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Case Report

A child locked-in due to iatrogenic osmotic demyelination syndrome

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ABSTRACT

Iatrogenic Osmotic demyelination syndrome (ODS) may follow aggressive correction of hyponatremia with hypertonic saline. Locked-in syndrome (LIS), is an entity rarely encountered in ODS, and has been infrequently reported in children. LIS has variable outcomes, although associated with significant morbidity and a protracted course. The authors present a report of a 5 year old, developmentally normal female- who developed features of ODS, progressing to LIS in a matter of days. Recurrent seizures necessitated mechanical ventilation and the administration of propofol. Assessment of her mentation, ocular movements and phonation were done on a daily basis post-extubation. Early enteral feeds were started and rehabilitation was initiated involving the healthcare staff as well as the child's parents. The outcome was fortunate in spite of the fact that the illness had a prolonged and difficult course. The patient made a full recovery, and did not suffer from any sequele after 3 months.

Keywords: Osmotic demyelination syndrome, Locked in syndrome, Hypertonic saline, Hyponatremia, Quadriparesis, Dysarthria

INTRODUCTION

Central pontine myelinolysis, which constitutes the spectrum of ODS was first described by Victor and Adams in 1959. The link between ODS and rapid correction of hyponatremia was proposed by Tomlinson and demonstrated by Kleinschmidt-DeMasters and Norenberg in 1981. Clinical features such as quadriparesis, altered sensorium, dysphagia, dysarthria etc. are encountered in ODS.[1] The reason why certain areas of the brain such as the pons, are more vulnerable to develop ODS is still obscure.

LIS or pseudocoma is one of the rare scenarios encountered in ODS, and as per Bauer- may be classified into classical, incomplete and complete forms.[2] LIS - a term coined by Plum and Posner[3], is a state of wakefulness with detectable awareness within a non-functional body and is defined by the American Congress of Rehabilitation Medicine as the presence of: (1) sustained eye opening (bilateral ptosis should be ruled out as a complicating factor); (2) preserved basic cognitive abilities; (3) aphonia or severe hypophonia; (4) quadriplegia or quadriparesis; and (5) a primary mode of communication that uses vertical or lateral eye movement or blinking of the upper eyelid.[4]

Bilateral ventral pontine lesions are the most frequent cause of LIS[5], and the first pediatric case was reported by Golden et al in 1976.[6]

CASE REPORT

A 5 year old developmentally normal female 'B', was referred to us with history of moderate intermittent fever, reduced appetite, recurrent episodes of vomiting since 1 week, altered sensorium since 3 days and recurrent generalized tonic clonic seizures (GTCS) since 2 days. She had been admitted elsewhere, and was being treated for possible meningo-encephalitis.

We reviewed her records and were able to ascertain that she had been admitted to the paediatric intensive care unit (PICU) of the referral centre. Initial MRI Brain

performed there at the time of admission was normal. In the PICU, she was detected to have hyponatremia-necessitating correction with 3% hypertonic saline. Twenty six hours after correction, B started having GTCS, which continued unabated in-spite of administration of multiple anticonvulsants (Phenytoin, Phenobarbitone and Sodium Valproate). She was subsequently referred to our centre for further care.

We encountered B in the ER with Glasgow coma scale (GCS) of 7/15. She was afebrile, had blood sugars of 148mg/dL, was tachycardic (114 bpm) and had sluggishly reacting pupils as well as bilateral extensor plantar responses. Optic fundi were hyperaemic, blood pressure was normal, and remainder of the physical examination was unremarkable. She had two episodes of GTCS in the ER, each lasting approximately two minutes in spite of administration of intravenous Midazolam.

B was admitted to the ICU. Blood investigations revealed only marginally elevated total WBC counts (12000cells/cmm), serum Sodium (141 mEq/L) and deranged hepatic transaminase levels (SGOT: 82 IU/L, SGPT: 76 IU/L). CSF analysis showed mild pleocytosis (14 cells/cmm, 100% lymphocytes) and a CSF-PCR was negative for infectious agents (JE Virus, Dengue 1-4, HSV, Measles, Mumps, Chikungunya, West Nile Virus, Toxoplasmosis, Pneumococcus, H. influenza, meningococcus, Cryptococcus, M. Tuberculosis and Filamentous fungi). No CSF Oligoclonal Bands were seen. Arterial blood gas analysis (ABGA) showed compensated metabolic acidosis, while renal function tests were normal. Three more episodes of GTCS occurred and after discussing with B's parents, it was decided to electively intubate her and administer Propofol infusion with supportive mechanical ventilation.

