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Case Report

Case Report on Thiazide-induced Hyponatremia Leading to Extra Pontine Myelinolysis

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ABSTRACT

Extra Pontine Myelinolysis (EPM) is a type of neurological disorder characterized by altered sensorium, movement abnormalities, seizures, and parkinsonian-like symptoms. It is a rare disorder involving wide etiological factors of which the most common is hyponatremia and its correction. Hyponatremia usually develops as a result of the use of certain medications like benzodiazepines, diuretics, etc. other causes include chronic kidney disease, heart disease, and metabolic disorders. EPM can be diagnosed with MRI and CT scans. In order to prevent this fatal disease, it is recommended to closely monitor the patients on medication like thiazides or benzodiazepines for serum sodium levels and maintain adequate amounts with adjuvant therapies and follow recent guidelines for the controlled correction of existing hyponatremia. Myelinolysis can only be treated symptomatically with neurological agents and physical therapies as no specific cure exists.

Keywords: Extra pontine myelinolysis, Hyponatremia, Benzodiazepines.

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INTRODUCTION

The term demyelination also called myelinolysis, refers to the loss of myelin sheath without any damage to the axons. Demyelination occurs as a result of diseases with the potential to harm myelin sheaths and the cells that produce them.[1]

Osmotic Demyelination Syndrome (ODS), is a severe and potentially fatal condition that has two components, Central Pontine Myelinolysis (CPM) and Extra Pontine Myelinolysis (EPM). The CPM symmetrically includes the basis pontis and pontocerebellar fiber, leaving the ventrolateral pons essentially unaffected, whereas EPM mainly affects the basal ganglia, thalami, and cerebral white matter.[2]

Etiologically, there are a large number of underlying causes and relevant comorbidities in the development of osmotic demyelination syndrome, which most commonly occurs as a result of a prior disease or its treatment such as chronic alcohol use and alcohol withdrawal, severe hyponatremia, and its aggressive correction, and liver transplantation.[3]

Extrapontine osmotic demyelination occurs when extracellular sodium levels rise rapidly, inducing dehydration or death of astrocytes and oligodendrocytes, resulting in non-inflammatory demyelinating lesions in the pontine and extrapontine areas.[4-6] Reports of osmotic demyelination have mostly been limited to patient reports and small studies.[7-9] Thus, it remains unclear, how often the rapid correction of sodium levels leads to osmotic demyelination in patients with severe hyponatremia.[10]

Slow correction of sodium is paramount. There is no recommendation to increase the serum sodium by more than 6-8 mEq/24 hr.[11-14] Quick correction especially >12 mEq/24 hr might lead to Osmotic Demyelination Syndrome (ODS).[15-18]

Osmotic Demyelination Syndrome (ODS) is a collection of mobility abnormalities and psychiatric symptoms that was first discovered in chronic alcoholics in 1959.[19-21] Seizures, Parkinsonian-like movement disorders, Encephalopathy, and locked-in syndrome are some of the hallmarks of osmotic demyelination syndrome.[10]

In EPM, a number of clinical characteristics can surface, ranging from spastic paraparesis with postural limb tremor and myoclonic jerks to a parkinsonian picture with choreoathetosis and eventually leading to a persistent parkinsonian condition with dystonia.[22]

The most common clinical manifestations (CPM and EPM) are encephalopathies, characterized by vigilance disorders, qualitative impairment of consciousness, delirium, and disorders of drive, memory, and concentration, among others.[3] Mutism, parkinsonism, dystonia, and catatonia have also been described as symptoms of EPM.[22]

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Electrolytes should be assessed after one week, one month, and then every three months upon starting thiazide diuretics[8,23] and should be stopped if hyponatremia occurs, rechallenging the patient is contraindicated.[18]

In individuals at high risk for osmotic demyelination (serum sodium 105 mEq/L, hypokalemia, malnutrition, or liver disease), recent US guidelines indicate that correction rates should not exceed 8 mEq/L for any 24-hr period however European guidelines suggest limiting correction to <10 mEq/L in the first 24 hr and < 8 mEq/L for any 24-hr period thereafter.[10] The American expert panel also recommended aggressive therapy with 3% saline for seizures and coma, regardless of known chronicity, a 10-min infusion of 100 mL of 3% saline repeated three times as needed was recommended.[18]

