Case Report

Extrapontine Myelinolysis in Preoperative Sellar Region Tumor: Report of Two Cases

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This manuscript was presented at Annual Meeting of the Neurological society of Thailand, March 2009
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Osmotic demyelination syndrome (ODS) is a well-known disorder caused by rapid correction of serum sodium. Many conditions including hormonal abnormality are associated with this syndrome. The authors describe two cases of preoperative sellar region tumor associated with hypopituitarism and secondary adrenal insufficiency. These two patients had hyponatremia. Neurological manifestations in both of them were generalized dystonia. Magnetic resonance imaging (MRI) revealed a characteristic extrapontine myelinolysis (EPM). The first case was a 35-year-old man with craniopharyngioma who developed generalized dystonia after rapid correction of hyponatremia. The second case was a 24-year-old man with gonadotroph pituitary adenoma who developed generalized dystonia, dysarthria, and dysphagia in the course of hyponatremia. Hormonal changes will cause fluctuation in hyponatremia and correction of hyponatremia, even if the recommended rate may be hazardous and will promote ODS. Patients with sellar region tumors are at risk of developing ODS and correction of hyponatremia in these cases should be closely monitored.

Keywords: *Extrapontine myelinolysis, Sellar region tumor, Generalized dystonia, Hypopituitarism, Adrenal insufficiency*

J Med Assoc Thai 2009; 92 (11): 1548-53
Full text. e-Journal: *http://www.mat.or.th/journal*

Osmotic demyelination syndrome (ODS) is characterized by selective destruction of myelin sheath at the basis pontis (central pontine myelinolysis, CPM)[1] or destruction of myelin outside the pons (extrapontine myelinolysis, EPM)[2]. Clinical features of the syndrome vary from asymptomatic to full-blown neurological deficits in the affected central nervous system. ODS is usually related to a rapid correction of hyponatremia. Other associated conditions include chronic alcoholism, malnutrition, debilitating diseases, post hepatic transplantation, and hormonal disturbance[3-7]. Magnetic resonance imaging (MRI) is a diagnostic test of choice in ODS[2]. Characteristic imaging features include symmetrical hyperintensity on T2 weighted image (T2WI) within the pons in typical CPM or symmetrical hyperintensity on T2 weighted image within caudate and putamen, sparing globus pallidus in EPM[2]. The most common hormonal disturbances related to ODS are secondary adrenal insufficiency and inappropriate antidiuretic hormone (ADH) secretion[6-9]. These hormonal changes usually occur in the setting of panhypopituitarism secondary to sellar and parasellar tumors[8-10]. Interestingly most of ODS related to hormonal disturbances in sellar-parasellar tumors occur postoperatively. The authors reported two cases of sellar region tumors that developed generalized dystonia associated with EPM during the preoperative period.

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Case Report

Case 1

A 35-year-old unemployed man with paranoid schizophrenia presented with delusion and paranoid 7 months before this admission at King Chulalongkorn Memorial Hospital. He had been treated with clozapine and trihexyphenidyl. One month later, he developed diffuse headache, low-grade fever, and vomiting. One

month after the onset of headache, he went to a district hospital. Physical examination disclosed neck stiffness and the results of lumbar puncture were as follow: open pressure /close pressure of 20/19 cmH_2O, white blood cell count 1013 cells/$mm^3$with 74% lymphocyte and 26% neutrophil, protein 101 mg%, cerebrospinal fluid (CSF) glucose/plasma glucose 59/98 mg%. AFB stain, Gram stain, India ink preparation, as well as CSF culture for bacteria and fungus detected no organisms. Tuberculous meningitis was diagnosed and anti-tuberculous drugs were started and continued for 4 months. Two months before admission, the headache did not improve and he became drowsy and confused. Elevated liver enzyme and hyponatremia were detected. Drug induced hepatitis was diagnosed and antituberculous drugs were changed. Serum sodium was corrected from 123 to138 mmol/L within one day. His consciousness improved but he could not resume his activity of daily living. Two weeks before this admission, he became drowsy again. Physical examination revealed hypotension and generalized dystonia. His electrolytes were in normal limit. CT scan of the brain revealed isodense mass at suprasellar region with chronic and acute hemorrhage in the mass. Hormonal evaluation revealed: FT4 0.629 ng/dl (0.8-1.8 ng/dl), FT3 1.49 pg/ml (1.6-4.0 pg/ml), TSH 1.44 uIU/ml (0.3-4.1 uIU/ml), his serum morning cortisol was 11.4 ug%(definite adrenal insufficiency < 3 ug%, undetermined 3-18 ug% and exclude if > 18 ug%). Shock from adrenal insufficiency was suspected and the patient dramatically responded to corticosteroid therapy. Hormonal replacement therapy for secondary hypothyroidism and secondary adrenal insufficiency consisted of thyroxin 0.1ug/day and prednisolone 10 mg/day. The patient regained consciousness but abnormal movement persisted. Neurological examination revealed generalized dystonia and generalized brisk deep tendon reflexes. MRI of the brain showed gadolinium enhancing suprasellar mass extended anteriorly to part of the third ventricle (Fig. 1A). Symmetrical hypersignal intensity lesions in the caudate and putamen with pallidal sparing in T2WI compatible with extrapontine myelinolysis were also detected. (Fig. 2A). Craniectomy and nearly total removal of the tumor was performed. Pathological diagnosis of the tumor was craniopharyngioma WHO class I. Eleven days after the surgery, he developed diabetes insipidus (DI) and nasal spray desmopressin acetate was added. Unfortunately, he expired from aspirated pneumonia.

