

# An Interesting Case Report of Complete Neurological Recovery in Osmotic Demyelination Syndrome

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**Abstract:** We report a case of osmotic demyelination syndrome happened because of rapid correction of severe chronic hyponatremia occurred after use of 0.9% normal saline. He had all the risk factors for development of osmotic demyelination syndrome like chronic alcoholism, malnourishment, liver disease, very low baseline sodium level and hypokalemia. Sodium relowering therapy with help of 5% dextrose and desmopressin was immediately started to prevent development of ODS. Despite of this patient developed classical symptoms of ODS on 5th day. MRI brain showed characteristic T2 weighted hyper intensities in pons as well as in extra pontine regions confirmed the diagnosis of ODS. Aggressive supportive therapy along with systemic steroids was started to reverse this. As opposed to dismal prognosis mentioned in the literature for established ODS, our patient had full neurological recovery in four months period. This report emphasizes on importance of timely recognition and anticipation of this illness, immediate use of dextrose and desmopressin to relower sodium levels and aggressive supportive therapy for prevention and treatment of ODS.

**Keywords:** ODS, Sodium, Potassium, Hyponatremia, Hypokalemia, MRI Brain, Dextrose and Desmopressin

## 1. Introduction

ODS occurs due to overt rapid correction of sodium specially in cases of chronic hyponatremia. Chances of rapid correction are more in patients with history of chronic alcoholism, malnourishment, very low baseline sodium level and presence of hypokalemia along with hyponatremia<sup>[1, 2]</sup>. Though the risk of overcorrection is more with the use of hypertonic saline but even free water restriction and use of normal saline can lead to rapid correction<sup>[3]</sup>. Hence it is prudent to monitor sodium levels closely while correcting hyponatremia specially severe and chronic hyponatremia. Though prevention of ODS is of utmost importance but in case of any anticipated rise in initial trajectory of sodium or any unexpected rapid rise in sodium, immediate sodium relowering therapy should be started. In case of established ODS, aggressive rehabilitative and supportive care has the potential to reverse this illness and many patient's make full neurological recovery as happened in our case too. There is some controversy in literature on prognosis of this illness and long term outcome of patients of ODS is variable in different studies<sup>[4]</sup>. However in this case early anticipation, aggressive relowering therapy trial and supportive care in intensive care unit helped in making complete neurological and radiological recovery. Therefore regardless of the initial severity of illness, early and consistent aggressive management should be done for patients of ODS.

## 2. Case Presentation

A 41 year old male with a history of smoking, chronic alcoholism and hypertension on regular anti-hypertensives {Telmisartan (40 mg) and Chlorthalidone (12.5 mg) combination} is presented to Emergency Department with complaints of pain abdomen, multiple episodes of loose stools and vomiting for one day.

Vital parameters are as follows: BP was 110/70 mm of Hg, pulse 108/min, respiratory rate 32/min with spo2 of 98 % on room air. Systemic examination was normal except for presence of mild epigastric tenderness. He was fully

conscious and oriented at the time of presentation. His initial laboratory findings were significant for leukocytosis, neutrophilia, mild thrombocytopenia, transaminitis (ALT/AST 167/389), raised amylase (123u/l) and lipase (130u/le). Electrolytes were grossly deranged with sodium of 101mmol/l, potassium of 2.6 mmol/L and chloride of 60 mmol/L. Kidney function was normal with Creatinine of 0.7 mg/dl.

Thyroid profile, s. cortisol level, urine osmolality and urine spot sodium were sent for evaluation of hyponatremia. Thyroid profile and serum cortisol were within normal limit. Urine osmolality (360mOsm/kg) and urine spot sodium (39mmol/L) were suggestive of presence of SIADH, further worsened with use of thiazide diuretic.

Chest x ray was normal and USG abdomen showed bulky pancreas suggestive of mild pancreatitis, as also evident biochemically with raised amylase and lipase level. ECG showed T wave inversions in anterior chest leads though cardiac enzymes were within normal limits.

