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Case Report

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With a grain of salt; A cautionary reminder. A case report of osmotic demyelination syndrome

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Abstract

Osmotic Demyelination Syndrome (ODS) is a demyelinating disease typically seen in the central pons, often associated with a rapid correction of hyponatraemia. This case describes iatrogenic central pontine and extrapontine demyelination secondary to rapid correction of hyponatraemia in a 45-year-old man with a history of chronic alcohol misuse and malnutrition. We report how this patient improved dramatically with physical rehabilitation therapy despite significantly abnormal clinical and radiological findings.

Keywords: Hyponatraemia; Osmotic demyelination syndrome; Central pontine myelinolysis.

Introduction

Osmotic Demyelination Syndrome (ODS) is a disabling, iatrogenic disorder associated with rapid correction of hyponatremia [1-4]. The original case series in 1959 described non-inflammatory demyelination of the central pons in a group of patients with alcoholism and malnutrition, leading to pseudobulbar palsy, quadriplegia and death [5]. In the 1970s an association with hyponatremia was reported [4,6]. Subsequent case studies have denoted a broad clinical spectrum, and extension of disease to include extra-pontine foci [2,7]. There may also be clinico-radiological paradox, with more dramatic myelinolysis on imaging compared with clinical severity [8,9]. A large systematic review reported that although mortality can reach 25%, outcomes have improved since earlier descriptions, and more than half of patients make a good recovery [8,10,11]. Although factors such as alcoholism, hypokalemia, malnutrition and liver transplantation are associated with ODS, it is rapid correction of hyponatremia which is of principal significance [1,3,7,9,11,12]. Sterns et al reported in 1986 that a rise in serum sodium by more than 12 mmol/L over 24 hours in patients with critical hyponatremia (<106 mmol/L) resulted in adverse neurological outcomes [2].

Chronicity of hyponatremia is integral to the risk of developing ODS [13]. This relates to the concept of cerebral adaptation, which is achieved within 48 hours of hyponatremia onset [1]. Efflux of cerebral intracellular osmolytes maintains osmotic equilibrium between intra and extra-cellular spaces, and is necessary to reduce harmful outcomes from cerebral edema. In ODS, rapid correction of hyponatremia once cerebral adaptation is completed, precipitates water movement out of cells, resulting in brain shrinkage and demyelination, with damage to astrocytes and glial cells [1,14,15].

Hyponatremia is frequently encountered in the hospital environment, and improved treatment protocols have resulted in iatrogenic ODS being uncommon [13,16]. In this case report we describe the presentation, diagnosis and clinical trajectory of a patient with ODS. We hope this case can serve as a reminder of

the gravity of this disorder, the necessity of hypervigilance in its prevention and recognition, and the importance of clinical cautiousness in the management of hyponatremia.

Case presentation

A 45-year-old man presented to the Emergency Department in an Australian quaternary referral hospital on 9th of March with a 3-day history of lethargy, confusion and reduced mobility, in the context of subacute decline over 3 months with anorexia and weight loss. He had a history of alcohol abuse and associated cardiomyopathy, diagnosed 8 years prior. Medications included bisoprolol, bumetanide, spironolactone and ramipril. The patient denied recent alcohol consumption. He had no other co-morbidities, nor family history. On examination, he was hypotensive with blood pressure 71/35 mmHg, heart rate was 84 in sinus rhythm, and temperature measured 36.3°C. He appeared cachectic and dehydrated. Biochemistry revealed critical hyponatremia; sodium measured 102 mmol/L, hypokalemia 2.8 mmol/L and hypochloremia 60 mmol/L. Serum osmolality was 215 mmol/Kg, urine sodium < 10 mmol/L and urine osmolality 119 mmol/kg. Blood glucose was 5.4 mmol/L. Renal impairment was present, with serum creatinine 184 micromol/L and eGFR 38 ml/min/1.73 m^2; baseline renal function was unknown. Venous lactate measured 1.6 mmol/L. GGT was 52 U/L, ALP 138 U/L. Transaminases were within normal range as was thyroid function. Serum cortisol measured the following morning was 289 nmol/L. The patient's confusion and lethargy was attributed to hyponatremia and 70 mls hypertonic 3% saline was administered by the emergency physician. The case was discussed with the admitting nephrologist; considering the insidious onset of symptoms, concurrent alcoholism and malnutrition, a provisional diagnosis of chronic hypovolaemic hyponatremia with total solute depletion was made. The patient was admitted to the Intensive Care Unit for further management. It was advised to correct the hyponatremia cautiously with isotonic saline solution (0.9% NaCl) at a rate of 80 mL/hour with biochemistry sampled every 4 hours, aiming for no more than 1mmol rise per every 2-3 hours, and no more than 8-10mmol/L total over the first 24 hours.

During the first 14 hours of admission the sodium incremented appropriately from 102 mmol/L to 107 mmol/L. The rate of correction then accelerated and reached 113 mmol/L by the 24-hour mark and 124 mmol/L by 48 hours; a total increase of 22 mmol/L (Figure 1). This was despite attempts to slow the rate of rise by changing from isotonic saline to a 5% dextrose infusion. However, the patient clinically improved, his acute kidney injury resolved, and he was transferred to a medical ward 48-hours after admission.

