Effective treatment of osmotic demyelination syndrome with corticosteroid therapy: A case report

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Summary

Background: Osmotic demyelination syndrome (ODS) is characterized by widespread degeneration of myelin within the central nervous system (CNS) and has no established treatment. A limited number of cases have reported positive outcomes with corticosteroid in the treatment of ODS. We report the case of complete recovery of ODS with corticosteroid. *Case presentation:* A 48-year-old man presented with a stupor condition and exhausted. He was hospitalized at the Endocrinology Department with hyponatraemia, which was rapidly corrected with hypertonic saline from 103 to 116mmol/L. He was transferred to the Stroke Department because of worsening consciousness, arising rigidity and bradykinesia of the extremyties, worsening dysarthria and bradyphrenia. A brain magnetic resonance imaging (MRI) scan revealed later on pontine myelinolysis. He was commenced on corticoid 11 days after rapid correction of sodium. His status began to improve gradually after 10 days from starting of corticosteroid therapy and at 44 day-follow-up had no neurological deficit. *Conclusion:* Corticosteroid therapy can be considered as an effective treatment modality in osmotic demyelination syndrome.

Keywords: Hyponatraemia, osmotic demyelination, corticosteroid therapy.

1. Background

Osmotic demyelination syndrome (ODS), which embraces central pontine myelinolysis (CPM) and extrapontine myelinolysis (EPM), is often underdiagnosed in clinical practice, but can be fatal. Overall, ODS accounts for 0.4% to 0.56% of all neurological admissions to tertiary referral hospitals and 0.06% of all medical hospital admissions [1]. ODS is associated with rapid correction of hyponatraemia, and occurring sometimes at normal level of serum-sodium. Brain adapts to chronic hyponatraemia by movement of organic and inorganic particles through extracellular matrix [3]. During rapid correction of hyponatraemia (more than 12mmol/l per day), organic osmolytes cannot re-enter the intracellular environment as quickly as ionic movement creating an osmotic disequilibrium [3]. This leads to collapse of brain cells including astrocytes and oligodendrocytes causing accelerated apoptosis. As a result, the blood brain barrier (BBB) is destructed and demyelination is activated [4]. Microscopically, the lesions show symmetrical myelin destruction affecting all the fibre tracts, with a loss of oligodendrocytes [5]. A recent study has shown substantial axonal damage in central pontine myelinolysis, which is also present in other demyelinating diseases, where it is associated with an inflammatory infiltrate [6]. Therefore, symptoms related cerebral demyelination typically appears after two to six days of rapid sodium correction. Generally, established ODS is associated with a poor prognosis. Apart from

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supportive therapy, sodium re-lowering therapy has shown some benefits in the acute condition [4]. Other treatment methods reported for ODS included thyrotrophic releasing hormone, corticosteroids, immunoglobulins and plasmapheresis. Therapeutic effects of steroid in osmotic demyelination syndrome have been found in few case reports, including adults and pediatrics [7-8]. Besides, dexamethasone has been shown to have a beneficial response in osmotic demyelination syndrome in animal studies [9]. We report a case of complete clinical recovery of ODS with corticosteroid, initiated 11 days after rapid sodium correction.

2. Case presentation

A 48-years-olds man with alcohol abuse and hypertension (used perindopril 5mg per day and indapamide 1.25mg per day for treatment), presented with exhausted, stupor condition and hiccup. On admission to the department of endocrinology he was afebrile, pulse rate was 98 bpm and blood pressure was 137/85mmHg. His Glasgow coma scale score (GCS) was 14/15, pupils were equally reactive to light and there was no stiff neck. His haematological and biochemical investigations done at hospitalization are shown in Table 1. He was noted to have plasma sodium of 103 mmol/L which was increased with hypertonic saline (500ml NaCl 3%) up to 116mmol/L in the first day of the treatment and corrected up to 138mmol/l after seven days. His plasma sodium level and plasma osmolality in the first ten days are shown in Figure 1 and Figure 2 correspondingly. Non contrast computed tomography (NCCT) brain was normal at this time.

