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Case Report

Quadriplegia, due to hypokalaemia and related osmotic demyelination syndrome, as an initial presentation of Sjogren's syndrome

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Abstract...

We report a case of a 25-year-old lady who presented with quadriplegia and was found to have renal tubular acidosis and refractory hypokalaemia; serological investigations later revealed an underlying Sjogren's syndrome as the root cause for her problems. Her weakness, although initially attributed solely to hypokalaemia, was evaluated further and imaging evidence of Osmotic Demyelination Syndrome (ODS) was obtained. Although ODS is associated most often with rapid correction of hyponatremia, there are studies showing that osmotic demyelination can occur in the absence of hyponatremia. The case is unique in that quadriplegia as an initial manifestation of Sjogren's syndrome is rare, and may have more than a single causal mechanism, hence a high degree of clinical suspicion is necessary to arrive at the right diagnosis. Moreover, in contrast to the overall poor prognosis in ODS, our patient, despite a prolonged hospital stay, recovered well in a few weeks. In addition, a spurious dengue serology related to auto immunedisorder confounded the whole clinical scenario.

Keywords: Osmotic demyelination syndrome; Hypokalaemia; Sjogren's syndrome; Quadriplegia; Renal tubular acidosis.

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Introduction

Sjogren syndrome (SS) is a chronic, systemic autoimmune disease characterized by lymphocytic infiltration of the exocrine glands [1]. It commonly presents with dryness involving the eyes and mouth due to involvement of lacrimal and salivary glands and up to one-half of affected individuals also develop extra-glandular disease [2]. Renal involvement in SS is not uncommon and its spectrum includes interstitial nephritis, which can manifest as distal RTA, proximal RTA, tubular proteinuria, nephrogenic diabetes insipidus, glomerular diseases, or renal failure. Hypokalaemia is the most common electrolyte abnormality in most cases [3,4]. Hypokalaemia can produce muscle weakness by different mechanisms including hypokalaemic periodic paralysis, acute motor axonal neuropathy, myopathy, and may rarely cause Osmotic Demyelination Syndrome (ODS) resulting in quadriplegia. ODS, an often-underdiagnosed entity, is most often related to severe hyponatremia but has been reported to occur even in its absence. Correctly identifying the cause of weakness in these patients is important therapeutically and prognostically.

Case report

A 25-year-old female, with no known comorbidities, presented with a history of decreased food intake for 2 weeks, vomiting and abdominal pain of 4 days duration, later developing altered sensorium and weakness of all four limbs since a day prior to admission. She was initially evaluated elsewhere and detected to have severe hypokalaemia (1.4 mEq/L) and positive Dengue IgM. When she presented in the ER, she was drowsy (GCS 4/15) with laboured breathing. Her vitals were stable with a pulse rate of 78/min, BP of 110/60 mmHg and oxygen saturation of 99% in room air. Neurological examination revealed quadriplegia with normal deep tendon reflexes, and plantar reflex showing no response bilaterally. There was no neck stiffness.

Table 1: Laboratory profile of the patient during the course of illness.

Laboratory investigation	Day 1	Day 2	Day 5
Hemoglobin	9.3 g/dL		
ESR	72 mm/hr		
Total leukocyte count	19,030 cells/mm^3		12,000
Platelet count	516,000 cells/mm^3		
Serum potassium	1.7 mmol/L	2.4	3.8
Serum sodium	141 mmol/L	147	141
Serum phosphorous	1.4 mg/dL	1.8	3.4
Serum calcium	9.8 mg/dL	7.7	9.2
Serum creatinine	1 mg/dL		
Serum chloride	123 mmol/L	128	108
AST	26 IU/L	655	113
ALT	16 IU/L	175	123
Amylase	597 IU/L		
Lipase	729 IU/L		
Serum HCO_3^-	9 mmol/L	14	21

She underwent CT imaging of the brain which did not reveal any significant abnormalities. Arterial blood gas analysis revealed severe metabolic acidosis with normal anion gap. She had major electrolyte abnormalities including severe hypokalaemia (1.7 mmol/L), hypophosphatemia (1.4 mg/dL), hyperchloremia (123 mmol/L) with normal sodium levels (141 mEq/L) (Table 1). Total counts were initially elevated (19,000 cells/mm^3) with neutrophilic predominance (Table 1). Platelet count was normal. Renal parameters were normal. Transaminases were elevated from the second day. Increased serum amylase and lipase levels were also seen. Serum calcium was initially normal, later decreased. Creatine kinase was elevated (1450 IU/L). Dengue IgM was repeated and found to be positive with a high titre (42; >11 unitsconsidered significant) (Table 1). Chest X-ray and CT abdomen did not reveal any major abnormalities.