We started Propofol with a loading dose of 3mg/kg, followed by infusion at 1 mg/kg/hr which was continued for 36 hours, following which levetiracetam was introduced into the treatment regimen. No further seizures occurred thereafter. Intravenous fluids (Dextrose-normal saline) and antibiotic (Ceftriaxone) were given. Early nasogastric (NG) feeds were initiated. Renal function and Serum electrolyte levels were monitored on a daily basis. All the limbs remained hypotonic and she had hypoactive deep tendon reflexes. Spontaneous eye opening and blinking were observed on day 4 of hospitalization, lateral and vertical eyeball movements were noticeable. In view of satisfactory respiratory efforts, B was extubated and provided oxygen support via nasal prongs. Periodic suctioning of the oral cavity was performed to clear pooled secretions. We observed that she could comprehend basic questions and give appropriate responses by blinks albeit phonation was impaired. At this stage, we encouraged direct parental involvement in her care, and advised them on providing necessary visual, tactile and auditory stimuli.

MRI Brain was done on day 5, which showed an ill-defined, irregular central pontine lesion measuring 1.9 x1.9 x 2.1 cms which was iso to hypo intense on T1, mildly hyper intense on T2, FLAIR weighted sequences. There was no evidence of diffusion restriction, hemorrhage, perilesional edema or mass effect. There was no significant enhancement of the lesion post-contrast. Spectroscopy of the lesion showed increased choline peak, choline: creatinine (2.84) and choline: N-Acetyl aspartate (1.59) ratios. Mild lipid lactate peak was also observed. A diagnosis of Osmotic demyelination syndrome was made.

B was transferred to the wards on day 7. NG feeds were continued till day 24, while spoon feeds were started from day 14 in small quantities. Limb and truncal hypotonia persisted-necessitating physiotherapy. Phonation was impaired, although B was able to produce a few vowel sounds by day 13. The main mode of communication was through her eye movements and blinks. We extensively reviewed available literature on locked-in syndrome and were able to attribute the same diagnosis to our patient. Twitching limb movements were observed on day 16, which progressed to partial limb flexion. Ambulation with support was encouraged from day 22. She was discharged on day 29, and the parents were taught exercises by the physiotherapist. Levetiracetam was continued for a further six week period. Proper feeding and supportive care methods were also taught. We reviewed the patient on a weekly basis, noticing gradual improvement in her phonation and physical activity. Orientation and comprehension remained intact. B's recovery was complete by three months, and she resumed her scholastic pursuits. No cognitive or motor deficits were observed. An MRI brain was repeated at 4 months- which showed resolution of the pontine lesion.

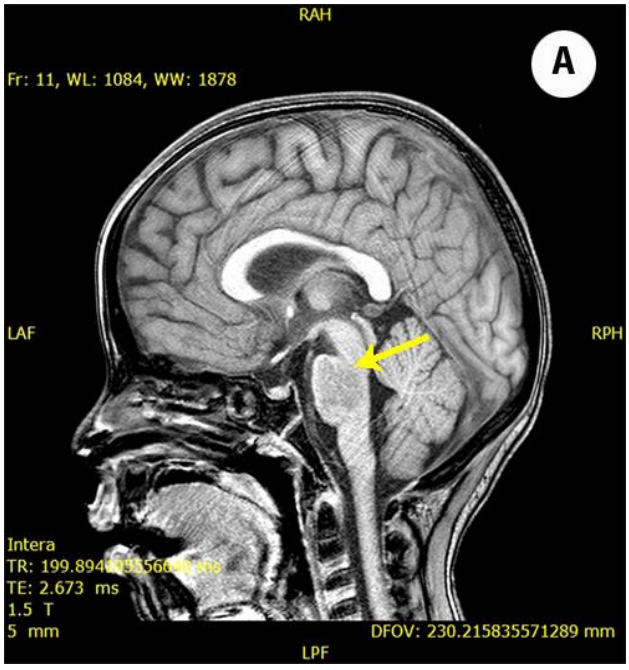

Figure 1: Sagittal T1-weighted brain MRI image shows pontine lesion with low signal intensity.