Although premorbid function was poor, the patient initially made good progress with mobility and cognition. His condition deteriorated with new, frequent falls 9 days into admission. The serum sodium was 131 mmol/L at this time. Neurological examination revealed dysarthria, upper and lower limb resting tremor, and ataxia. He had full power in limbs and normal sensory examination. Severe dysphagia was demonstrated by video fluoroscopy. Given the significant rise in sodium that had occurred earlier in admission, concern was raised for ODS. Differential diagnoses included alcohol withdrawal and alcohol related brain injury.

A cerebral MRI on 20th March demonstrated abnormal restricted diffusion within the central pons with sparing of the periphery. There was increased restriction on the left and corresponding T1 hypointensity and T2/FLAIR hyperintensity. There were small foci of restricted diffusion in the right and left mesial temporal lobes inkeeping with extra-pontine myelinolysis. A background of cerebral atrophy was noted (Figure 2).

Osmotic demyelination syndrome was diagnosed and the patient underwent rehabilitation therapy. Neurology and function improved dramatically and he progressed to become independently mobile and able to climb stairs 3 weeks after diagnosis. Dysarthria, dysphagia and tremor also resolved and he was discharged home.

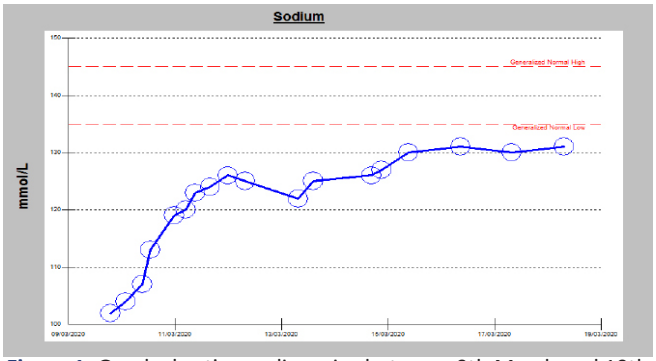

Figure 1: Graph charting sodium rise between 9th March and 19th March 2020.

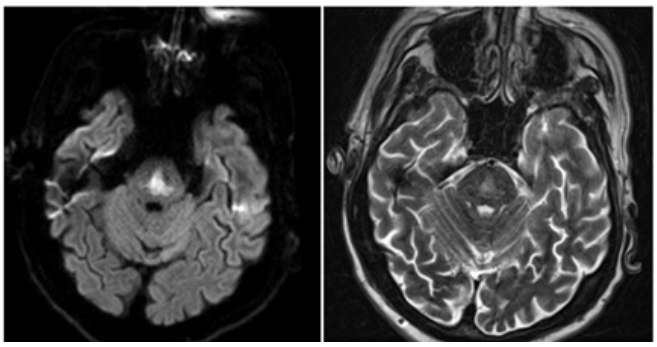

Figure 2: MRI Brain performed 20th March 2020.
Left: DWI. Right: T2

Discussion

ODS is a rare clinical entity, however given its premise as preventable and iatrogenic in nature, with grave outcomes for the patient, this case provides several timely lessons for clinicians. Our case demonstrates three key points in the management of chronic hyponatremia and ODS. Firstly, slower correction of sodium over the initial 24 – 48 hours should be advocated. Whilst most clinical guidelines recommend correction of 8 – 10 mmols/L over 24 hours [17], we suggest lower targets (i.e. 4 – 6 mmol over 24 hours) particularly in patients likely to have chronic hyponatremia who are at high risk of ODS. Secondly, early recognition that a patient is at risk of ODS may reduce the clinician's urge to correct hyponatremia. Our patient exemplifies an 'at-risk patient' in his history of alcoholism, malnutrition and hypokalemia. Lastly, ODS is often delayed, in our case 9 days after presentation, thus we advise monitoring of neurological status, in at-risk patients, for a prolonged period.

This case also highlights some of the pitfalls encountered when treating hyponatremia and can offer practical guidance to clinicians. Guidelines for treatment often vary between centres, and clear cohesive agreement is frequently lacking [17]. As we found, the rate of increase in serum sodium can be difficult to predict; whilst our patient experienced only a modest rise after hypertonic saline, the sodium rose rapidly on the second day of admission, despite attempts to attenuate this by changing to a 5% dextrose infusion. This is consistent with a retrospective study which found that only 6 out of 83 patients were corrected at a rate of <8 mmol/L per 24 hours [11]. Close monitoring is essential, even if initial biochemistry tracks as planned. In patients with critical hyponatremia, this should portend an extended critical care stay.

ODS occurs more commonly in the context of co-morbid alcoholism, malnutrition and hypokalemia [5,12], all of which were present in our patient. In addition, the majority of patients have an initial serum sodium <120 mmol/L [10], with one retrospective study demonstrating the mean sodium at presentation to be 104 mmol/L [11]. When encountering a patient with a concerning risk factor profile, targeting lesser increments in serum sodium is advisable. Early recognition of these risk factors in the current case may well have led to less aggressive sodium replacement and prevention of ODS.