In view of low GCS and laboured breathing she was electively intubated and ventilated. Her hypokalaemia was initially refractory and needed continuous intravenous potassium supplementation of 20 mEq/h over the first 72 hours to reach a value above 3.0 mEq/L. Concurrent hypophosphatemia was also intravenously corrected. On the first day calcium level was normal but she developed symptomatic hypocalcemia (7.7 mEq/L) on the second day with carpopedal spasm and positive Chvostek's sign, and was given IV correction. An initial diagnosis of proximal renal tubular acidosis, pancreatitis and probable hypokalaemic paralysis was considered. By day 2, on withdrawal of sedation, her sensorium improved with spontaneous eye opening and response to simple verbal commands. By the 5th day of admission her metabolic parameters had normalised and she could be extubated the next day; but her limb weakness only improved partially and she had significant residual paralysis.

An autoimmune assay to look for the underlying pathology tested positive for ANA, Anti-Ro and Anti-La antibodies, suggestive of Sjogren's syndrome, which can produce both proximal RTA and pancreatic exocrinopathy.

Her limb weakness was initially considered to be due to hypokalaemic paralysis alone, but as some weakness persisted even after correction of serum potassium, further investigations were carried out to look for other causes. Cerebrospinal fluid analysis showed elevated protein (118 mg/dL), a cell counts of 8 cells/mm^3 (lymphocytes) and normal glucose. Nerve conduction studies were normal. An electroencephalogram showed only occasional triphasic waves. An MRI brain showed swollen pons with heterogeneously increased T2 and FLAIR signals, diffusion restriction and foci of microbleed, with heterogeneous post-contrast enhancement (Figures 1 and 2). The FLAIR high signal extended into the right and left middle cerebellar peduncles (Figure 1).

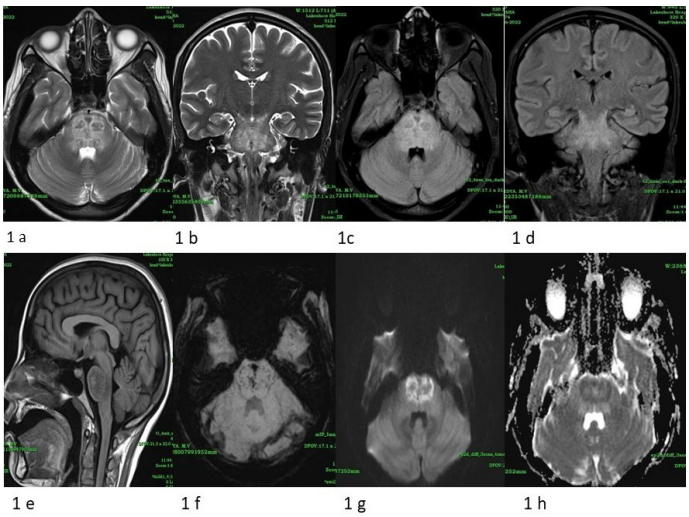

Figure 1: Axial and coronal T2 (a & b), axial and coronal FLAIR (c & d), T1 sag (e), SW (f), DW with ADC (g &h) images showing heterogenous increased T2 and FLAIR signal with T1 hypo intensity, foci of microbleed in SW sequence with diffusion restriction. FLAIR high signal extends into right and left middle cerebellar peduncles.

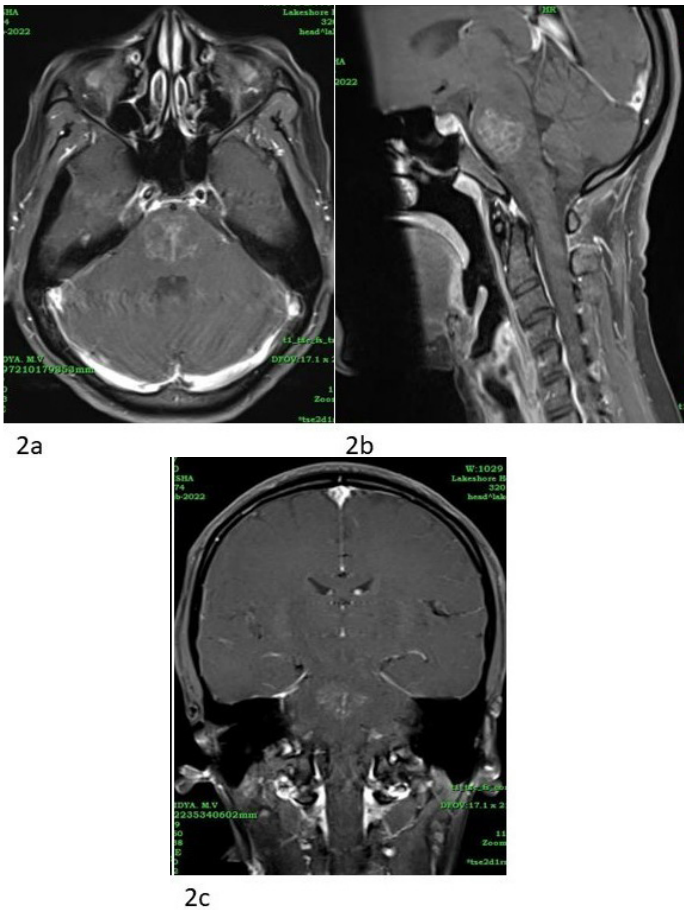

Figure 2: (a,b,c) Post contrast axial, sagittal and coronal images show heterogeneous enhancement.