Case 2

A 24-year-old man had a two-week history of severe vomiting and myalgia. He had neither abdominal pain nor headache. The vomiting subsided after taking antiemetic but myalgia persisted. He developed psychomotor retardation and could not perform his regular work one day after the vomiting. Three days later, he had a brief episode of syncope and was hospitalized. Physical examination and all routine biochemistry were unremarkable except for low level of serum sodium of 133 mmol/L (135- 145 mmol/L). Intravenous fluid was given and his general condition improved. Two days after the hospitalization he developed delirium. A single dose of intramuscular haloperidol was given. Delirium resolved on the next

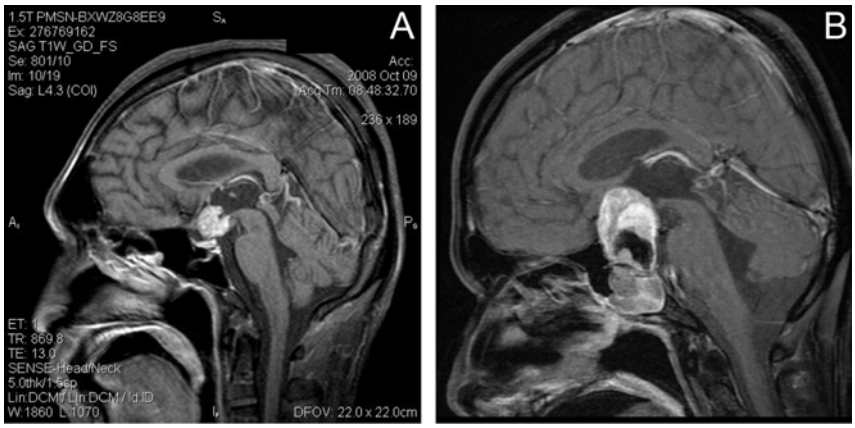

Fig. 1 MRI T1W galdolinium enhancement showed (A) galdolinium enhancing craniopharygioma extended to anterior part of the third ventricle. (B) galdolinium enhancing gonadotroph pituitary adenoma extended to suprasellar region

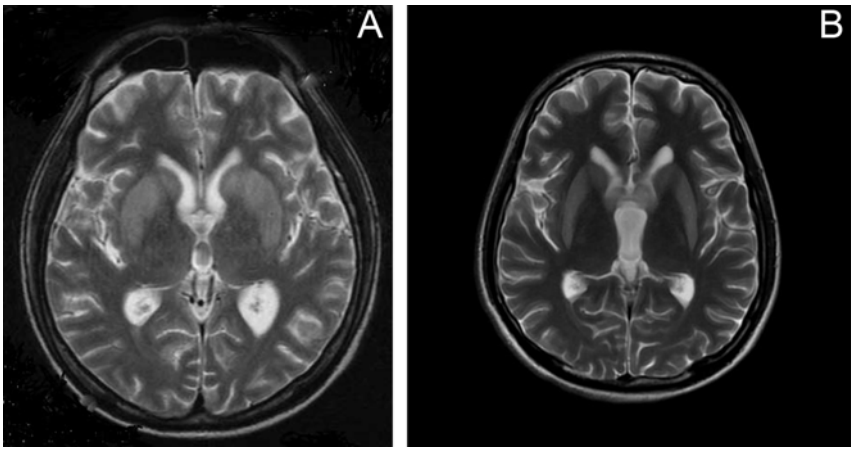

Fig. 2 MRI T2WI of case 1 (A) and case 2 (B) showed symmetrical hypersignal intensity lesions at caudate and putamen with pallidal sparing

day but mild generalized dystonia occurred. He was discharged without any medication. Eight days after the onset of the illness, the generalized dystonia deteriorated and dysarthria as well as dysphagia were observed. CT scan of the brain revealed a sellar mass with homogeneous enhancement. He was referred to King Chulalongkorn Memorial Hospital for further management.