He was started on IV fluids (0.9% saline), antibiotics and all supportive care including potassium supplementation. Hypertonic saline was not given despite of severe hyponatremia as patient was fully conscious and oriented. Serum sodium, Potassium and other electrolytes were monitored regularly at 8 hourly intervals. His serum sodium concentration rose to 110mmol/l by 8 hours. At this point his rate of 0.9% saline infusion was decreased from 100 ml to 60 ml per hour. By 16 hours his sodium level was 116 and then by 24 hours 123 mmol/L. Hence, in first 24 hours his sodium had risen from 101mmol/l to 123 mmol/l that is 22 mmol rise in first 24 hours. In view of significant rapid correction of sodium, attempts to re-lower the sodium further were initiated immediately with help of 5% dextrose with water at rate of 150 ml per hour. Sodium levels were monitored to see the response of re-lowering therapy. During re-lowering therapy target sodium was kept as 110-112 mmol/L in next 24 hours. Patient developed significant polyuria with urine output of more than 150-200 ml per hour and sodium started rising again despite dextrose infusion. It

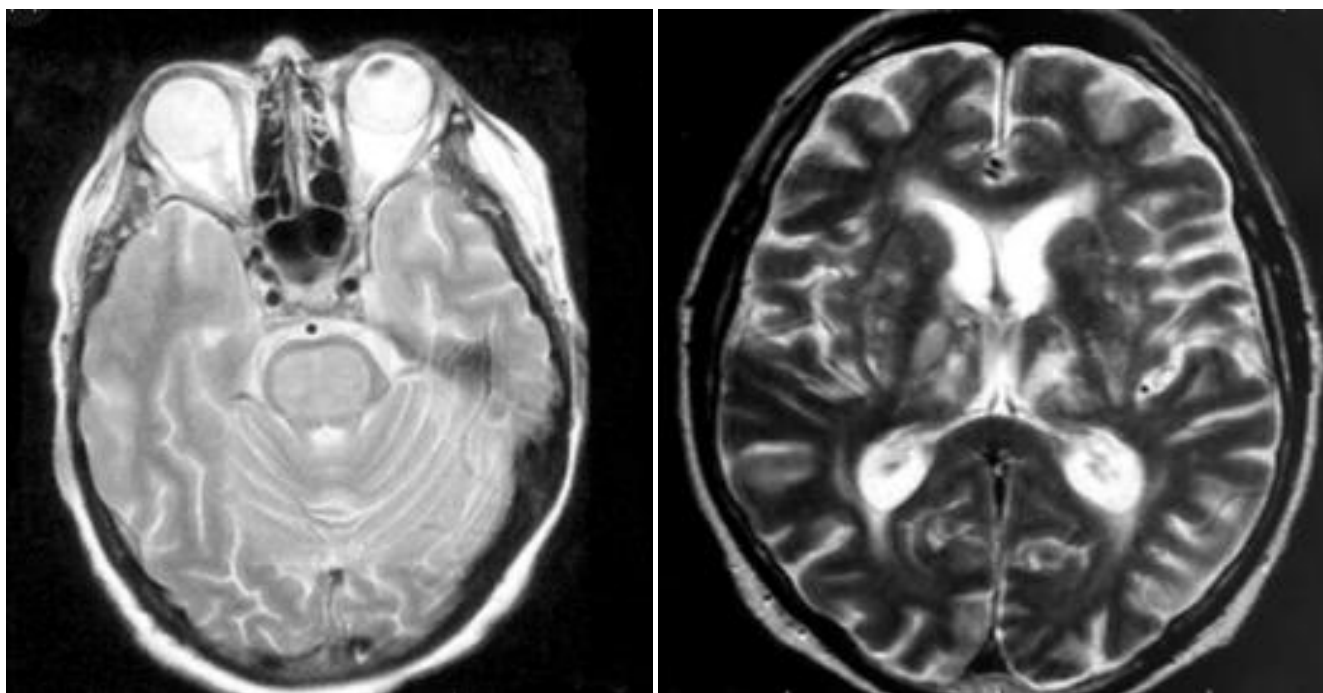
was tough to correct the sodium with 5% dextrose only and injection desmopressin was started to prevent further rise in sodium levels and to control polyuria. Over next 3 days we could achieve sodium levels between 116-118 mmol/L despite of continuous infusion of dextrose and intermittent desmopressin injections. Patient remained conscious, alert, and coherent with no evidence of any neurological involvement till day 4.

