

Isolated extrapontine myelinolysis with neuropsychiatric manifestation: A case report from Nepal

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Abstract

A referred case of a 34-year-old woman was brought to the emergency room with features of mutism and whole-body rigidity following rapid correction of hyponatremia. On presentation, she was ill looking with tremors on her both hands and legs. She was unresponsive to command and developed involuntary outbursts of laughter and crying. Based on clinical features and neuroimaging, diagnosis of isolated extrapontine myelinolysis was made. She was treated with quetiapine, vitamin B₁ and B₁₂ supplements, trihexyphenidyl, levodopa-carbidopa and physiotherapy of limbs. Due to lack of clinical trials for adequate diagnosis and management of extrapontine myelinolysis, this case report highlights the importance of extrapontine myelinolysis with neuropsychiatric manifestation in research world.

Keywords

Extrapontine myelinolysis, hyponatremia, osmotic demyelination

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Introduction

Central pontine myelinolysis (CPM) is a non-inflammatory demyelination of the pons while extrapontine myelinolysis (EPM) refers to demyelinating lesions occurring outside pons: cerebellum, lateral geniculate body, external capsule and so on. CPM and EPM are collectively known as osmotic demyelination syndromes (ODSs). EPM is one of the complications that occurs secondary to rapid correction of hyponatremia. In the vast majority of cases, it is associated with CPM, but rarely, it can also occur as an isolated entity. The pathology, time course and associations are shared among CPM and EPM, but they differ in clinical presentations.¹ We report a case of isolated EPM due to rapid correction of hyponatremia with neuropsychiatric features.

Case report

A referred case of 34-year-old female with history of migraine without aura who was apparently well 1 month back presented to the local hospital with the history of vomiting about 8–10 episodes per day for 10 days. Vomiting was associated with

bilateral headache which was persistent, throbbing in nature and used to get relieved on oral pain medication. Patient then visited nearby hospital where her routine blood examinations revealed hyponatremia (Na^+ = 108 mEq/L; reference = 135–145 mEq/L) along with borderline hypokalemia (3.4 mEq/L; reference = 3.5–5.2 mEq/L). Her blood glucose (5.5 mmol/L; reference = 3.8–7.8 mmol/L), creatinine (83 $\mu\text{Mol/L}$; reference = 40–110 $\mu\text{Mol/L}$) and urea (6.2 mmol/L; reference = 1.6–7 mmol/L) were within normal limits. She was admitted to intensive care unit (ICU) where she was symptomatically managed for 10 days. Hyponatremia was corrected from 108 to 132 mEq/L within 48 h of time. After 3 days, she was unable to speak and developed sustained stiff limbs. She was unresponsive to command

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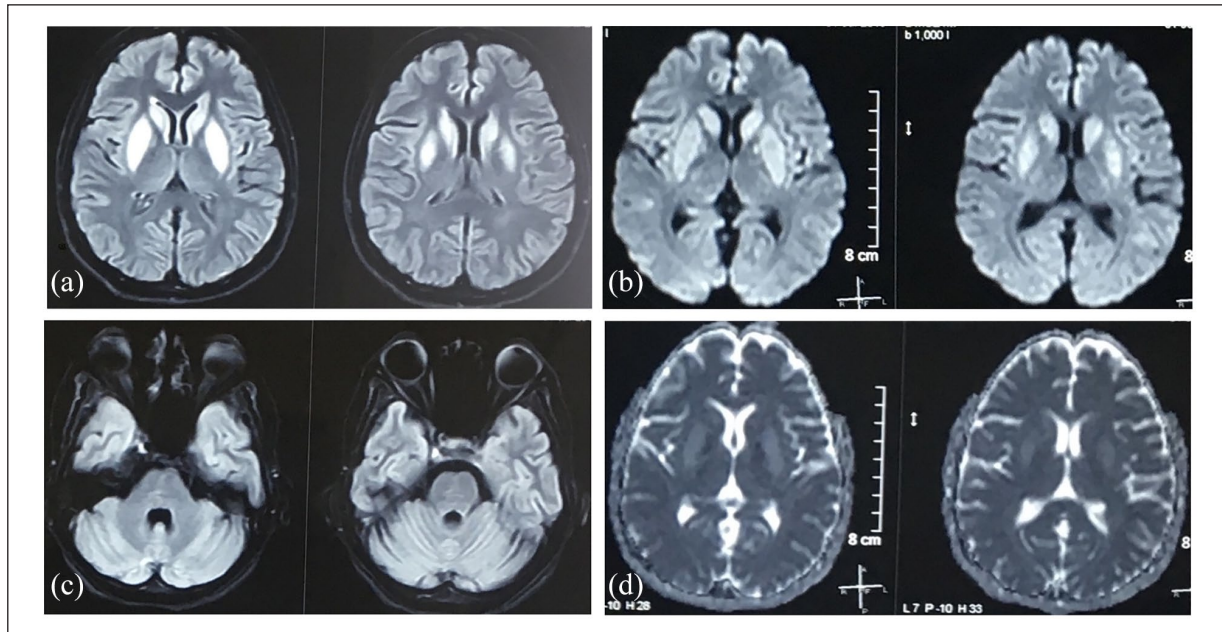