Even though her Dengue IgM was detected to be positive, she did not have any features suggestive of an acute dengue infection. Furthermore, her Dengue IgG tested on Day 3 and Day 19 of admission were negative, indicating a probable false-positive IgM result, which has been reported in autoimmune conditions. Thus, the final diagnosis was taken as an underlying Sjogren's syndrome presenting with proximal RTA, hypokalaemia and quadriplegia, with the weakness attributed to hypokalaemic paralysis and ODS.

She was started on steroids: pulse intravenous methylprednisolone followed by a course of oral steroids. Once her liver parameters had normalised she was initiated on immunosuppressants (Mycophenolatemofetil) and oral steroids were continued. During the course of her stay she also developed postural hypotension and urinary retention, thought to be due to autonomic dysfunction as a part of Sjogren's syndrome. She also had difficulty in vocalisation and video laryngoscopy showed a unilateral vocal cord palsy, probably as a result of endotracheal intubation. The patient had a gradual but definitive improvement with treatment, which included speech therapy, psychotherapy and physical therapy apart from medical management. By the time of discharge, she was vocalizing and able to walk without support. Follow up MRI screening showed significant reduction in the pontine swelling and T2 and FLAIR hyperintensities (Figure 3).

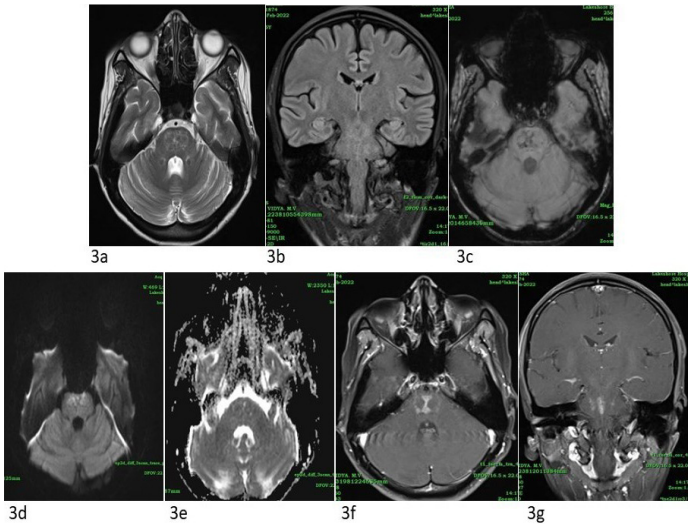

Figure 3 (Post treatment images): Axial T2 (a), FLAIR coronal (b), SW (c), DW with ADC (d & e), post contrast axial and coronal (f & g) shows significant resolution of findings.

Discussion

Primary Sjogren's syndrome is a progressive autoimmune disorder involving the exocrine glands, usually presenting with sicca symptoms such as keratoconjunctivitis and xerostomia. Extra glandular manifestations may be non-specific with involvement of different organ systems, with renal disease being the most common among them. Tubulointerstitial nephritis is the typical presentation and is often characterized by Renal Tubular Acidosis (RTA), of which distal (type I) RTA is more common than proximal (type II) RTA. Although hypokalaemia is a common occurrence in both these varieties, it is usually mild, and severe hypokalaemia with paralysis is rare, even more so as an initial manifestation of the disease. There are case reports describing hypokalaemic paralysis in Sjogren's syndrome, but most of them highlight scenarios in which the weakness had fully resolved after potassium correction [5-8].

In our case, a 25-year-old female patient, later detected to have SS, presented with quadriplegia (with normal deep tendon reflexes) and was found to have refractory hypokalaemia, normal anion gap metabolic acidosis along with hypophosphatemia, hyperchloremia and glucosuria indicative of proximal RTA. In contrast to the other cases mentioned earlier, the persistence of her weakness in spite of correction of dyselectrolytemia prompted us to investigate for other causes.

Hypokalaemiais known to cause weakness in different ways. It can result in a radiculoneuropathy kind of presentation mimicking GBS - AMAN (acute motor axonal neuropathy) variant [9]. Here the reflexes will be depressed with normal sensations and NCS will show reduction of CMAP amplitudes of motor nerves. Hypokalaemia can also lead to hypokalaemic periodic paralysis in susceptible individuals. Chronic or persistent hypokalaemia can lead to myopathy [10]. In our case, nerve conduction studies were normal, deep tendon reflexes were well elicited with an equivocal plantar response, hence central causes had to be ruled out. The MRI brain revealed findings of pontine T2 and FLAIR hyperintensities, diffusion restriction and microbleeds.