CASE REPORT

A 56-years-old male was admitted to the department of internal medicine with complaints of decreased daily activities from 2 to 3 days, associated with decreased food intake, vomiting, and loose stools. He had a previous history of hiccups and shortness of breath (insidious in onset) one week back. The patient had a past medical history of Coronary artery disease for which he underwent Percutaneous transluminal coronary angioplasty surgery twice, and he was a known case of Hypertension for which he was on tablets Rosuva Gold (Aspirin 75 mg/ Rosuvastatin 20 mg/clopidogrel 75 mg), Prolomet XL 50 mg, Sartel-C (Telmisartan 40 mg/Chlorthalidone 12.5 mg) and Amlong 5 mg.

Provisionally he was diagnosed to have Metabolic encephalopathy secondary to Hyponatremia (which was suspected to be diuretics induced) as blood biochemical examination showed sodium (Na+) levels as 90 mEq/L and on examination, the patient was drowsy, less response to verbal commands, and was in a confused state. Initially, the patient was treated with hypertonic solutions like an injection of Potphos 5mL in 45mL normal saline infused at the rate of 5mL per hour and 3% Normal saline at the rate of 20mL per hour along with antibiotics and symptomatic treatment.

By day 2 sodium levels reached 104 mEq/L with improved sensorium, and NaCl infusion was stopped on day 4 as normal levels of sodium i.e., 127 mEq/L were achieved. On day 5 patient suddenly threw seizures, involving shaking of bilateral upper limbs with up rolling of eyeballs and deviation of mouth to left side, CT brain and EEG were done which were grossly normal. On day 7 Patient was treated with anti-epileptics for the new onset seizures. His Na+ levels were133 mEq/L on day 7.

On day 8, the patient was suspected to have slurred speech and had complaints of generalised myalgias. By day 9, the patient was unable to speak or follow verbal commands. On examination, it was known that the patient had decreased movements, reduced speech intensity. Trihexyphenidyl 1mg twice daily was started in order to treat the movement defects. On day 10 patient presented with dyskinesias, low voice, and rigidity of limbs, MRI brain showed subtle hyperintensities in bilateral basal ganglia but no features of ODS. By day 11 he developed generalized bradykinesias, mild tremors throughout the night, dizziness, and headache so were suspected of Parkinson's disease and added Carbidopa and levodopa to his treatment. The patient's sensorium didn't improve and rigidity still persisted, so DW-MRI (Diffusion Weighted-Magnetic resonance imaging) of the brain was done which showed Demyelination of bilateral caudate nuclei, putamen, thalamus, external capsule, and left cerebellar hemisphere with relative sparing of globus pallidus, hence was suggestive of Expontine Demyelination. The patient was continued on the same medication along with physiotherapy and rehabilitation. Within 3 to 4 days of Trihexyphenidyl, Carbidopa, and levodopa treatment patient's sensorium improved to some extent, he was able to move all limbs and follow commands. So patient was discharged with advice to continue physiotherapy and rehabilitation with bowel and bladder care to prevent bedsores. At discharge time, the patient was conscious, obeying simple commands, and was on Ryles tube feeding.

DISCUSSION

This case demonstrates how a simple adverse drug reaction (Diuretic-induced Hyponatremia) can lead to a life-threatening disease (Myelinolysis) through a series of agonizing events. Despite the fact that Osmotic demyelination syndrome is considered to be rare, it is more prevalent than herniation which occurs due to untreated hyponatremia.[24]