Figure 1. (a) T2 FLAIR image of brain showing symmetrical increased signal intensity in bilateral lenticular and caudate nucleus. (b) DWI image showing symmetrical increased signal intensity in bilateral lenticular and caudate nucleus. (c) T2 FLAIR image showing normal signal in pontine and cerebellar region. (d) ADC image showing bilateral hyperintensity in lenticular and caudate nucleus.

and developed involuntary outbursts of laughter and crying. She was then treated with gradually increased dose of lorazepam, but there was no improvement.

For further neuropsychiatric evaluation, she was referred to our center. On examination in the emergency room, the patient was ill looking with tremors on both hands and legs with involuntary outbursts of laughter and crying. Her Glasgow Coma Scale (GCS) was 12/15; eye opening was 4, verbal was 3 and motor was 5.² Her pulse rate was 123/min, blood pressure was 120/90 mmHg, and was afebrile. Other systemic examinations were within normal limits. Brain magnetic resonance imaging (MRI) scan, done on 10th day of her neuropsychiatric symptoms, showed symmetric T2/fluid-attenuated inversion recovery (FLAIR) and diffusion-weighted imaging (DWI) hyperintense signals at bilateral lentiform nucleus and head of caudate nucleus and normal signal in pons (Figure 1(a)–(c)). Apparent diffusion coefficient (ADC) scan also showed hyperintensity in bilateral lentiform and caudate nucleus (Figure 1(d)). With the clinical history of rapid correction of hyponatremia, clinical manifestations and neuroimaging findings, diagnosis of isolated EPM was made.

Patient was treated with quetiapine 75 mg/day, thiamine 400 mg/day, methylcobalamin 1500 mcg/day, trihexyphenidyl 6 mg/day, levodopa-carbidopa 250 mg/day and physiotherapy of limbs. During hospital stay, the patient's sensorium and crying episodes were gradually improved. At the time of discharge (10th day of admission), the patient had GCS of 15/15, was able to walk with support, feed by herself, tremor and rigidity were reduced. She started communicating with

her family members with unresolved dysarthria. Medicines were reduced to quetiapine 25 mg/day, thiamine 100 mg/day, methylcobalamin 500 mcg/day, trihexyphenidyl 2 mg/day and static dose of levodopa-carbidopa at 250 mg/day. On follow-up after 3 months, the patient had resolution of all other symptoms except rigidity in left hand and mild dysarthria that were improving in its course. Levodopa-carbidopa was prescribed to continue at the same dose (250 mg/day), and the rest of the medications were stopped.

Discussion

Isolated EPM is a rare condition. Necropsy series done in 58 cases showed isolated CPM in half of the cases, EPM and CPM in three-fifth cases and only EPM was present in remaining two-fifth of the cases.¹ It is commonly seen in chronic alcoholics followed by patients with rapid correction of hyponatremia, liver transplant patients under immunosuppression particularly with cyclosporine³ and less commonly in burns, hypophosphatemia, systemic lupus erythematosus, porphyrias, cytomegalovirus hepatitis, anaphylactic shock, ketosis and hyperosmolar hyperglycemic state.^{4–6} In 1950, measurement of serum electrolyte was not in routine examination. Hence, the researchers were not able to appreciate the role of Na^+ involved in EPM. In 1976, Tomilson suggested that the rapid correction of hyponatremia was a causative factor for EPM. So, it is suggested to correct serum sodium level slowly and cautiously, and not to exceed 8 mEq/L per day.¹ But even with normal sodium levels and correction of serum sodium levels within safe limits, demyelination may occur.⁷

