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# Case Report

# A case of Parkinsonism secondary to Osmotic Demyelination Syndrome

**Wasundara S Wathurapatha, P M Jayawardana, Upul Dissanayake**

National Hospital of Sri Lanka

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Corresponding Author: Wasundara S Wathurapatha, E-mail:<wsevwandi@hotmail.com> https://orcid.org/0000-0002-2291-5995
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## Introduction

Osmotic demyelination syndrome (ODS) refers to the neurological manifestations occurring secondary to focal demyelination in the brain as a consequence of rapid changes in serum osmolality and encompasses both central pontine myelinolysis (CPM) and extra-pontine myelinolysis (EPM) depending on the site of demyelination. The incidence of ODS as demonstrated by MR imaging-based studies ranges from 0.3% -1.1%. Although initially thought to occur exclusively in the malnourished and in chronic alcoholics, rapid correction of hyponatremia is increasingly being recognized as the most common cause of ODS. Early detection of ODS leading to early intensive rehabilitation and supportive therapy has improved the prognosis of ODS which was initially thought to be a fatal illness. EPM occurs in 10% of cases of ODS and it is an uncommon cause of secondary parkinsonism. We report a case of ODS presenting with prominent parkinsonism following rapid correction of hyponatremia. Usually, the symptoms of ODS begin to appear within 1 week of correction of hyponatremia. Our case is unique because symptoms of ODS appeared 2 weeks after correction of hyponatremia and he did not have any typical risk factors for ODS such as malnutrition, alcoholism or evidence of chronic liver disease.

## Case Report

A 65-year-old man presented to our medical ward with generalised slowness, slurring of speech and difficulty in walking for 1-week. He was a known patient with hypertension and hypothyroidism and was on losartan, hydrochlorothiazide and thyroxine. Three weeks previously he had been admitted to the local hospital with recurrent episodes of positional vertigo associated with severe vomiting which progressed to confusion and altered behavior. He was found to have hyponatremia of 107 mmol/L and hypokalemia of 2.9 mmol/L. Non

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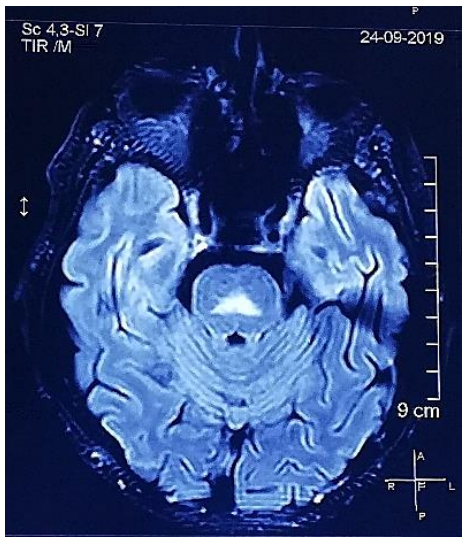
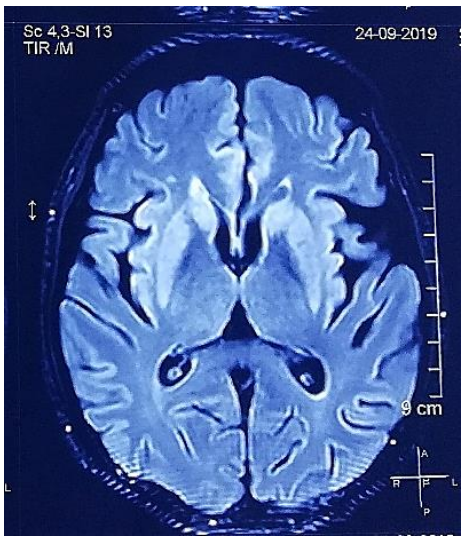
contrast CT brain and other investigations were normal. He was diagnosed to have hyponatremic encephalopathy precipitated by excessive vomiting due to benign paroxysmal positional vertigo in the background of thiazide diuretics induced chronic hyponatremia. His sodium level was corrected to 133 mmol/L over 48 hours using 3% saline and the potassium level to 3.6 mmol/L with oral potassium chloride. He was asymptomatic until he developed the current symptoms. He is a teetotaler with no family history of movement disorders or chronic liver disease. He was not on any dopamine depleting drugs.