On day 5, he suddenly developed confusion, disorientation and agitation. On examination he had tremors, dysarthria, dysphagia and weakness in all four limbs. As patient already had history of overtly corrected sodium level in first 24 hours with risk factors for development of ODS like chronic alcoholism and hypokalemia, MRI brain was ordered to confirm the diagnosis. In MRI Brain T2 / FLAIR images showed symmetrical hyper-intensity involving bilateral caudate nucleus, putamen and thalamus. Small focal area of DWI restriction was seen in lower central part of pons showing subtle hyper-intensity on FLAIR suggestive of

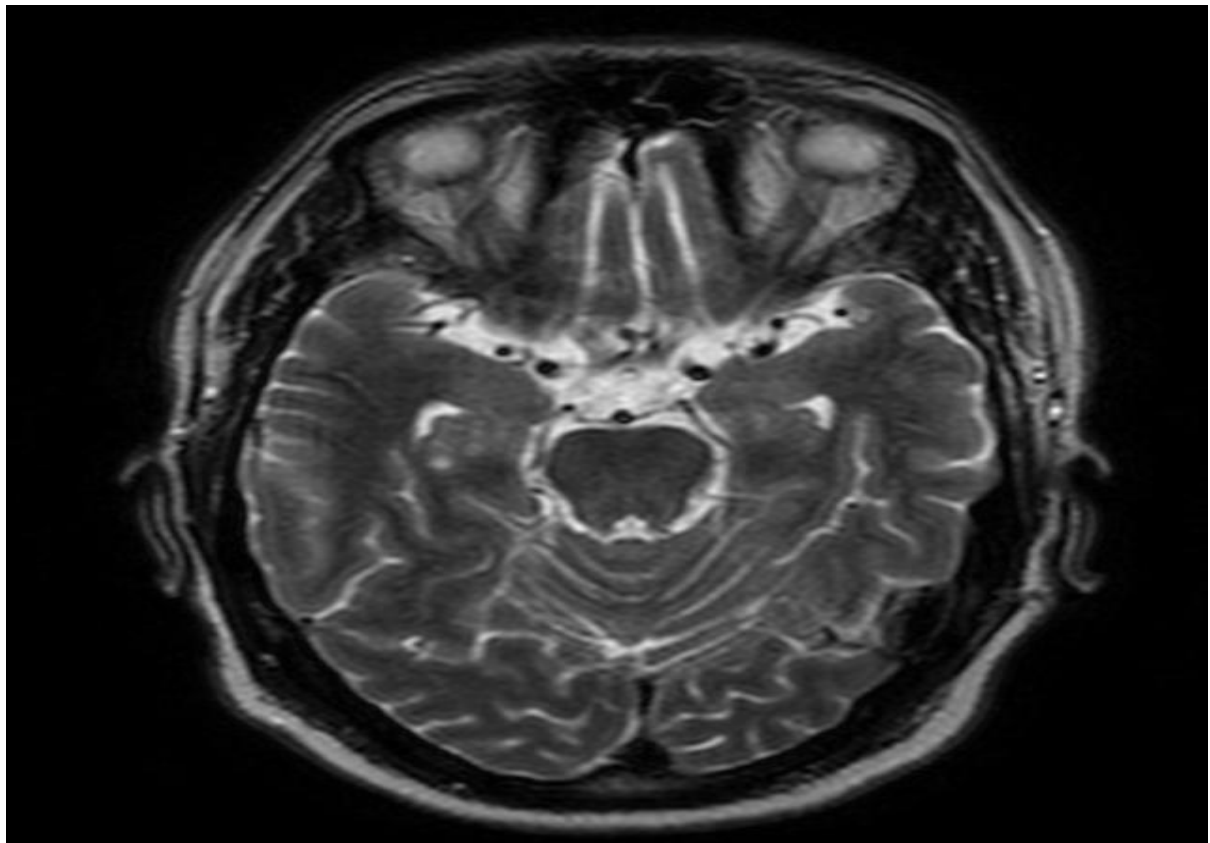
ODS. MRI demonstrated features of both central pontine and extrapontine myelinolysis, which, when occur together is considered virtually pathognomonic of ODS. He was started on intensive supportive therapy along with steroids. Supportive therapy was offered in form of aggressive limb physiotherapy, speech therapy and nutritional support. He gradually improved in next 2 weeks in form of improvement in speech, dysphagia and quadriparesis. At the time of discharge he was swallowing soft diet and walking with the help of walker. He was discharged with some residual neurological deficits in the form of mild dysarthria, tremors, mild dysphagia and slight gait ataxia. Patient was followed up regularly for next 4 months. He gradually improved with the help of physiotherapy, tapering dosages of steroids and multivitamins. At the end of 4 months, he had remarkable improvement in the form of normal eating, normal speech and no support required to walk. His MRI brain was repeated; showed no evidence of residual brain damage.