General physical examination was unremarkable. Neurological examination revealed an alert young man with severe generalized dystonia, dysphagia, dysarthria, and normal deep tendon reflexes. Other neurological examinations were limited by severe dystonia. MRI of the brain depicted a well defined round shape gadolinium enhancing sellar mass extending to the suprasellar region in T1 weighted image (Fig. 1B). Symmetrical hypersignal intensity lesions in the caudate and putamen with pallidal sparing in T2WI were compatible with extrapontine myelinolysis (Fig. 2B). The laboratory testing showed serum FT4 of 0.69 ng/dl (0.8-1.8 ng/dl), FT3 of 0.33 pg/ml (1.6-4.0 pg/ml), TSH of 0.41 uIU/ml (0.3-4.1 uIU/ml), morning cortisol of 2.3 ug% (definite adrenal insufficiency < 3 ug%, undetermined 3-18 ug% and exclude if > 18 ug%) and prolactin of 1.7 ng/ml (2-25 ng/ml). Panhypopituitarism from a pituitary tumor with secondary adrenal insufficiency and secondary hypothyroidism were diagnosed. Hormonal supplements, consisting of thyroxin 0.1 ug/day and prednisolone 7.5mg/day, were started. Lioresal and trihexyphenidyl were prescribed for generalized dystonia and were titrated up to 30 mg and 14 mg per day, respectively.

Transphenoidal pitutitary tumor resection was performed and the pathological diagnosis was gonadotroph pituitary adenoma. Generalized dystonia was markedly improved and mild dystonia of the right hand was detected at 6 months follow-up.

Discussion

ODS was first described under the term "central pontine myelinolysis or CPM" in 1959[1]. Extrapontine myelinolysis (EPM) with similar pathology in the basal ganglia, thalamus, and subcortical white matter was added in 1962[2]. ODS includes CPM, EPM, and other osmotic demyelinating lesions *i.e.* cerebral cortical sclerosis and posterior column involvement, which have been linked to CPM and EPM[2]. In ODS the relative proportions of CPM, EPM and CPM with EPM were 50%, 30% and 20% respectively[2]. Pathophysiology of ODS was not well understood. However, correlation between ODS and rapid correction hyponatemia were documented in clinical as well as animal experimental studies[8,9]. Currently, myelinolytic lesion is believed to be the result of osmotic change rather than electrolyte imbalance[8,9]. ODS has also been reported in diseases that are predisposed to the genesis of hyponatremia and osmotic change including chronic liver disease, post hepatic transplant, malnutrition, debilitating diseases, burns, and hormonal disturbances[3-7]. Hormonal disturbances associated with ODS include hypopituitarism[10], adrenal insufficiency[7,8], and inappropriate antidiuretic hormone (ADH)[6] secretion. The most common situation in which ODS associated with hormonal disturbances is postoperative pituitary tumor resection[6,9]. Even in

this situation, hormonal disturbances are usually accompanied with prolongation, fluctuation, or rapid correction of hyponatremia. Clinical manifestations of CPM consisting of coma, locked-in syndrome, quadriparesis, dysphagia, dysarthria, diplopia, ataxia, and pseudobulbar syndrome[11]. These clinical syndromes have clinicopathological correlation with pontine lesions[1]. On the other hand, EPM has diverse clinical presentations including progressive dystonia[12], parkinsonism[7,13], spastic paralysis[13], dysarthria[1], confusion, and abnormal behavior[2]. The variations in these syndromes are due to a wide spread lesion involving the basal ganglia, thalamus, subcortical white matter, and cerebellum in EPM[1,7]. MRI is the neuroimaging of choice in ODS. In CPM, MRI T2-WI shows hypersignal intensity at the basis pontis. In EPM, MRI reveals hypersignal intensity changes in the basal ganglia, thalamus, subcortical white matter, and cerebellum with typical pallidal sparing[1,7]. The sparing of globus pallidus can differentiate EPM from other systemic and metabolic disorders[14] *e.g.* hypoxemia, carbon monoxide poisoning, Wilson's disease, and Leigh's disease[7].