Table 1. Haematological and biochemical parameters of the patient

Laboratory parameter	Admission	Discharge	Reference range
Total white cell count (G/l)	11.27	09.72	4-10
Neutrophil count (%)	85.8	73.2	40-74
Lymphocyte count (%)	3.7	12.6	19-48
Red blood cell count (T/l)	4.85	3.94	4.2-6
Haemoglobin level (g/l)	146	119	130-170
Platelet count (G/L)	133	491	140-350
Serum glucose (mmol/l)	10.29	6.61	4.1-5.9
Serum urea (mmol/l)	5.04		3.8-8.3
Serum creatinine (µmol/L)	35	49	62-106
Serum potassium (mmol/l)	1.9	137.6	3.5-5.0
Plasma sodium (mmol/l)	103	3.6	135-145
Serum osmolality (mOsm/L)	221.3	293	280-296
pH	7.61	7.44	7.35-7.45
pCO_2 (mmHg)	42	32	35-48
pO_2 (mmHg)	74	86	83-108

At the admission, this patient had alkalosis and severe electrolyte disorder when hospitalized. White blood cell count and neurophil proportion were higher than normal range, it might be consequences of an unknow infection. When discharged, his biochemical parameters were in general limitation and blood cultures showed the infection was improved.

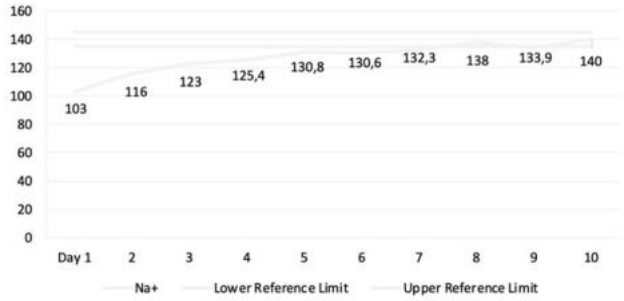

Figure 1. Plasma sodium level (mmol/l) in the first ten days of treatment.

His plasma sodium level was very low in admission then increased quickly in first 3 days. Specially, it rose 13mmol/l at the first day and reached the normal range from day 8.

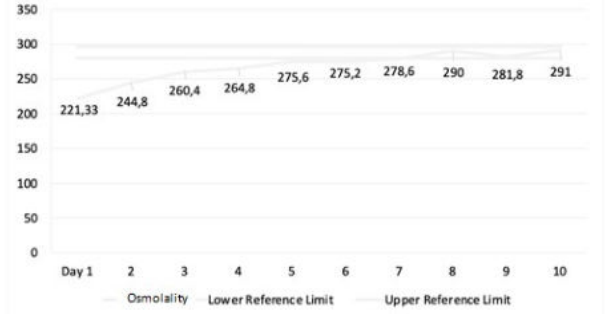

Figure 2. Plasma Osmolality (mOsm/L) in the first ten days.

Patient's plasma osmolality was corected rapidly in firt 3 days and reached normal limitation in the eighth day.

After 3 days of sodium-correction he developed bradykinesia and tremors in all of four limbs symmetrically. He remained sparse speech and there were no seizures.

After 6 days, his consciousness level was reduced (GCS was 12/15). At the same time, he developed dysphagia and dysarthria. After 10 days, MRI of the brain showed bilateral symmetrical T2 FLAIR (fluid-attenuated inversion recovery) high signal involving thalami, lentiform nuclei, and external capsules. Furthermore, the characteristic central trident shaped T2 FLAIR high signal area was found in the pons (Figure 3).

The diffusion tensor imaging (DTI) showed some damages at tractus pyramidalis (Figure 4).

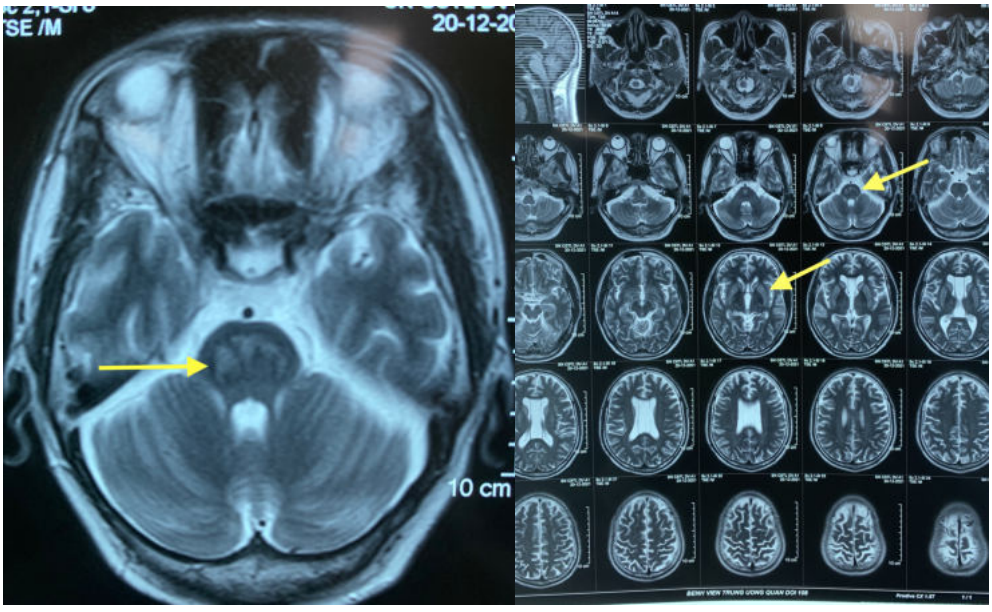

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Figure 3. Brain MRI at 10th-day. Fig. 3a. Classic trident-shaped appearance in pontine. Fig. 3b. Image of damages in thalamic, pontine, lenticular and caudate nucleus.