On examination, he was conscious and oriented in time, place and person. He had dysarthria and a 'mask' like face with lack of facial expression. There was increased tone in all four limbs with lead-pipe rigidity and cogwheel rigidity in bilateral upper limbs. All reflexes were exaggerated and the "Babinski sign" was positive bilaterally. Muscle power was normal. There was severe bradykinesia but no resting tremors. He had a shuffling gait with small stride length, slow turns and reduced arm swinging. Sensory examination was normal and he didn't have any cerebellar signs. Cranial nerve examination and eye movements were normal. Ophthalmic examination revealed no Kayser-Fleischer rings. There was no significant postural hypotension. Cardiovascular, respiratory, and abdominal examinations were normal.

Baseline investigations including serum electrolytes, thyroid function tests and serum ceruloplasmin levels were normal. Cerebrospinal fluid examination revealed no abnormality. MRI brain revealed hyperintense lesions in the central pons and in the bilateral caudate nuclei and putamen (Figure 1) in T2 weighted and FLAIR sequences suggestive of demyelination.




(a)




(b)

Figure 1: MRI-FLAIR sequences showing a hyperintense lesion in the central pons (a) and hyperintense lesions in bilateral basal ganglia with sparing of globus pallidi (b)

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A diagnosis of secondary parkinsonism due to osmotic demyelination syndrome (ODS) was made based on the characteristic MRI appearance in the background of rapid correction of hyponatremia prior to the development of parkinsonism. He was started on Syndopa (Levodopa/Carbidopa) 125mg 4-times a day. Physiotherapy and gait training were commenced. He had a marked improvement in his symptoms in 2 weeks. At follow up after 6months, patient was independent in his activities of daily living and there were no residual Parkinsonian features.

## Discussion

Parkinson's disease is mainly a clinical diagnosis. The presence of bradykinesia with at least one of the other 2 cardinal features, tremor or rigidity, is defined as parkinsonism. In the presence of parkinsonism, the diagnosis of Parkinson's disease (PD) requires absence of red flags and absolute exclusion criteria as per the Movement Disorder Society diagnostic criteria [1]. Our patient had significant bradykinesia and lead-pipe rigidity associated with cogwheeling but no tremor. Therefore, he was diagnosed as having parkinsonism. He had bilateral symmetrical involvement, impaired gait and dysarthria from the beginning of the illness. Absence of asymmetry, gait impairment or severe dysarthria within 5 years of onset of illness are considered as red flags [1]. Rapid disease progression and absence of tremors are predictive of atypical parkinsonism [2]. Therefore, he was evaluated for secondary parkinsonism or possible atypical parkinsonism. However, he didn't have other features to suggest common atypical parkinsonism syndromes such as ocular movement abnormalities, autonomic dysfunction, apraxias or cerebellar signs. There is a wide variety of aetiology, including infective, metabolic and toxic insults and brain space occupying lesions, that result in secondary parkinsonism while drug induced parkinsonism due to anti-dopaminergic drugs are the most common cause[3]. EPM is an uncommon cause of secondary PD [3].

Magnetic resonance imaging of the brain is a useful and non-invasive diagnostic tool in discriminating the differential diagnosis of parkinsonism. In PD, extranigral structures are typically normal in the MRI brain whereas involvement of basal ganglia, especially the putamen, is in favor of atypical parkinsonism syndromes or secondary PD [4]. Our patient's MRI brain showed evidence of EPM involving the basal ganglia, the caudate nuclei and the putamen. It did not reveal any space occupying lesions, evidence of CNS infection or typical MRI features of atypical parkinsonian syndromes. Therefore, a diagnosis of secondary parkinsonism due to EPM was made.