Areas of brain involved in EPM are cerebellum, lateral geniculate body, external capsule, hippocampus, putamen, cerebral cortex/subcortex, thalamus and caudate nucleus. Other less commonly involved sites are claustrum, internal capsule, midbrain, internal medullary lamella, mammillary body and medulla oblongata.¹ Clinical manifestations in EPM can be variable, could be either pure motor, neuropsychiatric, extrapyramidal or overlapping type.^{1,8–10} Extrapyramidal features have been frequently reported in patients with both CPM and EPM such as Parkinsonism, chorea, dystonia, spasms and ballismus which are likely due to demyelination of nerve fibers containing dopamine receptors in basal ganglia and its connections.^{1,9–11} Neuropsychiatric manifestations such as inappropriate affect, emotional lability, personality changes, paranoia, poor judgment, emotional incontinence and disinhibition are prominent features in EPM along with movement disorders.^{1,11} Our patient presented with agitated delirium and a pseudobulbar state with pathological laughing and crying, likely due to diffuse bilateral basal ganglia lesions and impairment of various neurotransmitter systems.^{11,12} Although cognitive and behavioral manifestations in CPM have not been clearly associated, it is suggested that the disruption of reticular activating system, corticopontine and neurotransmitter pathways might have caused the cognitive impairment and cortical features in CPM.^{12,13} Furthermore, patient's comorbid condition and its complications can also worsen neuropsychiatric manifestations.¹³

The progression of disease may not be same in all the cases of EPM, that is, in some patients, there is progression from spastic paraparesis with postural limb tremor and myoclonic jerks to a Parkinsonian feature with choreoathetosis, and finally progress to permanent Parkinsonian state with dystonia. In other group of patients, there might be signs of pyramidal dysfunction which resolve over certain months and are replaced by transient retrocollis and oromandibular dystonia and a permanent focal dystonia of the arm with spasmodic dysphonia.¹ Our patient showed a significant improvement in her neuropsychiatric manifestations, but extrapyramidal features were persistent even in 3-month follow-up.

MRI is the imaging of choice for EPM where hyperintense lesions are seen on T2 and DWI, and hypointense lesions are seen on T1-weighted images with no enhancement in contrast scan. The lesions may not be apparent on early scan; hence, repeated imaging might be needed after 10–14 days of onset of symptoms.¹⁰ Since MRI was done on 10th day of illness in our case, findings showed symmetrical hyperintense lesions in T2, DWI and ADC of bilateral lenticulate and caudate nucleus sparing pons. Hyperintensity in DWI and reduced signal in ADC are typical MRI findings in ODS.^{4,10} A case study with series of MRI follow-up showed hyperintensity in DWI and rapid normalization to increased ADC signal could be seen within a month correlating ADC changes and clinical improvement.¹⁰ Hence, recent advancement of neuroimaging has helped in the early diagnosis and management causing better survival and clinical outcome in EPM.

Due to lack of clinical trials, there is a gap in the formulation of definitive treatment protocol for EPM. Supportive measures like extensive physiotherapy and rehabilitation, ventilatory support and medicines for symptomatic relief are the current effective treatments. Case reports have been published showing the benefits of steroids, immunoglobulins and thyrotropin-releasing hormone, but they lack evidence. In cases of ODS with hyponatremia, hypokalemia has been found to be a predisposing factor and thus needs to be corrected earlier.¹⁴ Clinical and radiological findings are inconclusive for morbidity or mortality. In a large case series of 34 cases, only 2 died and 30 survived: 10 were left dependent, 11 had some deficit but were independent and 11 recovered completely among survivors.¹

One of the limitations of this case report is that follow-up MRI could not be done due to financial constraints. Furthermore, patient was followed-up at 3 months which is comparatively a short period. A long-term follow-up will be required to see if any extrapyramidal sequela persists.

Conclusion

Isolated EPM is a rare neuropsychiatric disorder. Patient presenting with neuropsychiatric disorder might also have ODS despite normal level of serum sodium and irrespective of rate of correction of hyponatremia. Brain MRI might be beneficial in initial diagnosis. There is a lack of definitive clinical management of EPM. Due to lack of clinical trials for adequate diagnosis and management of EPM, this case report highlights the importance of EPM with neuropsychiatric manifestation in research world.

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Author contributions

S.K., S.A. and A.P. drafted the manuscript, reviewed the literature and edited the manuscript. R.O. did the supervision, revised and edited the manuscript. B.P.G., R.K., R.R., N.G., S.P. and A.S. were in charge of the case and reviewed the manuscript.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

Our institution does not require ethical approval for reporting individual cases.

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Informed consent

Written informed consent was obtained from the patient's husband (inability of the patient due to her condition) in English as well as Nepali language to publish her clinical details.

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