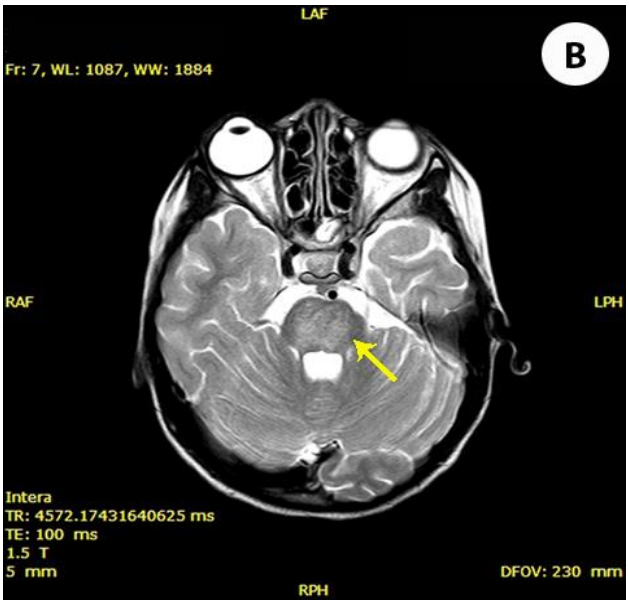

Figure 2: Axial T2- weighted image showing central pontine lesion with high signal intensity.

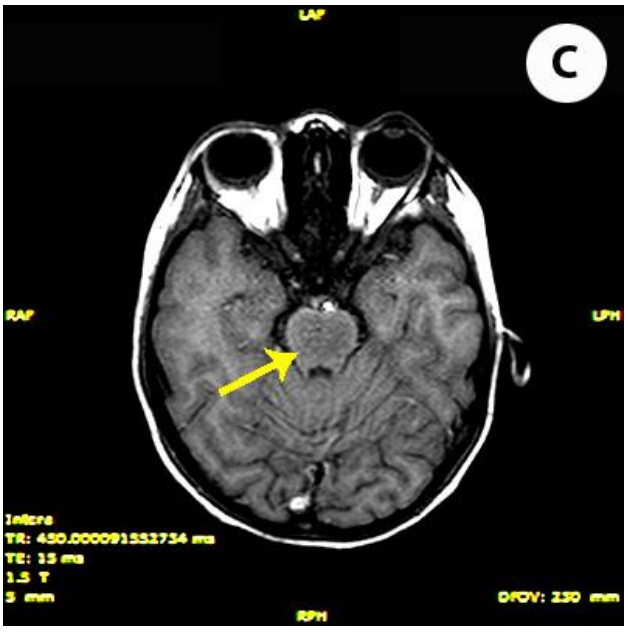

Figure 3: Axial T1- weighted image showing pontine lesion with low signal intensity.

DISCUSSION

Existing literature on paediatric LIS have reported up to 40% of the patients having poor outcome.[5] There is no definitive treatment for this condition, and care is mostly supportive, with anticipation of difficulties encountered during feeding, ambulation and phonation. As the posterior pons containing the reticular activating system, is uninvolved-sleep-wake cycle and consciousness are unaffected. Lack of involvement of the mesencephalon permits preservation of convergence and eye movements in the vertical plane.[7]

In case of B, the time of onset of symptoms suggestive of ODS after correction of hyponatremia was twenty-six hours. Other reports have described clinical manifestations classically occurring five to seven days after correction of sodium levels, but may even occur after two or more weeks.[8] The differential diagnoses for ODS in the general population include encephalitis, meningitis, multiple sclerosis, stroke, primary brain tumors, metastases, radiotherapy, chemotherapy, Wernicke encephalopathy, hepatic encephalopathy etc.[9] however, in the paediatric population-the first three would be more relevant. CSF analysis showed a mild pleocytosis, which can be confounding for viral infections, while such a phenomenon might be associated even with a benign condition such as HaNDL.[10] Classic pathological findings in ODS include symmetrical demyelination. There occurs oligodendroglial loss and reactive astrocytosis. Inflammation is not a prominent feature, and axonal cylinders and nerve cells and vasculature are relatively preserved.[11] ODS in children may occur at any age, with the youngest case reported being that of a 40- day old infant.[12]