Pathophysiology of ODS has been reported as follows. Low serum osmolality secondary to hyponatremia leads to inflow of water into the brain across the osmotic gradient resulting in cerebral oedema. As an adaptation to that, the brain loses intracellular and interstitial fluid osmotically active solutes including electrolytes and reaches the same tonicity as plasma thereby ameliorating the increased water content. This adaptation begins within minutes of hyponatremia and completes within two days. With rapid correction of hyponatremia, brain

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re-accumulates electrolytes rapidly but organic solutes slowly. Rapid overshoot of extracellular electrolytes in the setting of depleted organic solutes causes a hypotonic intracellular compartment which leads to shrinkage and death of brain cells due to loss of water. Injury to astrocytes and oligodendrocytes results in focal brain myelinolysis [5-7].

Our patient's hyponatremia had been corrected at a rate of 13 mmol/L/day and was the most likely culprit for ODS. Several authors have documented that there is no safe rate of correction of hyponatremia [8-10]. However, the majority of reported cases have occurred when the rate of correction exceeded 8 mmol/L/ day and when the initial serum sodium concentrations were very low i.e, ≤ 105 mmol/L. Therefore, the rate of correction of hyponatremia should not exceed 6-8 mmol/L/day [11]. Furthermore, coexistent hypokalemia has been found to increase the risk of developing ODS due to hyponatremia correction [12]. Our patient had hypokalemia and this may have contributed to ODS.

CPM predominantly involves the basis pontis causing dysarthria, dysphagia and spastic quadriparesis due to involvement of corticobulbar and corticospinal fibers. In severe cases, 'locked-in syndrome" can occur due to involvement of the ventral pons [10]. EPM most commonly affects the cerebellum and lateral geniculate body. It also affects the thalamus, cerebral white matter, basal ganglia and hippocampus [10,13]. Our patient had EPM involving bilateral caudate nuclei and putamen with sparing of the globus pallidi, which is a characteristic finding reported in previous case reports [8,14-16]. EPM typically results in extrapyramidal symptoms, movement disorders, parkinsonism, dystonia, tremors, choreoathetosis, mutism and catatonia [10]. Hence the presenting features of our patient can be explained by CPM and EPM. CPM and EPM appear in MRI brain as hypointense lesions on T1 sequence and hyperintense lesions on T2 weighted and FLAIR sequences. These lesions are typically bilateral, symmetrical and non-contrast enhancing [10,17]. We report similar findings in our patient.

Our patient had a biphasic clinical sequence. He presented to us with features of parkinsonism of 1 weeks duration after being asymptomatic for 2 weeks following symptomatic hyponatremia. This biphasic nature has been described in the literature. Almost all previously reported patients have developed symptoms of ODS within about 1 week of correction of hyponatremia [8,9,14,15,18]. Our patient was late to present and developed symptoms of ODS after 2 weeks of correction of hyponatremia and hence the diagnosis could have been missed. However, previous authors have reported that ODS can cause symptoms 7-14 days after correction of hyponatremia [14].

There is no trial-proven specific treatment for ODS and the treatment is mainly supportive. Parkinsonism due to ODS typically shows a good clinical response to dopaminergic therapy and has a good prognosis. Many patients recover completely and become independent [9]. This is because, relative dopamine deficiency due to reduced presynaptic striatal dopamine

transporters as a result of EPM is the main reason for parkinsonism in ODS [19]. However, progressive parkinsonism despite dopaminergic treatment has been reported [20].

In conclusion, ODS should be considered as a cause of secondary PD and hence a recent history of hyponatremia correction should be sought in such cases. Also, symptoms of ODS can appear as late as 2 weeks after correction of hyponatremia. As the parkinsonism secondary to EPM is potentially treatable, it is an important diagnosis to make. Chronic hyponatremia should be corrected with great caution in order to prevent ODS especially when there is coexistent hypokalemia.

## Consent

Written and verbal consent was obtained from the patient for publication of this case report.

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