Both cases in the present report presented with generalized dystonia and MRI were compatible with EPM. The first case of craniopharyngioma had a strong evidence of rapid correction of hyponatremia. However, the second case of gonadotrophpituitary tumor had only mild hyponatremia. In the first case, hypoadrenalism was suggested by a dramatic response of shock to corticosteroid therapy while in the second case, low level of morning cortisol was documented. Hypopituitarism may affect sodium homeostasis via the mechanism of secondary adrenal insufficiency. In normal physiology, cortisol exerts a physiologic tonic inhibitory effect on ADH secretion[15]. ADH physiologically controls reabsorption of water from extracellular compartment to intravascular compartment, and results in relative reduction in serum sodium. Hypopituitarism with secondary adrenal insufficiency results in ADH hypersecretion with consecutive renal water retention and hyponatremia[15]. The fluctuation in hormonal level due to pituitary tumor will cause unpredictable fluctuation in serum sodium. Even the recommended or slower than recommended rate of sodium correction can promote ODS[8,15]. In the second case, hyponatremia was not overt and there was no detail of the correction of fluid and electrolyte imbalance. ODS in the present case may be related to fluctuation of serum sodium during the intravenous fluid infusion and hormonal effect. According to the literature review, most cases of ODS associated with pituitary tumor and hypopituitarism with secondary adrenal insufficiency, usually occurred postoperatively. However, both of these presented cases developed ODS preoperatively. It should be concluded that ODS related to pituitary tumor, hypopituitarism and secondary hypoadrenal insufficiency can occur in the perioperative period and careful management of hyponatremia as well as close monitoring of serum sodium level are advocated.

Treatment of ODS are mainly supportive and symptomatic. High dose corticosteroid had been used in a case of pituitary adenoma with hypopituitarism and CPM, which occurred after surgical removal of the tumor[16]. The investigator claimed a dramatic clinical response in this case[16]. However, cortico-steroid replacement in panhypopituitarism can be complicated by ODS due to rapid change in sodium homeostasis and careful correction as well as critical monitoring of serum sodium should be advocated if rapid correction of hypopituitarism with cortico-steroid was planned[9]. The overall prognosis of ODS varies from complete recovery, minimal to severe disability and death[1,2]. The prognostic outcomes of movement disorders related to EPM were also varied from resolution of the syndrome within four months to permanent abnormal movements[2]. Extent of lesion detected from initial MRI was not correlated with clinical outcomes. Follow-up MRI could not predict the final outcome as well and some cases that had persistent MRI abnormality in spite of complete clinical recovery[17]. The first case in the present report died from aspirated pneumonia within one month after ODS while the second case had a mild right hand focal dystonia and had been successfully treated with trihexyphenodyl and lioresal during the 6 months follow up period.

Conclusion

The authors report two cases of EPM related with hypopituitarism and secondary adrenal insufficiency occurred before the operation of sellar region tumors. The sellar region tumors are a risk of ODS during the perioperative period. Careful corticosteroid replacement therapy and correction of hyponatremia as well as a close monitoring of serum sodium are the Keyes practical issue for the prevention of ODS in this situation.