MRI remains the diagnostic tool of choice, and can reveal pontine and extrapontine hyperintensities on T2 and hypo intensities on T1 weighted images.[13]When such lesions are symmetrical, they support the diagnosis of ODS. These lesions may be ideally seen one to two weeks after onset of symptoms. The complete resolution of MRI findings is rarely seen.[14]

B had seizures refractory to most anticonvulsants, necessitating the use of propofol. We selected propofol in the background of B's altered liver function test, considering the fact that the pharmacokinetics of propofol is not altered by liver failure, and that metabolism of the drug also occurs through alternate extra hepatic pathways. The use of Propofol may thus, offer a viable alternative in similar scenarios. The ventilatory strategy we opted for reduced the chance of respiratory compromise. Enteral feeds were started early; physiotherapy and supportive care were provided. We did not use steroids during the course of treatment. B had a fortuitous recovery, and no sequele were detectable four months after her discharge from the hospital. Other reports of paediatric LIS conveyed far less favourable outcomes.[5]

CONCLUSION

Although rarely encountered, ODS should be considered as a differential diagnosis in any patient with a history of new-onset altered sensorium, quadriparesis and dysphagia after correction of hyponatremia. The diagnosis of paediatric LIS poses a significant challenge

and careful attention must be paid on a daily basis to the child's mentation and ocular movements. There are no clear guidelines for the management of paediatric LIS, and hence it can only be through perusal of literature documenting course of the illness and adopted interventions, that treating physicians and nursing staff may formulate and modify strategies for patient care. Early rehabilitation improves outcome and it should be a concerted effort by the treating staff as well as the child's relatives, since the provision of long term care and attention is inevitable. Although majority of the literature describes a long, tortuous course of illness and poor outcome in majority of the patients, complete recovery is possible, and the future should hold promising insights into this condition.

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REFERENCES

1. Martin RJ. Central pontine and extrapontine myelinolysis: the osmotic demyelination syndromes. J Neurol Neurosurg Psychiatr. 2004;75(Suppl 3):iii22-8.
2. Bauer G, Gerstenbrand F, Rumpl E. Varieties of the locked-in syndrome. J Neurol. 1979;221:77-91.
3. Plum F, Posner JB. The diagnosis of stupor and coma. 3rd ed. Philadelphia: F. A. Davis Co., 1983;363-4.
4. American Congress of Rehabilitation Medicine. Recommendations for use of uniform nomenclature pertinent to patients with severe alterations of consciousness. Arch Phys Med Rehabil. 1995;76:205-9.
5. Bruno MA, Schnakers C, Damas F. Locked-in syndrome in children: report of five cases and review of the literature. Pediatr Neurol. 2009;41(4):237-46.
6. Golden GS, Leeds N, Kremenitzer MW, Russman BS. The ''locked-in'' syndrome in children. J Pediatr. 1976;89:596-8.
7. Smith E, Delargy M. Locked-in syndrome. BMJ. 2005;330:406-9.
8. Walterfang M, Goh A, Mocellin R. Peduncular hallucinosis secondary to central pontine myelinolysis. Psychiatry and Clinical Neurosciences. 2012;66(7):618-21.
9. Ashrafian H, Davey P. Review of the causes of central pontine myelinosis: yet another apoptotic illness? European Journal of Neurology. 2001;8(2):103-9.
10. Suresh I, Deb P, Chandra BD, Jeevan HR. Syndrome of transient headache and neurological deficits with cerebrospinal fluid lymphocytosis mimicking dengue encephalitis in a child. Int J Res Med Sci. 2015;3:2481-4.
11. Love S. Demyelinating diseases. J Clin Pathol 2006;59:1151-9.
12. Karakaş HM, Erdem G, Yakinci C. Osmotic demyelination syndrome in a 40-day-old infant. Diagn Interv Radiol. 2007;13(3):121-4.
13. Miller GM, Baker HL Jr, Okazaki H, et al.Central pontine myelinolysis and its imitators: MR findings. Radiology 1988;168:795-802.
14. Menger H, Jörg J. Outcome of central pontine and extrapontine myelinolysis (n = 44). J Neurol. 1999;246(8):700-5.

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