

Journal of Nephrologist



Osmotic demyelination syndrome after bone marrow transplantation

Fatemeh Yaghoubi^{1#}, Davood Babakhani^{2#}, Farnoosh Tavakoli³, Farnaz Tavakoli^{1*}

¹Nephrology and Kidney Transplantation Ward, Dr. Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran

²Hematology, Oncology Research Center and Stem Cell Transplantation (HORCST), Dr. Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran

³Endocrinology and Metabolism Research Institute (EMRI), Tehran University of Medical Sciences, Tehran, Iran

#Equally contributed as first authors.

ARTICLE INFO

Article type:
Original Article

Article history:
Received: 7 January 2021
Accepted: 9 April 2021
Published online: 20 July 2021

Keywords:
Osmotic demyelination syndrome
Bone marrow transplantation
Hyponatremia

ABSTRACT

A 14-year-old boy with a past medical history of bone marrow transplantation (BMT) was referred to the emergency department with the loss of consciousness and seizure. On admission, the blood test indicated strict hyponatremia with hypokalemia, hypomagnesemia, hypophosphatemia, hypoglycemia, and low-serum low-density lipoprotein cholesterol (LDL-C). After six days, the patient suffered from dysarthria, dysphagia, behavioral disturbances, disorientation, and obtundation. Based on the physical examination, hyperreflexia and upward bilateral plantar reflexes were outstanding. Lumbar puncture, spiral brain CT scan, and MRI were normal. Hence, MRI repeated 2 weeks later, and the T2-weighted image indicated the bilateral symmetric hyperintense lesions in the basal ganglia. The osmotic demyelination syndrome (ODS) is a scarce and serious neurologic complication of the quick correction of chronic strict hyponatremia.

Implication for health policy/practice/research/medical education:

Osmotic demyelination syndrome risk is highest in the patients with serum sodium of ≤ 120 mEq/L, especially if hyponatremia is associated with hypokalemia, low-plasma osmolality and other electrolyte disorders.

Please cite this paper as: Babakhani D, Yaghoubi F, Tavakoli F, Tavakoli F. Osmotic demyelination syndrome after bone marrow transplantation. J Nephrologist. 2021;10(x):exx. DOI: 10.34172/jnp.2021.xx.

Introduction

Hyponatremia is one of the most common electrolyte abnormalities in patients referred to the hospital. Clinical symptoms and signs of hyponatremia depend on the severity of hyponatremia (1-3). Hyponatremia commonly indicates weakness, nausea, headache, muscle cramps, cognitive disorders, confusion, lethargy, seizure, and coma (1,4-6). Focal neurologic signs are scarce (6). The approach to first therapy of hyponatremic patients depends upon hyponatremia severity, the presence, and severity of symptoms, the presence of preexisting intracranial pathology, and the prevention of quick correction of hyponatremia (7-9).

Case Presentation

A 14-year-old boy with the past-medical history of

common variable immunodeficiency (CVID), ulcerative colitis, and lichen planus was referred to the emergency department with loss of consciousness and seizure two hours ago. Considering CVID about 6 weeks ago, he had undergone bone marrow transplantation (BMT). He took some medications, involving cyclosporine, acyclovir, risperidone, citalopram, mesalamine, voriconazole, and prednisolone.

Due to the admission, the blood test indicated strict hyponatremia (serum Na:115meq/L) with hypokalemia (K: 3.1 meq/L), hypomagnesemia (Mg: 1 mg/dL), hypophosphatemia (Ph: 1.3 mg/dL), hypoglycemia (BS: 55 mg/dL) and low-serum LDL-C (LDL-C: 40 mg/dL). Other tests were serum Ca 7.5 mg/dL, serum albumin 2.87 g/dL, serum total protein 5.3 g/dL, and serum total cholesterol 102 mg/dL. Complete blood count

*Corresponding author: Farnaz Tavakoli, Email: farnaztavakkoli@gmail.com, f-tavakkoli@farabi.tums.ac.ir

(CBC) diff revealed hypochromic-microcytic anemia with hemoglobin 9.5 g/dL and thrombocytopenia (plt: 22000/ μ L). In PBS (peripheral blood smear), there was no schistocyte or platelet aggregation. Serum creatinine, arterial blood gas, and liver enzyme were in the normal ranges. Cyclosporine trough level was high (260 ng/mL). He was treated with only 50 cc hypertonic saline 5% along with 2 mcg of desmopressin, 4 cc MgSO₄ 50%, 10cc KCl 15%, 50cc hypertonic glucose 50%, and 10 cc calcium gluconate. Then, the seizure stopped. Serum Na, K, BS, was controlled every 4 hours. Serum Mg, Ca, Ph was controlled every 12 hours. Hypertonic saline was not prescribed for the patient again.

Plasma sodium concentrations via the first 48 hours were 115, 118, 123, 126, 124, 132, 134, 138, 136, 140, 138, 142, respectively (Table 1). After six days, the patient suffered from dysarthria, dysphagia, behavioral disturbances, disorientation, and obtundation. On physical examination, hyperreflexia and upward bilateral plantar reflexes were outstanding.