References

1. Adams RD, Victor M, Mancall EL. Central pontine myelinolysis: a hitherto undescribed disease

occurring in alcoholic and malnourished patients. AMA Arch Neurol Psychiatry 1959; 81: 154-72.
2. Martin RJ. Central pontine and extrapontine myelinolysis: the osmotic demyelination syndromes. J Neurol Neurosurg Psychiatry 2004; 75 (Suppl 3): iii22-8.
3. Laureno R, Karp BI. Myelinolysis after correction of hyponatremia. Ann Intern Med 1997; 126: 57-62.
4. Huq S, Wong M, Chan H, Crimmins D. Osmotic demyelination syndromes: central and extrapontine myelinolysis. J Clin Neurosci 2007; 14: 684-8.
5. Yu J, Zheng SS, Liang TB, Shen Y, Wang WL, Ke QH. Possible causes of central pontine myelinolysis after liver transplantation. World J Gastroenterol 2004; 10: 2540-3.
6. Sata A, Hizuka N, Kawamata T, Hori T, Takano K. Hyponatremia after transsphenoidal surgery for hypothalamo-pituitary tumors. Neuroendocrinology 2006; 83: 117-22.
7. Sajith J, Ditchfield A, Katifi HA. Extrapontine myelinolysis presenting as acute parkinsonism. BMC Neurol 2006; 6: 33.
8. Pradhan S, Jha R, Singh MN, Gupta S, Phadke RV, Kher V. Central pontine myelinolysis following 'slow' correction of hyponatremia. Clin Neurol Neurosurg 1995; 97: 340-3.
9. Choe WJ, Cho BK, Kim IO, Shin HY, Wang KC. Extrapontine myelinolysis caused by electrolyte imbalance during the management of suprasellar germ cell tumors. Report of two cases. Childs Nerv Syst 1998; 14: 155-8.
10. Lasheen I, Doi SA, Al Shoumer KA. Glucocorticoid replacement in panhypopituitarism complicated by myelinolysis. Med Princ Pract 2005; 14: 115-7.
11. Defebvre L, Rogelet P, Destee A, Verier A. Regressive dystonia and cerebellar ataxia: two unusual symptoms in central pontine myelinolysis. J Neurol 1995; 242: 450-4.
12. Yoshida Y, Akanuma J, Tochikubo S, Hoshi A, Matsuura Y, Homma M, et al. Slowly progressive dystonia following central pontine and extra-pontine myelinolysis. Intern Med 2000; 39: 956-60.
13. Wright DG, Laureno R, Victor M. Pontine and extrapontine myelinolysis. Brain 1979; 102: 361-85.
14. Miller GM, Baker HL Jr, Okazaki H, Whisnant JP. Central pontine myelinolysis and its imitators: MR findings. Radiology 1988; 168: 795-802.
15. Diederich S, Franzen NF, Bahr V, Oelkers W. Severe hyponatremia due to hypopituitarism with adrenal insufficiency: report on 28 cases. Eur J Endocrinol 2003; 148: 609-17.
16. Nakano H, Ohara Y, Bandoh K, Miyaoka M. A case of central pontine myelinolysis after surgical removal of a pituitary tumor. Surg Neurol 1996; 46: 32-6.
17. Menger H, Jorg J. Outcome of central pontine and extrapontine myelinolysis (n = 44). J Neurol 1999; 246: 700-5.

Extrapontine myelinolysis ก่อนการผ่าตัดเนื้องอกบริเวณ sellar รายงานผู้ป่วย 2 ราย

ดวงพล ศรีมณี, รุ่งโรจน์ พิทยศิริ, กัมมันต์ พันธุมจินดา

กลุ่มอาการ osmotic demyelin เป็นกลุ่มอาการที่ทราบกันดีว่าเกิดจากการแก้ไขระดับโซเดียมในกระแสเลือดอย่างรวดเร็ว โดยมีหลายภาวะที่เกี่ยวข้องรวมถึงภาวะการทำงานที่ผิดปกติของฮอร์โมนร่วมด้วย รายงานผู้ป่วย 2 ราย ที่มีเนื้องอกในสมองบริเวณเซลล่าร่วมกับมีภาวะพร่องการทำงานของต่อมใต้สมองและภาวะพร่องการทำงานของต่อมหมวกไตอันเนื่องมาจากการพร่องการทำงานของต่อมใต้สมอง ผู้ป่วย 2 รายนี้มีระดับโซเดียมในกระแสเลือดที่ผิดปกติ และทั้งสองมีอาการบิดเกร็งทั้งตัว การตรวจสนามแม่เหล็กไฟฟ้าพบลักษณะเข้าได้กับภาวะ extrapontine myelonolysis ผู้ป่วยรายแรกเป็นชายอายุ 35 ปี เป็นเนื้องอกชนิด craniopharyngioma มีอาการบิดเกร็งทั้งตัวภายหลังจากแก้ไขระดับโซเดียมในกระแสเลือด ผู้ป่วยรายที่ 2 เป็นชายอายุ 24 ปีเป็นเนื้องอกชนิด gonadotroph pituitary adenoma มีอาการบิดเกร็งทั้งตัว ร่วมกับอาการพูดไม่ชัด กลืนลำบากหลังจากการแก้ไขระดับโซเดียมในกระแสเลือด ฮอร์โมนเป็นสาเหตุของการเปลี่ยนแปลงระดับโซเดียมในกระแสเลือด และการแก้ไขระดับโซเดียมในกระแสเลือดตามแนวคำแนะนำปกติอาจเกิดอันตรายและนำไปสู่กลุ่มอาการ osmotic demyelination ได้ผู้ป่วยเนื้องอกในบริเวณ sellar เป็นปัจจัยเสี่ยงในการเกิดกลุ่มอาการ osmotic demyelination และการแก้ไขระดับโซเดียมในกระแสเลือดจำเป็นต้องได้รับการดูแลใกล้ชิด