In our patient he initially had symptoms of hyponatremia like dehydration, then his condition improved as normal serum sodium concentration was restored, followed by sudden onset of seizures and subsequent deterioration of neurological profile. According to Saurab Gupta, *et al.* clinical presentation of Demyelination syndrome involves 2 phases where, in phase-I patient presents an altered sensorium due to hyponatremic encephalopathy, after the correction of hyponatremia (leading to improvement), they undergo phase-II in which they develop neurological symptoms due to myelinolysis.[19] However there is no evident explanation behind the pathogenesis of OSD (Osmotic demyelination syndrome), but Pervaiz M Zunga *et al.* state in their study that Osmotic demyelination syndrome is brought on by a lack of adaptive mechanisms to prevent brain swelling. As a result, the brain shrinks as a result of solute redistribution and hyponatremia correction, which disrupts tight junctions and the blood-brain barrier, damaging oligodentrocytes and resulting in neuronal demyelination.[9]

In our case patient's, serum sodium concentration increased by 12 mmol/L in the first 24 hr and 19 mmol/L in 48 hr, these levels are partially in compliance with the recommended guidelines for hyponatremia correction. S Tandukar and H Randon-Berrios and other researchers in their study states the limits of sodium

correction as less than 10 to 12 mmol/L in 24 hr and 18 mmol/L in the first 48 hr with the help of desmopressin.[24,25] Richard H Sterns concluded that excessive treatment of severe hyponatremia leads to osmotic demylenation[25] which was seen in our case report too as during the aggressive treatment of hyponatremia the patient had developed seizures.

Heng AE, *et al*. has concluded that there is no association of hypokalemia with the treatment of hyponatremia with Centro pontine myelinolysis.[23]