Lumbar puncture was handled and the results of cerebrospinal fluid (CSF) were normal.

A spiral brain computerized tomography (CT) scan (without contrast) and magnetic resonance imaging (MRI) was done and found normal. MRI repeated 2 weeks later, and T2-weighted image indicated the bilateral symmetric hyperintense lesions in basal ganglia (Figure 1). His neurologic abnormalities in MRI relatively recovered about two months later (Figure 2).

Discussion

The osmotic demyelination syndrome (ODS) is a scarce and serious neurologic complication of the quick correction of chronic strict hyponatremia (especially when serum sodium concentration is ≤ 120 mEq/L) (9, 10). ODS can include central pontine and extrapontine demyelination (11,13). ODS risk elements are serum sodium concentration at presentation, duration of hyponatremia, quick correction of strict chronic hyponatremia, hypokalemia, hypoxia, alcoholism, malnutrition, history of advanced liver disease or liver transplantation (12-16).

The existence of concomitant metabolic derangements,

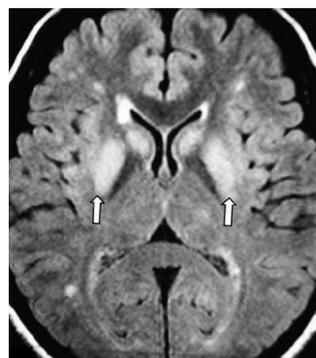


Figure 1. Axial FLAIR image shows bilateral symmetric hyperintense lesions in the basal ganglia (observation; the arrows are showing the lesions).

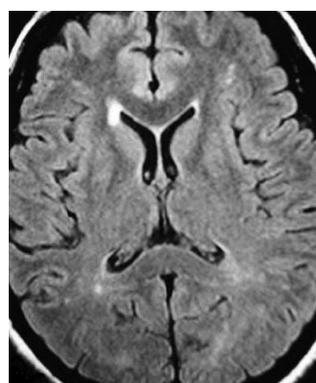


Figure 2. Axial FLAIR image two months later indicates the lesions had disappeared.

involving hypokalemia, hypophosphatemia, hypomagnesemia, and hypoglycemia may disrupt the normal activity of active transport pumps at the cell membrane included in the regulation of intracellular osmolarity, restricting the ability of brain to respond to osmotic stress (17). Moreover, the correction of hypokalemia or other metabolic disorders may cause a quick increase in serum Na through cellular Na⁺/K⁺ exchange and other mechanisms. Serum Na must be closely controlled when correcting these abnormalities (17-19).

Moreover, low pre-transplant serum cholesterol was

Table 1. Laboratory assessment through hyponatremia correction

	1st	2nd	3rd	4th	5th	6th	7th	8th	9th
Na (meq/L)	115	118	123	126	124	132	134	138	136
K (meq/L)	3.1	2.5	3.2	3.5	3.6	3.4	3.4	3.5	4
BS (mg/dL)	55	82	105	120	122	145	130	126	134
Ca (mg/dL)	7.5			6.8			7.8		7.6
Ph (mg/dL)	1.5			1.8			2.3		2.5
Mg (meq/L)	1			1.3			2.5		2.8

associated with ODS in post liver transplantation. It may show the malnutrition or increase the susceptibility to calcineurin inhibitor toxicity in the post-liver transplantation which was associated with ODS in case reports (11,16,19,20)

ODS's clinical manifestations are typically delayed for two to six days after the rapid elevation of the serum sodium concentration has occurred (9,10). The symptoms involve dysarthria, dysphagia, paraparesis or quadriparesis, behavioral disturbances, movement disorders, seizures, lethargy, confusion, disorientation, obtundation (10,11).

Strictly influenced the patients may become "locked in"; they are awake, but cannot move or verbally communicate. They can commonly move their eyes and blink (10, 12).

In patients with pontine involvement, speech abnormalities early occur and persist, and patients often become mute. Corticospinal signs (hyperreflexia and bilateral Babinski signs) and corticobulbar signs (brisk jaw jerk) are usual. Swallowing dysfunction may result in the aspiration pneumonia and respiratory failure (9,11).

Other usual physical findings involve increased muscle tone, facial weakness, and snout, grasp, or rooting reflexes. Extra-pontine involvement can lead to various findings, involving the psychiatric disturbances, catatonia, postural limb tremor, myoclonic jerks, and a parkinsonian picture with choreoathetosis or dystonia, which responds to the dopaminergic treatment (10-13).

Conclusion

Considering the severity, permanent adverse consequences, and high mortality rate of ODS, the inhibition is necessary. Among the patients with hyponatremia more than two days or with hyponatremia of unknown duration, we proposed that the serum sodium must not increase 6 to 8 mEq/L in any 24-hour period to inhibit ODS. ODS risk is highest in the patients with serum sodium of ≤ 120 mEq/L, especially if hyponatremia is associated with hypokalemia, low-plasma osmolality, and other electrolyte disorders.

Authors' contribution

Initial draft and data gathering was handled by Farnoosh Tavakoli. Fatemeh Yaghoubi and Davood Babakhani presented the case and contributed to case discussion and figures. Manuscript was edited by Farnaz Tavakoli. All authors read and signed the final version.