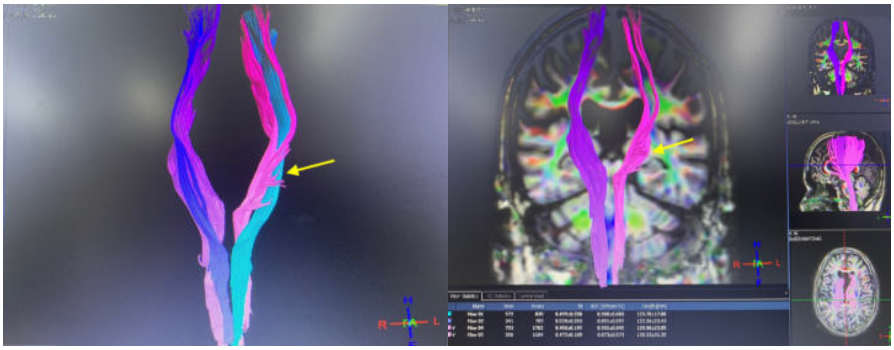

Figure 4. DTI at 10th-day

Disruptions of tractus pyramidalis

A diagnosis of ODS was made based on the history of rapid sodium correction and abnormalities detected on the brain MRI [2]. After 12 days of admission and no improvement in his neurological status patient was transferred to Stroke Department of 108 Military Central Hospital.

On examination, he was afebrile and there was no neck stiffness. GCS was 11/15 (best motor response -6, best verbal response 2, and eye opening 3). He had characteristics of Parkinsonism including tremors, rigidity and bradykinesia symmetrically involving in all four limbs. Increased muscle tone and hyperreflexia were noted in both upper and lower limbs with bilateral extensor plantar responses. He had tetra paralysis with muscle strength was 2/5. Speech and swallow disorder were recognized. Cardiovascular and abdominal examinations were normal. When he was transfered to stroke department, screening for sepsis including blood cultures and chest radiograph showed a mild pneumonia at right lung. Sodium level was 138mmol/L on admission to our department. Cerebrospinal fluid (CSF) analysis was normal.

A diagnosis of ODS was concluded, it based on the history of rapid sodium correction, followed-neurological deficit and abnormalities detected on the brain MRI [2]. After that, the patient started treatment with methylprednisolone (1.5mg/kg/day) and levodopa (250mg/day) from 14th-day. An antibiotic (Cefoxitin 6g/day) was used to treat pneumonia. The clinical status was improved significantly at 21th-day. He was discharged at 28th-day in when he had an increased muscle strength (4/5) and narrow-based shuffling gait. Parkinsonism, speech and swallow disorder were disappeared at this time. He could walk without any assistance at 58th-day. Brain-MRI image showed remaining core damage at pontine central area but surrounding edema parts were faded (Figure 5).

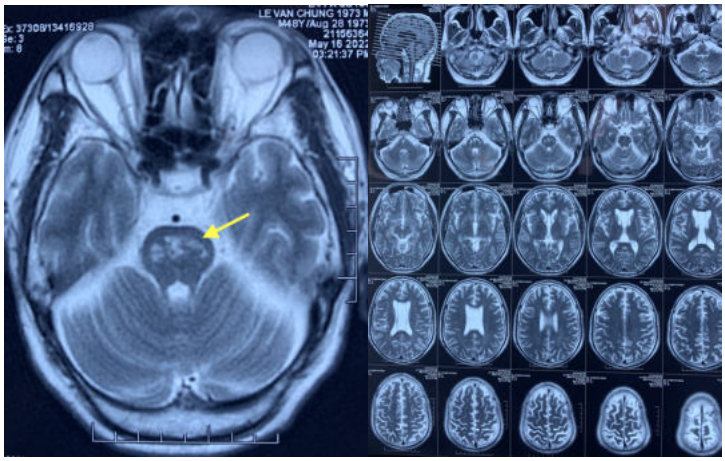

Figure 5. Brain MRI at 58th-day

Trident-shaped remained in pontine but with smaller size.

