Cortical Visual Impairment (CVI): An Atypical Manifestation of Osmotic Demyelination Syndrome in a Child

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Introduction

Osmotic Demyelination Syndrome (ODS) is a unique process of selective demyelination and destruction of oligodendrocytes and astrocytes in specific areas of the brain that usually occurs a few days after an osmotic stress [1]. ODS has been described most frequently in association with a rapid correction of hyponatremia, though it may occur with other electrolyte or metabolic abnormalities [1]. ODS is a rather uncommon disorder in childhood [2,3] and encompasses central pontine and extra pontine myelinolysis. ODS may be associated with neurological impairment in the form of ataxia, bulbar dysfunction, gait disturbances, spasticity, seizures, encephalopathy and even coma and death. It may result in long term neurodevelopmental sequelae [2,3].

We present a 12-year-old boy with ODS, who’s most disabling manifestation was cortical visual impairment (CVI). Treatment included immunomodulation with steroids and IVIG. This may have contributed to his relatively good outcome.

Case Presentation

The child presented to an emergency department (ED) after a brief generalized tonic seizure. He had been unwell for 8 weeks (well child prior). There was history of intermittent vomiting, lethargy, sleep disturbances, craving for sugary drinks, and polydipsia (drinking up to 15 liters of water/day). Urea, electrolytes, creatinine and blood glucose had been normal when checked at a general practice two weeks earlier.

In ED he was initially thought to be postictal, with stable vital signs. Mild hypertonia and intermittent posturing of right upper limb was noted. His initial sodium level was 118 mmol/L on capillary blood gas (121 mmol/L on venous sample); 10 ml/kg bolus of 0.9% sodium chloride and 3 ml/kg of 0.9% sodium chloride resulted in improvement in consciousness. He had marked respiratory alkalosis (pH 7.84; CO₂ 14 mmHg; HCO₃ 25 mmol/L) and hypokalemia (2.7 mmol/L on venous gas). His serum osmolality was 257 mmol/kg; urine osmolality was 114 mmol/kg and urinary sodium concentration was 114 mmol/L.

He received another bolus of 3% sodium chloride, after experiencing a second seizure. An hour later he remained drowsy and experienced a third seizure which was terminated by midazolam. After seizure resolution the patient was loaded with 40mg/kg of levetiracetam. He was intubated at the peripheral hospital for transfer to a tertiary hospital (in view of recurrent seizures and his encephalopathic state).

At the tertiary hospital his sodium concentration fluctuated and in the course of 24 hours varied from 118 mmol/L to 158 mmol/L. Figure 1 depicts the changes in sodium concentration over the first few days. Considering diabetes insipidus, desmopressin (DDAVP) was commenced, as was free water via nasogastric tube, both were titrated based on the urine output and serum sodium level which were closely monitored. Over the course of the next 36 hours, he was extubated and later transferred to the ward in a stable condition. With DDAVP (200 mcg twice daily) the polydipsia had settled and he remained normonatremic. He did not have ongoing seizures so levetiracetam was not continued.
He had initial improvement for nearly 24 hours post extubation and was less encephalopathic. Over subsequent days, he became more restless, agitated and had sleep disturbance prompting a neurology consult on day 5 of admission at tertiary hospital. Neurologic assessment revealed markedly impaired visual acuity limited to perception of light with normal fundus and pupillary reactions. His other cranial nerves were intact. He had no obvious motor deficits. EEG (Figure 2) on day 5 showed an encephalopathic background with no epileptiform discharges.

A CAT scan of the brain was normal. 3T MRI Brain on day (Figure 3) revealed subcortical U fiber hyper intensity in the anterior temporal lobes, bilateral corpus striatum and subcortical white matter of occipital lobes (primary visual

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**Figure 1:** Graph Depicting Fluctuation in Serum Sodium level.

**Figure 2:** The background on an EEG done on day five showed excessive asymmetric diffuse slowing more marked on the left side; suggestive of an encephalopathy. No epileptiform activity was seen. (HFF: 70Hz, LFF:0.5Hz)
cortex) consistent with the ODS, and absent posterior pituitary bright T1 spot with mildly thickened pituitary stalk. MRI spine was unremarkable.

Other investigations including work up for infectious, para infectious, immune mediated and metabolic disorder showed no significant abnormality. CSF examination showed 1 WBC, 4 RBC, glucose 4.4 mmol/L and protein 0.86 g/L. Oligoclonal bands were not detected. Endocrine investigations including thyroid function, ACTH, GH, IGF-1, IGFBP3, cortisol, short synacthen test, aldosterone, and aldosterone/renin ratio were all normal. Serum and CSF ACE was also normal.

The clinical profile; the neurological deterioration days after correction of the low sodium and the radiologic features led to the diagnosis of ODS. Acute disseminated encephalomyelitis was considered unlikely in view of neuro-radiological and CSF finding. Considering severity of the visual impairment, we treated him with 20 mg/m²/day of dexamethasone for three days followed by gradual weaning over two weeks and 2 g/kg of IVIG divided over three days.