Though dengue is not primarily a neurotropic virus, dengue encephalitis as a rare occurrence has been reported [11]. It is thought to be benign, but can be fatal at times, and usually presents with a diminished level of consciousness, headache, seizures, disorientation, and behavioural symptoms.The spectrum of MRI findings in dengue encephalitis include hyperintensities on T2-weighted and FLAIR sequences with the most commonly affected site being the basal ganglia-thalamus complex. Other sites are the cerebellum, cerebral cortex, white matter and brainstem. Patchy areas of diffusion restriction and focal areas of haemorrhage may also be present [12]. A repeat serology showed absent dengue IgG antibodies almost three weeks following her initial presentation, which highlighted the likelihood of a false-positive IgM result. Studies backing this possibility in autoimmune conditions have been reported. In a case report published in 2020, Supitcha et al. demonstrated a false-positive dengue IgM test in a patient with SLE [13]. A study by Tomohiko et al. suggested that a possibility of false positive reaction should be considered when serum samples from autoimmune disease patients are tested for dengue IgM by some commercial dengue IgM test kits [14].

Adams et al. were the first to describe pontine myelinolysis in 1959 [15]. Today, it is known as ODS, which embraces central pontine myelinolysis (CPM) and extrapontine myelinolysis (EPM), and although considered to be a rare condition, is often underdiagnosed in clinical practice and can be fatal [16]. The most common cause of ODS is hyponatremia and its pathophysiology consist of cerebral apoptosis and loss of myelin due to osmotic stress [18]. Other factors that may cause rapid rise in serum osmolality can also be associated with its development. Malnutrition, alcoholism, hypokalaemia, use of diuretics, and fluid resuscitation are known risk factors for ODS. There are rare reports of ODS cases with mild or no hyponatremia. Carolina et al. reported a case of a patient with multiple risk factors for ODS who developed hypokalaemia, without hyponatremia, and subsequent ODS with eventual recovery [17]. In a retrospective study by Parnandi et al., of patients admitted in an ICU over a period of 5 years, 2.5% were diagnosed as having ODS. The most common associated factor seen in this study was severe hypokalaemia defined as serum potassium level ≤1.5 mEq/L (41%) [17].

MRI is the preferred diagnostic modality in ODS and reveals T1-hypointense, T2-hyperintense, and FLAIR-hyperintense signals mainly in the pons in CPM and in the basal ganglia, thalamus, cerebellum, hippocampus, and cerebral cortex in EPM. Moreover, there can be a typical sign of osmotic demyelination syndrome - “the trident sign” - where the symmetrical high T2/FLAIR signal abnormality appears located in central pons. This reflects the prevalent involvement of the transverse pontine fibres and relative sparing of the descending corticospinal tract. The earliest change is diffusion restriction in the lower pons, which is apparent within 24 hours of the beginning of quadriplegia [15]. The MRI finding of pontine microbleeds in our patient was odd and did not fit into the classical ODS picture. However, in a review of literature we found a case report by Yuya et al. of a 23-year-old man with type 1 RTA and hypokalaemia who developed ODS with pontine haemorrhage. It has been suggested that osmotic vascular injuries induced by elevated levels of serum potassium and osmolarity give rise to oedema and vascular endothelial damage, consequently leading to haemorrhagic necrosis [18].

Overall, ODS has a poor prognosis with a high mortality rate. Patients who survive may not recover if in a coma and irreversible sequelae may persist [15]. The recovery pattern in ODS, as evidenced by the retrospective ICU study mentioned earlier, showed complete recovery in 24% of patients, recovery with some deficit in 47% and a vegetative state in 18% of patients. While the mortality in this study was 12%, literature evidence varies widely ranging from 6% to 90% [17].

Sjogren’s syndrome presenting initially with quadriplegia is a rare occurrence. Identification of the cause may be a diagnostic challenge, but necessary for accurate management and a favourable prognosis. As no clinical or radiological features can predict the outcome, a high level of suspicion for ODS is the most important factor for early diagnosis and better progression. In addition, the possibility of elevated serological markers of common diseases should be kept in mind when dealing with autoimmune disorders and a detailed clinical history and targeted investigations are needed to avoid a misdiagnosis. Such cases with multiple co-existing metabolic and neurological abnormalities usually have a poor prognosis, hence awareness of all the possible aetiologies and therapeutic options is crucial. Furthermore, apart from pharmacological management, timely supportive interventions like physiotherapy, speech therapy, psychotherapy, and optimal nutrition play a key role in their rehabilitation.

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