The interval between sodium correction and development of ODS has been well documented [3,7]. We have described a case of ODS occurring on day 9 of admission, and whilst this phenomenon is reported, it may not be common knowledge for clinicians. The relevance of this is multi-factorial. The serum sodium measured 131 mmol/L at the onset of ODS in our patient, and had been stable at this level for some days. Although evidence in rat studies suggest a role for re-lowering serum sodium in established ODS [18], data in humans is lacking, and we elected aggressive rehabilitation rather than attempting to re-precipitate hyponatremia.

It is interesting to note that despite MRI revealing striking pontine abnormalities in our patient, plus corresponding clinical symptoms, he progressed exceptionally well with rehabilitation, and was discharged with better function than his premorbid status. This finding has been echoed in other recent literature, and is converse to the terminal prognoses outlined in earlier reports [10]. This emphasises the importance of continued good care following diagnosis and demonstrates that a favourable outcome can be achieved. We must not let our preconceptions about the disorder lead to an overly pessimistic approach as, highlighted in this case, it is possible to make an excellent recovery.

References

1. Greenstein AJ, et al. Amyloidosis and inflammatory bowel disease. A 50-year experience with 25 patients. Medicine. 1992; 71: 261-270.
2. Lachmann HJ, et al. Natural history and outcome in systemic AA amyloidosis. New England Journal of Medicine. 2007; 356: 2361-2371.
3. Kuroda T, et al. Long-term mortality outcome in patients with reactive amyloidosis associated with rheumatoid arthritis. Clin Rheumatol. 2006; 25: 498-505.
4. Denis MA, et al, Control of AA amyloidosis complicating Crohn's disease: a clinico-pathological study. Eur J Clin Invest. 2013; 43: 292-301.
5. Pukitis A, et al. Effect of infliximab induction therapy on secondary systemic amyloidosis associated with Crohn's disease: Case report and review of the literature. Journal of Gastrointestinal & Liver Diseases. 2013; 22.
6. Hawkins PN. Studies with radiolabelled serum amyloid P component provide evidence for turnover and regression of amyloid deposits in vivo. Clin Sci (Lond). 1994; 87: 289-95.
7. Moroni G, et al. Chronic dialysis in patients with systemic amyloidosis: the experience in northern Italy. Clinical nephrology. 1992; 38: 81-85.
8. Gottenberg JE. et al. Anti–tumor necrosis factor α therapy in fifteen patients with aa amyloidosis secondary to inflammatory arthritides: A followup report of tolerability and efficacy. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology. 2003 48: 2019-2024.
9. Fernández-Nebro A. et al. Treatment of rheumatic inflammatory disease in 25 patients with secondary amyloidosis using tumor necrosis factor alpha antagonists. The American journal of medicine. 2005; 118: 552-556.
10. Livneh A, et al. Colchicine prevents kidney transplant amyloidosis in familial Mediterranean fever. Nephron. 1992; 60: 418-22.
11. Trabulus S, et al. Canakinumab treatment in kidney transplant recipients with AA amyloidosis due to familial Mediterranean fever. Clin Transplant. 2018; 32: e13345.
12. Dengu F. et al. Bilateral Nephrectomy for Autosomal Dominant Polycystic Kidney Disease and Timing of Kidney Transplant: A Review of the Technical Advances in Surgical Management of Autosomal Dominant Polycystic Disease. Exp Clin Transplant. 2015; 13: 209-13.
13. Solak Y. et al. When urine is no longer beneficial: renal artery embolisation in severe nephrotic syndrome secondary to amyloidosis. Amyloid. 2010; 17: 24-26.
14. Özdemir, B., et al. Among therapy modalities of end-stage renal disease, renal transplantation improves survival in patients with amyloidosis. in Transplantation proceedings. 2006. Elsevier.
15. Pasternack AJ. Ahonen And B. Kuhlbäck. Renal Transplantation In 45 Patients With Amyloidosis. Transplantation. 1986; 42: 598-601.
16. Sherif AM. et al. Long-term outcome of live donor kidney transplantation for renal amyloidosis. Am J Kidney Dis. 2003; 42: 370-5.
17. Kofman T, et al. Renal transplantation in patients with AA amyloidosis nephropathy: results from a French multicenter study. American Journal of Transplantation. 2011; 11: 2423-2431.
18. Lovat LB. et al. Long-term survival in systemic amyloid A amyloidosis complicating Crohn's disease. Gastroenterology. 1997; 112: 1362-1365.
19. Ueda M. et al. FK506 inhibits murine AA amyloidosis: Possible involvement of T cells in amyloidogenesis. J Rheumatol. 2006; 33: 2260-70.
20. Grupper A, et al. Kidney transplantation in patients with inflammatory bowel diseases (IBD): analysis of transplantation outcome and IBD activity. Transpl Int. 2019; 32: 730-738.