The patient had total recovery at 88th-day. He could walk as common and play some sports like jogging, volleyball… His cranial MRI at this time was similar with 30 days before.

3. Discussion

3.1. Osmotic demyelination syndrome

ODS is a rare acute demyelination development with a prevalence of 0.25% to 0.5% in the general residents. It is known to evolve following a rapid increase in serum sodium, usually more than 12mEq/mL in a 24-hour period [1]. Our patient had a fast corection in the first day of treatment (13mEq/mL).

The rick factors of ODS are manutrition, liver disease, alcohol use disorder, hypokalemia and starting serum sodium of ≤ 105mmol/L [5]. This patient had alcohol abuse. Althought his liver function was in normal range, but drinking too much alcohol to did harm to his metabolism. As a consequence, he had some sigh of manutrition: serum creatinin was low (35-49mml/l) and anemia. Because of using diuretic drug, he had several hypokalemia (serum potassium: 1.9mmol/l) and hyponatremia. So, we could find almost of ODS-rick factors in this patient.

Clinically, osmotic demyelination syndrome may present with a wide range of symptoms, including spastic tetraplegia, dysarthria, dysphagia, Parkinsonism, dystonia, altered mental status, emotional lability, pseudobulbar palsy, ophthalmoplegia, nystagmus, ataxia, and cranial nerve palsies. Severe cases may encounter "locked-in" syndrome or death. The first 5 symptoms were found in our case.

On cranial MRI, the earliest change is seen on DWI with limitation in the lower pons. This is met within 24 hours of the onset of tetraplegia. This same region authenticates ultimate high T2 signal and later a low T1 signal. The T1 and T2 changes usually take up to two weeks to develop. Injury-images of this region make a classic trident-shaped appearance. On T2/FLAIR axial MR images, the overall appearance has also been likened to the face of a pig, referred to as piglet sign. Infrequently gadolinium enhancement is also authenticates, just as in the acute stage of multiple sclerosis (MS) plaque. Similar appearances are seen in other parts of the brain: midbrain, basal ganglia and subcortical white matter [6]. Our patient had trident-shaped appearance at porn and other damages at basal ganglia.

3.2. Steroids in ODS

Therapeutic effects of steroid in osmotic demyelination syndrome have been reported in human in few case reports [7-8]. In rats model also, Sugimura and partners showed that dexamethasone had a beneficial response in ODS [9].

Disruption of the BBB is thought to be one of ODS's underlying pathogenesis. Rapid rise of serum sodium causes water to move into the extracellular space, causing shrinking and dehydration of brain vascular endothelial cells and glial cells, thus causing disruption of BBB and axonal sheer damage. Destruction of BBB allows access to lymphocytes, cytokines, complement proteins, and vasoactive amines to central nervous system tissue which may later lead to inflammatory demyelination. Steroids are known to regulate the BBB permeability and thus prevent BBB disruption induced by hyperosmolality [7]. Base on these incidences, we decided to use corticoid therapy with methylprednisolone (1.5mg/kg/day) in ten days. Patient's clinical status improved after some days of treatment.

With regard to steroids in ODS, they could be effective by reducing BBB permeability and prevent its disruption, given that BBB disruption after sodium correction plays a significant role in the pathogenesis of the syndrome. Methylprednisolone may also contribute to reversal of vasogenic edema. Sugimura et al (2005) found that dexamethasone treatment administered early (0–6 hours after rapid sodium correction) to animal models of ODS could

prevent demyelinating lesions. Intravenous steroids may take four to 10 days to improve symptoms. In our case the improvement started 7 days after completion of steroids. Of note, most ODS cases treated with steroids reported an improvement on follow-up, which nevertheless occurred months after the initial event.

In some case reports, levodopa was used like a good method to antagonize Parkinsonism symptoms in ODS [10]. Our patient had been treated with this drug until Parkinsonism was disappeared.

4. Conclusion

Osmotic demyelination syndrome remains a neurological complication that is difficult to treat and may result in permanent neurological sequelae or even death. Although rapid osmolar correction, mainly in the setting of hyponatremia is the main risk factor, the pathogenesis of the syndrome is not fully elucidated. Due to the variety of its presentation, ODS is not initially suspected in most cases. As findings may not be evident for up to two weeks, repeat imaging is needed to diagnose the syndrome. This is a particular case of ODS with successful recovery after corticoid therapy. It provides a new document and evidence about therapeutic of steroid in ODS treatment. However, there are alot of difficulties in ODS management and prevention is better than cure.

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