CONCLUSION

Osmotic myelinolysis, a rare but potentially life-threatening syndrome can develop during or as a result of treatment of hyponatremia regardless of the rate of sodium correction. In our case and when compared to other cases regarding the correction of hyponatremia patients developed osmotic demyelination without any hypokalemia. There should be a constant observation during the correction of hyponatremia in order to avoid the demyelination. Thus, further clinical studies must be conducted on a larger scale so as to identify the other possible mechanisms involved in the process of Demyelination, for early detection and prevention.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Love S. J Clin Pathol, demyelinating diseases; Department of Neuropathology. J Clin Pathol. 2006;59(11):1151-9. doi: 10.1136/jcp.2005.031195, PMID 17071802.
2. Garg P, Aggarwal A, Malhotra R, Dhall S. Osmotic demyelination syndrome - evolution of extrapontine before pontine myelinolysis on magnetic resonance imaging. J Neurosci Rural Pract. 2019;10(1):126-35. doi: 10.4103/jnrp.jnrp_240_18, PMID 30765988.
3. Lambeck J, Hieber M, Dreßing A, Niesen WD. Central pontine myelinosis and osmotic demyelination syndrome. Dtsch Ärztebl Int. 2019;116(35-36):600-6. doi: 10.3238/arztebl.2019.0600, PMID 31587708.
4. Paz P, Pan J, Somedeb Ball MD. Teaching NeuroImages: extrapontine osmotic demyelination in hypernatremia. 2020;94:1-2. doi: 10.1212/WNL.0000000000009299.
5. Han MJ, Kim DH, Kim YH, Yang IM, Park JH, Hong MK. A case of osmotic demyelination presenting with severe hypernatremia. Electrolyte Blood Press. 2015;13(1):30-6. doi: 10.5049/EBP.2015.13.1.30, PMID 26240598.
6. Barhaghi K, Molchanova-Cook O, Rosenburg M, Deal B, Palacios E, Nguyen J, *et al*. Osmotic demyelination syndrome revisited: review with neuroimaging. J La State Med Soc. 2017;169(4):89-93. PMID 28850553.
7. Gankam Kengne FG, Decaux G. Hyponatremia and the brain. Kidney Int Rep. 2018;3(1):24-35. doi: 10.1016/j.ekir.2017.08.015, PMID 29340311.
8. Zhao P, Zong Xuyi, Wang X, Zhang Y. Extrapontine myelinolysis of osmotic demyelination syndrome in a case of postoperative suprasellar arachnoid cyst. Case Rep Med. 2012;2012:Article ID 679257, 3 pages doi:10.1155/2012/679257. doi: 10.1155/2012/679257, PMID 23326275.
9. Zunga PM, Farooq O, Dar MI, Dar IH, Rashid S, Rather AQ, *et al*. Extra pontine osmotic demyelination syndrome. Ann Neurosci. 2015;22(1):51-3. doi: 10.5214/ans.0972.7531.220212, PMID 26124552.
10. 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(7):984-92. doi: 10.2215/CJN.13061117, PMID 29871886.
11. Verbalis JG, Goldsmith SR, Greenberg A, Korzelius C, Schrier RW, Sterns RH, *et al*. Diagnosis, evaluation, and treatment of hyponatremia: expert panel recommendations. Am J Med. 2013;126(10):S1-42. doi: 10.1016/j.amjmed.2013.07.006, PMID 24074529.
12. Spasovski G, Vanholder R, Allolio B, Annane D, Ball S, Bichet D, *et al*. Clinical practice guideline on diagnosis and treatment of hyponatremia. Eur J Endocrinol. 2014;170(3):G1-G47. doi: 10.1530/EJE-13-1020, PMID 24569125.
13. Hsu YJ, Chiu JS, Lu KC, Chau T, Lin SH. Biochemical and etiological characteristics of acute hyponatremia in the emergency department. J Emerg Med. 2005;29(4):369-74. doi: 10.1016/j.jemermed.2005.02.014, PMID 16243191.
14. Sterns RH. Treating hyponatremia: why haste makes waste. South Med J. 1994;87(12):1283-7. doi: 10.1097/00007611-199412000-00016, PMID 7973932.
15. Sterns RH, Riggs JE, Schochet SS Jr. Osmotic demyelination syndrome following correction of hyponatremia. N Engl J Med. 1986;314(24):1535-42. doi: 10.1056/NEJM198606123142402, PMID 3713747.
16. Sterns RH, Cappuccio JD, Silver SM, Cohen EP. Neurologic sequelae after treatment of severe hyponatremia: a multicenter perspective. J Am Soc Nephrol. 1994;4(8):1522-30. doi: 10.1681/ASN.V481522, PMID 8025225.
17. Aegisdottir H, Cooray C, Wirdefeldt K, Piehl F, Sveinsson O. Incidence of osmotic demyelination syndrome in Sweden: A nationwide study. Acta Neurol Scand. 2019;140(5):342-9. doi: 10.1111/ane.13150, PMID 31343728.
18. Tinawi M. Hyponatremia and hypernatremia: A practical guide to disorders of water balance. Arch Intern Med Res. 2020;3(1):74-95. doi: 10.26502/aimr.0025.
19. Gupta S, Gupta S, Shroti A. Osmotic, demyelination syndrome presenting as extrapontine myelinolysis with or without central pontine myelinolysis: case series of five cases and review of literature. MAMC J Med Sci. 2021;7(3):218-24.
20. Adams RD, Victor M, Mancall EL. Central pontine myelinolysis: a hitherto undescribed disease occurring in alcoholics and malnourished patients. AMA Arch Neurol Psychiatry. 1959;81(2):154-72. doi: 10.1001/archneurpsyc.1959.02340140020004, PMID 13616772.
21. Niwa K, Matsushima K, Yamamoto M, Shinohara Y. A case of extrapontine myelinolysis demonstrated on MRI. Clin Neurol. 1995;31:327-30.
22. Martin RJ. Central pontine and extrapontine myelinolysis: the osmotic demyelination syndromes. J Neurol Neurosurg Psychiatry. 2004;75(S3):iii22-8.. doi: 10.1136/jnnp.2004.045906, PMID 15316041.
23. Heng AE, Vacher P, Aublet-Cuvelier B, Garcier JM, Sapin V, Deteix P, *et al*. Centropontine myelinolysis after correction of hyponatremia: role of associated hypokalemia. Clin Nephrol. 2007;67(6):345-51. doi: 10.5414/cnp67345, PMID 17598369.
24. Tandukar S, Rondon-Berrios H. Treatment of severe symptomatic hyponatremia. Physiol Rep. 2019;7(21):e14265. doi: 10.14814/phy2.14265, PMID 31691515.
25. Sterns RH. Treatment of severe hyponatremia. Clin J Am Soc Nephrol. 2018;13(4):641-9. doi: 10.2215/CJN.10440917, PMID 29295830.

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