**Table 1:** Showing Serial Serum Sodium and other significant lab parameters

Time	Sodium (mmol/L)	Potassium (mmol/L)	Chloride (mmol/L)	Bicarbonate (mmol/L)	Serum Osmolality (mOsm/Kg)	Urine Sodium (mmol/L)	Urine Osmolality (mOsm/Kg)	BUN mg/dL	Uric Acid (mg/dL)	Creat. mg/dL
0 hour	101	2.6	<60	21.7	210	39	259	12.9	7.8	0.7
8 hour	110	3.2	80	24	-	-	-	11.9	7.4	0.95
16 hours	116	3.5	85	22	-	-	-	15.7	7.0	0.74
24 hours	123	3.6	82	25	-	-	-	26.4	6.5	0.69
48 hours	116	4.0	90	24	-	129	173	23.8	5.8	0.82
12 days	120	3.8	88	22.5	219	170	480	21.4	3.6	0.69



**Image 1:** Showing T2 weighted Pontine and Extrapontine Myelinolysis MRI Scan



**Image 2:** Showing T2 weighted Normal MRI Scan

### 3. Discussion

Central pontine myelinolysis was first described by Adams in 1959, where he described that pons was the only area implicated<sup>[5]</sup>. Eventually it was found that demyelination also occurred in extra pontine areas and hence the term Osmotic Demyelination Syndrome was introduced. Osmotic demyelination syndrome (ODS) refers to central pontine myelinolysis and extrapontine myelinolysis<sup>[6]</sup>. In this injury to white matter tracts and myelin sheath occurs because of osmotic disturbances. Central pontine myelinolysis and extrapontine myelinolysis have distinct clinical features but they have similar timing of onset of illness.

ODS happens due to iatrogenic injury caused by rapid correction of sodium, more so in some vulnerable and sick patients. The rate of correction, the duration of hyponatremia (acute or chronic) and the severity of hyponatremia are important and critical factors in determining the risk of development of ODS<sup>[7]</sup>. Similarly Chances of ODS is more when initial serum sodium is very low  $< 105$ <sup>[8]</sup>. Various predisposing factors for ODS are alcoholism, malnutrition, liver disease and hypokalemia<sup>[9]</sup>. Patients who are Hyponatraemic for only few hours rarely developed ODS, in comparison to those who have it for  $> 48$  hours.