Conflicts of interest

The authors revealed no competing interests.

Ethical considerations

The authors have completely observed ethical issues (including plagiarism, data fabrication, double

publication). Written consent was prepared from the patient for the publication of study.

Funding/Support

None.

References

1. Adrogué HJ, Madias NE. Diagnosis and treatment of hyponatremia. *Am J Kidney Dis.* 2014;64(5):681-4. doi: 10.1053/j.ajkd.2014.06.001.
2. Halawa I, Andersson T, Tomson T. Hyponatremia and risk of seizures: a retrospective cross sectional study. *Epilepsia.* 2011; 52:410. doi: 10.1111/j.1528-1167.2010.02939.x
3. Sterns RH. Severe symptomatic hyponatremia: treatment and outcome. A study of 64 cases. *Ann Intern Med.* 1987;107:656. doi: 10.7326/0003-4819-107-5-656.
4. Rose BD. New approach to disturbances in the plasma sodium concentration. *Am J Med.* 1986;81:1033. doi: 10.1016/0002-9343(86)90401-8
5. Sterns RH. Treatment of Severe Hyponatremia. *Clin J Am Soc Nephrol.* 2018;13:641-649. doi:10.2215/CJN.10440917.
6. Vu T, Wong R, Hamblin PS, Zajac J, Grossmann M. Patients presenting with severe hypotonic hyponatremia: etiological factors, assessment, and outcomes. *Hosp Pract (1995).* 2009;37(1):128-36. doi: 10.3810/hp.2009.12.266.
7. Sterns RH. Disorders of plasma sodium--causes, consequences, and correction. *N Engl J Med.* 2015; 372:55-65. doi: 10.1056/NEJMra1404489.
8. Verbalis JG, Goldsmith SR, Greenberg A, Schrier RW, Sterns RH. Hyponatremia treatment guidelines 2007: expert panel recommendations. *Am J Med.* 2007;120:S1-21. doi: 10.1016/j.amjmed.2007.09.001.
9. Gankam Kengne F, Decaux G. Hyponatremia and the Brain. *Kidney Int Rep.* 2018;3:24. doi: 10.1016/j.ekir.2017.08.015.
10. Karp BI, Lauren R. Pontine and extrapontine myelinolysis: a neurologic disorder following rapid correction of hyponatremia. *Medicine (Baltimore).* 1993;72:359. doi: 10.1590/S0004-282X2007000500027.
11. Lee EM, Kang JK, Yun SC, Kim KH, Kim SJ, Hwang KS, et al. Risk factors for central pontine and extrapontine myelinolysis following orthotopic liver transplantation. *Eur Neurol.* 2009;62(6):362-8. doi: 10.1159/000242426.
12. Sterns RH, Riggs JE, Schochet SS Jr. Osmotic demyelination syndrome following correction of hyponatremia. *N Engl J Med.* 1986;314:1535. doi:10.1056/NEJM198606123142402.
13. Martin RJ. Central pontine and extrapontine myelinolysis: the osmotic demyelination syndromes. *J Neurol Neurosurg Psychiatry.* 2004;75P:22-8. doi: 10.1136/jnnp.2004.045906.
14. Koul PA, Khan UH, Jan RA, Shah S, Qadri AB, Wani B, et al. Osmotic demyelination syndrome following slow correction of hyponatremia: Possible role of hypokalemia. *Indian J Crit Care Med.* 2013;17(4):231-3. doi: 10.4103/0972-5229.118433.
15. George JC, Zafar W, Bucaloiu ID, Chang AR. Risk factors and outcomes of rapid correction of severe hyponatremia. *Clin J Am Soc Nephrol.* 2018; 13:984. doi: 10.2215/

- CJN.13061117.
16. Yun BC, Kim WR, Benson JT, Biggins SW, Therneau TM, Kremers WK, et al. Impact of pretransplant hyponatremia on outcome following liver transplantation. *Hepatology*. 2009;49(5):1610-5. doi: 10.1002/hep.22846.
 17. Pham PM, Pham PA, Pham SV, Pham PT, Pham PT, Pham PC. Correction of hyponatremia and osmotic demyelination syndrome: Have we neglected to think intracellularly? *Clin exp Nephrol*. 2015;19:489–495. doi: 10.1007/s10157-014-1021-y.
 18. Lohr JW. Osmotic demyelination syndrome following correction of hyponatremia: Association with hypokalemia. *Am J Med*. 1994;96:408-413. doi: 10.1016/0002-9343(94)90166-x.
 19. Liamis G, Filippatos TD, Liontos A, Elisaf MS. Hyponatremia in patients with liver diseases: Not just a cirrhosis-induced hemodynamic compromise. *Hepato Int*. 2016;10:762-72. doi: 10.1007/s12072-016-9746-1.
 20. Tan TC, Robinson PJ. Mechanisms of calcineurin inhibitor-induced neurotoxicity. *Transplant Rev (Orlando)*. 2006;20:49–60. doi: 10.1016/j.trre.2006.02.005

Copyright © 2021 The Author(s); Published by Society of Diabetic Nephropathy Prevention. This is an open-access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.