Despite extensive investigations (skeletal survey, CT chest abdomen and pelvis, tumor markers, serum and CSF ACE) etiology of the thickened pituitary stalk remained inconclusive. There was no evidence suggestive of Langerhans Cell Histiocytosis. Continued surveillance is planned.

Progress

Two weeks post immunomodulation therapy he was alert, cooperative, interactive, and cognitively intact. There was a gradual improvement in vision as he was able to finger count from half meter and differentiate colors.

At three-month review, he described himself as being “almost back to normal”, with ongoing need for DDAVP. His vision was 6/12 in right eye and 6/16 in left eye. There were no apparent functional limitations; he was participating and enjoying day-to-day activities at home and school. He had no focal neurological signs and his manual dexterity for complex fine motor tasks seemed marginally impaired. At five-month review his vision was 6/6 with both eyes open and 6/9 in each eye. He had 10-degree peripheral visual field loss in both eyes and had some difficulty identifying similar colors.

Repeat MRI after six months showed similar appearances of the temporo-occipital subcortical parenchymal abnormalities with normal orbits and anterior optic pathway, mildly bulky infundibulum and absent posterior pituitary bright spot.

Discussion

ODS is rare, reported in 0.4% to 0.56% of patients admitted to neurology services and 0.06% of all admission to general medical and neurology services [4]. ODS in
children is even more uncommon than in adults [2]. ODS usually presents with central pontine myelinolysis (CPM). In a pediatric series (Bansal and Zinkus et al.), 46% of all ODS had CPM and 28% had isolated extra pontine myelinosis (EPM) and 25% had combined EPM and CPM [2].

The common clinical presentation of ODS includes encephalopathy, bulbar dysfunction, and seizures. EPM presentation depends on location of lesion and may involve gait disturbance, myoclonus, dystonia. Cortical visual impairment is very rare and has not been previously described in children. In a series of 106 children with ODS, none of them had CVI [2]. CVI has been described in an adult with involvement of lateral geniculate body [5]. We attribute the CVI in our case to extra pontine myelin lysis with involvement of the visual cortex and subcortical U fibers in the occipital lobes (Figure 3).

ODS, as reported, in most cases, after rapid correction of subacute or chronic hyponatremia. It is difficult to explain the clinical presentation/profile in our child: the polydipsia for 8 weeks, normal sodium at two weeks prior to hospital admission, symptomatic hyponatremia on presentation to the hospital, the fluctuating sodium levels and the diagnosis and persistence of central diabetes insipidus (of unknown etiology). The optimal management of hyponatremia is still uncertain. Most guidelines advocate slow correction (<10 mmol/L in 24 hours) [6]. If the cause is identified the approach to correction may be tailored, e.g. use of vaptans for hyponatremia due to SIADH [6].

MRI brain in our patient showed subcortical U fiber hyper intensity in the anterior temporal lobes, corpus striatum subcortical white matter of the cuneus of both occipital lobes at the superior margins of the calcarine fissure (primary visual cortex. MRI brain and spine are diagnostic of ODS. Diffusion weighted imaging (DWI) may depict changes before conventional MRI imaging in ODS [7]. In CPM, lesions classically involve central pons, tegmentum and corticospinal tract, which produce a characteristic trident shaped appearance. In EPM most commonly noted changes are in cerebellar peduncle, globus pallidus, thalamus, splenium of corpus callosum [6,7].

There are no consensus guidelines for treatment of ODS, once it already occurred. Current treatment recommendations consist mainly of supportive care [8,9]. IVIG, steroid and plasmapheresis have been used anecdotally, with variable success [8,9]. Recovery after ODS may be incomplete [4]. Early immunomodulation with steroid and immunoglobin may have contributed to the good outcome in our child.

ODS is challenging to diagnose, the possibility has to be kept in mind in the relevant scenarios, neuroimaging may provide support to the diagnosis, though may not always be indicative of ODS. There are no well-established effective treatment modalities. Our aim in publishing this case report is to raise awareness of ODS in the pediatric age group and to suggest that early use of immunomodulation - IVIG/Steroids may be beneficial.

Summary

This child developed ODS after rapid overcorrection of hyponatremia. He developed CVI, with MRI showing extrapontine myelinosis. ODS in children is very rare and CVI due to ODS has not been reported in a child. There are no standard treatment guidelines for ODS, but given the excellent recovery in our case, immunomodulation should be considered early in treatment.

Practice Points

- ODS is a rare neurological disorder in children, seen mostly in the context of too rapid correction of subacute or chronic hyponatremia.
- Hyponatremia may be challenging to treat. It is important to be cautious with correction of hyponatremia, even when it is symptomatic: aim for < 10 mmol/L change in 24 hours.
- Seizures, altered conscious states, bulbar dysfunction, ataxia, hypertonia, hypotonia, hyperreflexia are some of the typical manifestations of ODS.
- Atypical manifestations may also occur – such as cortical visual impairment, gaze palsies, parkinsonian features.
- Treatment with steroid and immunoglobin was effective in our case and should be considered in the management of ODS.

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