In this case rapid correction of sodium happened in first 24 hours along with many pre-disposing factors for development of ODS like chronic alcoholism, malnourishment, hypokalemia and liver disease. At the time of presentation sodium was 101 mmol/L and potassium was 2.6 mmol/L. Reason to explain increased risk of ODS with low potassium is not clear but hypokalemia makes the cell

membrane vulnerable for osmotic stress related injury. When hypokalemia is associated with hyponatremia; the clinical outcome of ODS is poor<sup>[11]</sup>. All of these findings made him highly susceptible for development of ODS. As clinical consequences of ODS are severe and sometimes permanent, prevention of this illness is paramount. Hence it is being recommended that the sodium should never be corrected by 6-8 mmol/L in 24 hour period; especially in setting of chronic hyponatremia<sup>[12]</sup>.

A reactive and rescue strategy should be adopted in case of troublesome trajectory of rise in sodium or patients already exceeded the correction limits respectively. As a part of this strategy immediate re-lowering of sodium was planned with the help of 5% dextrose and intermittent shots of desmopressin, while keeping a close watch on sodium levels and urine output. Re-lowering of sodium can reverse the blood brain barrier injury and prevent brain damage<sup>[13]</sup>. During re-lowering the target sodium should be just below the initial 48 hours target correction from initial sodium level i.e. 110-112 in this patient. It is suggested that sudden cessation of excessive ADH stimulus can lead to water diuresis and prevent re-lowering of sodium and cause increase in sodium levels making it tough to achieve target sodium levels. Despite of vigorous use of 5% Dextrose and Desmopressin, it was tough to reach the target sodium level in our patient.

Clinical manifestation of ODS is usually delayed for initial 2-6 days following the insult. In this case patient remained clinically stable for next 4 days with no neurological involvement. On day 5 he developed neurological symptoms suggestive of ODS. MRI is the imaging modality of choice for diagnosis of ODS. Well described findings include focal



symmetric, trident or Mexican hat shaped, high signal in the basal pons on T2 weighted and fluid attenuation inversion recovery (FLAIR) sequences and corresponding decreased T1 -weighted signal. Corticospinal tracts are spared<sup>[14]</sup>. Similar appearances are also seen in other parts of the brain like basal ganglion, midbrain and subcortical white matter. This patient showed classical hyperintense lesion in pontine as well as extra pontine areas on T2 Weighted imaging in MRI brain. Patient with established ODS require aggressive supportive therapy in form of prevention of nosocomial infection, nutritional support, DVT prophylaxis, limb and speech physiotherapy. Along with that continuous attempt to relower the sodium to achieve target sodium levels is equally important. It has been seen in various studies that patient of ODS have the potential to recover completely after prolonged neurological impairment with the help of supportive therapy<sup>[15]</sup>. Plasmapheresis, IVIG and steroids have been tried as an experimental therapy to treat ODS and has been found to be useful in improving neurological deficits. Though the additional studies on larger number of patients is required to further prove the definitive role of these experimental therapies in treatment in ODS<sup>[16, 17]</sup>. Our patient's follow up MRI brain revealed no residual damage.

Learning points:

- 1) Prevention of ODS is of utmost importance by avoiding rapid correction of sodium. This can be achieved by close monitoring of sodium levels while hyponatremia correction. Rapid correction sometimes can happen with just free water restriction or administration of IV normal saline infusion as oppose to myth that it can happen only with use of hypertonic saline.
- 2) Clinician should keep a high index of suspicion in vulnerable patients like chronic alcoholic and malnourished patients.
- 3) Hypokalemia may predispose for development of ODS though the exact pathophysiology is not clear. Hypokalemia should be corrected first, prior to correction of sodium.
- 4) Therapeutic relowering of serum sodium should be started in case of rapid correction of sodium to prevent and treat ODS.
- 5) Long term clinical outcome of pontine and extrapontine myelinolysis is variable and complete neurological recovery is seen with aggressive supportive care in terms of prevention of hospital acquired infections, DVT, Limb and Speech physiotherapy, nutritional support. Role of IVIG, Plasmapheresis and Steroid therapy need further research and studies.

