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Case Series of Osmotic Demyelination Syndrome Treated With Plasmapheresis: Experience From Two Tertiary Hospitals

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Dear Editor,

Osmotic demyelination syndrome (ODS) is a demyelination process caused by a rapid increase in the serum sodium level, manifesting as central pontine myelinolysis (CPM), extrapontine myelinolysis (EPM), or both conditions. ODS has potentially detrimental and irreversible consequences. Plasmapheresis has been reported in the literature as a potential effective therapy.[1]

We conducted a descriptive study of iatrogenic ODS treated with plasmapheresis at two tertiary hospitals. The onset and symptoms of ODS and the outcome after plasmapheresis were reviewed from the medical records.

Seven cases of ODS were treated with plasmapheresis. Six patients partially recovered, three of whom remained able to independently perform the activities of daily living. The seventh patient remained vegetative. Table 1 summarizes all of the cases from both tertiary hospitals.

The symptoms of ODS usually begin 2–6 days after overcorrection of hyponatremia exceeding 10 mmol/L/day.[2] However, the symptoms can develop as early as 24 hours and as late as 17 days, as demonstrated in our case series. Typical clinical manifestations of ODS depend on the areas of involvement, namely CPM, EPM, and both conditions, whose relative proportions are reportedly 50%, 40%, and 60%, respectively.[3] In our case series these proportions were 14%, 29%, and 57%, respectively.

The classic mechanism of ODS involves the rapid correction of a chronic hypo-osmolar state, leading to the shrinkage of oligodendrocytes and hence demyelination.[4] However, a few reported cases of successful treatment with plasmapheresis and immunotherapy within 5 days of symptom onset suggested a mechanism of myelinotoxin production after the osmotic stress.[1]

ODS is usually diagnosed based on a history of serum sodium overcorrection followed by a typical clinical manifestation of CPM or EPM. Brain magnetic resonance imaging (MRI) is the imaging modality of choice to confirm the diagnosis. Hyperintense lesions on T2-weighted images are classic MRI findings in ODS, with these lesions typically located in the central part of the pons, medulla oblongata, and the mesencephalon.[5] The brain MRI findings can be reversed after appropriate treatment that results in clinical improvement.[6] There are some reports of hyperintense lesions in diffusion-weighted imaging with an elevated mean apparent diffusion coefficient in ODS, suggesting complex pathophysiologic changes beyond a demyelinating process, similar to multiple sclerosis.[7] Our case series demonstrates typical brain MRI findings of ODS (Supplementary Figs. 1-7 in the online-only Data Supplement); however, no posttreatment MRI was performed to allow comparisons with the pretreatment condition.

There is currently no specific efficacious treatment for ODS. Most patients who develop ODS will require long-term intensive supportive care while waiting for the possibility of

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Table 1. Summary of the seven cases of ODS

Case	Age (yr)/ sex	Comorbidities	Sodium level in mmol/L	ODS symptoms (onset from sodium correction)	Imaging features	Treatment (days after onset of ODS symptoms)	Outcome
1	61/F	Hypertension	<100 to 115 within 22 hours	Parkinsonism (17 days)	Both CPM and EPM	Plasmapheresis (4 days)	Residual parkinsonism requiring assistance for ADL
2	43/M	Hypertension	102 to 116 within 16 hours	Status epilepticus with left upper limb chorea (24 hours)	Both CPM and EPM	IV Methyl-prednisolone (6 days) Plasmapheresis (8 days)	Vegetative state and homebound
3	63/M	Hepatitis B	102 to 115 within 16 hours	Status epilepticus with facial twitching (24 hours)	CPM	Plasmapheresis (6 days)	Residual left hemiparesis and sensory ataxia, assisted ambulation with a walking stick
4	23/F	History of miscarriage	102 to 120 within 24 hours	Reduced GCS with hypomimia and generalized hypotonia and hyporeflexia (4 days)	EPM	Plasmapheresis (4 days)	Requires a wheelchair for ambulation
5	56/F	Hypertension Diabetes mellitus Dyslipidaemia	<100 to 115 within 13 hours	Reduced GCS with abnormal gait and tremors (11 days)	Both CPM and EPM	Plasmapheresis (2 days)	Ambulates without assistance Able to perform simple house chores
6	46/F	No known medical illness	110 to 127 within 12 hours	Parkinsonism (7 days)	EPM	Plasmapheresis (2 days)	Ambulates without assistance
7	54/F	Hypertension Dyslipidaemia	<100 to 116 within 20 hours	Altered behaviour with slow response (13 days)	Both CPM and EPM	Plasmapheresis (8 days)	ADL-independent Residual spastic gait

ADL, activities of daily living; CPM, central pontine myelinolysis; EPM, extrapontine myelinolysis; GCS, Glasgow Coma Scale; IV, intravenous; ODS, osmotic demyelination syndrome

complete or partial recovery. Thus, preventing ODS with close monitoring and extra caution in sodium correction in high-risk patients are of utmost important. Relowering of the serum sodium level after inadvertent overcorrection with desmopressin and 5% dextrose is another measure for preventing the development of ODS.[8] Other therapeutic options such as corticosteroids, myoinositol, and urea have shown benefit in animal models, but the lack of clinical experience and large multicenter trials hinders the development of effective ODS management protocols.[9]

Since an immunologic process with myelinotoxin production is postulated as the pathophysiology of ODS, plasmapheresis and immunomodulators such as intravenous immunoglobulin (IVIg) and steroids have been studied for the management of ODS. Most ODS cases treated with plasmapheresis, IVIg, or their combination have improved significantly as soon as 1 day after treatment that is initiated within 7 days of onset. However, the outcome is unclear with regard to steroids. Besides ceasing the production of myelinotoxic compounds, IVIg may help to promote myelin repair in ODS. Similarly, plasmapheresis exerts effects on the immune system beyond the mere removal of myelinotoxins from the circulation. It is postulated to be able to induce alterations in lymphocyte proliferation and function, and cytokine suppression, resulting in an anti-inflammatory outcome.[10]

Most of the patients in our case series achieved good recovery after plasmapheresis performed within 5 days of symptom onset, with the best outcome observed when plasmapheresis was performed within 2 days. One patient remained vegetative and bed-bound, possibly due to his presentation as status epilepticus of unknown onset contributing to a worse outcome.

Supplementary Materials

The online-only Data Supplement is available with this article at https://doi.org/10.3988/jcn.2022.18.1.117.

Ethics Statement

Informed consent to participate was obtained from the subjects or their caregivers.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

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Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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