrome following hyponatremia and its rapid correction; a manifestation of extra-pontine myelinolysis confirmed by magnetic resonance imaging. *Arch Neurol* 45:112-114.
11) Thompson AJ, Brown MM, Swash M, Thakkar C and Scholtz C (1988) Autopsy validation of MRI in central pontine myelinolysis. *Neuroradiology* 30: 175-177.
12) Thompson PD, Miller D, Glendhill RF and Rossor MN (1989) Magnetic resonance imaging in central pontine myelinolysis. *J Neurol Neurosurg Psychiatr* 52:675-677.
13) Ikeda M, Takahashi K, Matsunaga T and Tsukagoshi H (1994) Reversible white matter lesions in a patient with fulminant hepatitis and acute renal failure. *Intern Med* 33:360-362.
14) Rojiani AM, Prineas JW and Cho ES (1994) Electrolyte-induced demyelination in rats. *Acta Neuropathol (Berl)* 88:287-292.