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#### References

- [1] Sterns RH. Disorders of plasma sodium—causes, consequences, and correction. *New England Journal of Medicine*. 2015 Jan 1;372(1):55-65.
- [2] Sterns RH. Treatment of severe hyponatremia. *Clinical Journal of the American Society of Nephrology*. 2018 Apr 6;13(4):641-9.
- [3] Mohmand HK, Issa D, Ahmad Z, Cappuccio JD, Kouides RW, Sterns RH. Hypertonic saline for hyponatremia: risk of inadvertent overcorrection. *Clinical Journal of the American Society of Nephrology*. 2007 Nov 1;2(6):1110-7.
- [4] Louis G, Megarbane B, Lavoué S, Lassalle V, Argaud L, Poussel JF, Georges H, Bollaert PE. Long-term outcome of patients hospitalized in intensive care units with central or extrapontine myelinolysis. *Critical care medicine*. 2012 Mar 1;40(3):970-2.
- [5] Adams RD, VICTOR M, MANCALL EL. Central pontine myelinolysis: a hitherto undescribed disease occurring in alcoholic and malnourished patients. *AMA Archives of Neurology & Psychiatry*. 1959 Feb 1;81(2):154-72.
- [6] Martin RJ. Central pontine and extrapontine myelinolysis: the osmotic demyelination syndromes. *Journal of Neurology, Neurosurgery & Psychiatry*. 2004 Sep 1;75(suppl 3):iii22-8.
- [7] Laureno R, Karp BI. Myelinolysis after correction of hyponatremia. *Annals of Internal Medicine*. 1997 Jan 1;126(1):57-62.
- [8] Adrogué HJ, Madias NE. Diagnosis and treatment of hyponatremia. *American journal of kidney diseases: the official journal of the National Kidney Foundation*. 2014 Nov;64(5):681.
- [9] Liamis GL, Milionis HJ, Rizos EC, Siamopoulos KC, Elisaf MS. Mechanisms of hyponatremia in alcohol patients. *Alcohol and Alcoholism*. 2000 Nov 1; 35(6):612-6.
- [10] Berl T, Rastegar A. A patient with severe hyponatremia and hypokalemia: osmotic demyelination following potassium repletion. *American Journal of Kidney Diseases*. 2010 Apr 1;55(4):742-8.
- [11] Lohr JW. Osmotic demyelination syndrome following correction of hyponatremia: association with hypokalemia. *The American journal of medicine*. 1994 May 1; 96(5):408-13.
- [12] Adrogué HJ, Madias NE. The challenge of hyponatremia. *Journal of the American Society of Nephrology*. 2012 Jul 1;23(7):1140-8.
- [13] Kengne FG, Soupart A, Pochet R, Brion JP, Decaux G. Re-induction of hyponatremia after rapid overcorrection of hyponatremia reduces mortality in rats. *Kidney international*. 2009 Sep 2;76(6):614-21. On Whatsapp.
- [14] Osborn AG, Blaser SI, Salzman KL, Katzman GL, Provenzale J, Castillo M. Diagnostic imaging brain. Salt Lake City (Utah): Amirsys.
- [15] Rebedew DL. Is central pontine myelinolysis reversible?. *WMJ*. 2016 Dec.
- [16] Grimaldi D, Cavalleri F, Vallone S, Milanti G, Cortelli P. Plasmapheresis improves the outcome of central pontine myelinolysis. *Journal of neurology*. 2005 Jun 1;252(6):734.
- [17] Bibl D, Lampl C, Gabriel C, Jüngling G, Brock H, Köstler G. Treatment of central pontine myelinolysis with therapeutic plasmapheresis. *The Lancet*. 1999 Apr 3;353(9159):1155.