

Reversible parkinsonism in central pontine and extrapontine myelinolysis: A report of five cases from India and review of the literature

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Abstract

Parkinsonism with or without dystonia has been rarely described following central pontine myelinolysis and extrapontine myelinolysis. We report 5 cases of reversible parkinsonism and dystonia with imaging evidences of central pontine myelinolysis and extrapontine myelinolysis associated with hyponatremia from a center in Eastern India. Their presentations varied from mild masked facies to extra pyramidal syndromes characterized by progressive supranuclear palsy like feature and marked dystonia. Two cases presented with flaccid quadriplegia later evolved into spasticity and dystonia. The cause of hyponatremia was due to vomiting in two, diuretic-induced, nutritional and psychogenic polydipsia one each. The onset was acute in 4, and gradual in one from psychogenic polydipsia. They responded well to gradual correction of electrolyte imbalance, dopaminergic and antidystonic agents including botulinum toxin. The movement disorders of central pontine myelinolysis with extrapontine myelinolysis represent a treatable manifestation of the osmotic demyelination syndrome and rewarding result can be achieved.

INTRODUCTION

Osmotic demyelination syndrome or central pontine myelinolysis (CPM) with or without extrapontine myelinolysis (EPM) is a disorder associated with hyponatremia. This condition was first described by Adams in 1959 in an alcoholic and malnourished patient who suffered from hyponatremia.¹ Other known associations are prolonged use of diuretics, psychogenic polydipsia, burns, post hepatic transplants, malignancy and post surgical patients.²⁻⁴ EPM is associated with lesions in basal ganglia, thalamus, internal capsule, cerebellum, and subcortical white matter.⁵ It is clinically characterized by a variety of psychiatric and behavioral changes, different types of movement disorders such as ataxia, postural limb tremor, myoclonic jerks, choreoathetosis, dystonia and parkinsonism.⁵ These movement disorders are usually reversible, though rarely may become permanent.

Previous studies have documented this condition in autopsy studies. With advent of MRI, CPM with or without EPM are being increasingly diagnosed. Early diagnosis and the intensive care facilities have also reduced the mortality rate to 10-20%.⁶⁻⁸ However it is being expected that

with increasing salvaging of the patients, more and more cases with different sequel will be observed. We have recently seen 5 patients over last 2 years with imaging characteristics of CPM with EPM of acute and subacute onset presenting with features of extrapyramidal syndromes. There are very few case reports from India⁶⁻⁷ and progressive supranuclear palsy (a variant of Parkinson plus syndrome) due to CPM and EPM has rarely been reported. This is a report of the 5 patients with a brief review of literature (Table 1).

CASE REPORT 1

This was a 44 years old man who did not have past history of hypertension, diabetes mellitus, but was an alcoholic. He was admitted to the medical ward with recurrent vomiting for 4 days after an alcohol binge. There was no recent history of taking antipsychotic drugs. He was drowsy, malnourished without pyrexia, jaundice, systemic signs and focal neurological deficit. Routine complete blood count, blood biochemistry and ultrasound examination of the abdomen were all normal. Upper gastrointestinal endoscopy showed mild gastritis. The serum sodium and potassium on admission were 110 mEq/L and 2.8 mEq/L

Table 1: Published cases of central pontine myelinolysis and extrapontine myelinolysis

Author and year of publication	No. of patients' cohort evaluated	Predisposing factors/Presentation	Subjects with brain lesions of CPM with or without EPM	Outcome and other notes
Adam, 1959 ¹	4*	Alcoholics & malnourished-3 intractable diarrhea, with dermal feature of scleroderma	CPM-all 4 cases	Three cases had autopsy study
Estol, 1989 ⁴	85	Post hepatic transplant in 11 patients (adult-8, children-3)	CPM-11 (13%) EPM-4 (4.7%)	All autopsied patients
Fryer, 1996 ³	44	Post hepatic transplant with evidence of cyclosporine neurotoxicity	CPM-5 (11.3%) EPM-2 (4.5%) (MRI based)	All patients recovered
Brnster, 2000 ²	463	Orthotropic liver transplantation	CPM-6 cases (1.5%)	Two patients with CPM survived with neurologic sequel. One of the cases was diagnosed in repeat MRI, one on CT scan and in 4 patients, confirmation came from autopsy. The autopsied patients presented with stupor only and lacked the classical signs of CPM
Wright, 1979 ⁸	3,548	Alcoholic liver disease-9 Hodgkin disease-1 Burns-1	CPM-11 (0.25%)	All had autopsy study
Gocht, 1987 ⁹	58		CPM-50% EPM-40% CPM & EPM-60%	All had autopsy study
Menger, 1999 ¹⁸	44	Chronic alcoholics-42 Diabetes Mellitus-1 Malnutrition-1	CPM-38 (86.4%) EPM-1 (2.3%) CPM&EPM-5 (11.3%)	2-died 10-dependent 11-independent with residual deficit 11-completely recovered
Oh, 1995 ²³	200	Rapid correction of hyponatremia, both after bladder-glycine wash in prostatectomy	CPM-2	

*Details of fourth case has not been provided

respectively. The electrolytic imbalances were gradually corrected over the subsequent 9 days using intravenous normal saline and potassium chloride under ECG monitoring. The patient became fully alert and vomiting stopped.

Two days later, he became drowsy, developed tremulousness, abnormal posturing of all limbs, and one episode of generalized tonic clonic seizure. He was transferred to the neurological ward. Examination showed that he had aggressive behaviour, emotional lability, impaired attention span and incoherent speech. There was slow horizontal saccade and broken pursuit of eye movement, spasmodic dysphonia, cogwheel rigidity of all limbs, dystonia of face, axial musculature and all limbs; coarse rest and postural tremor. The tremor was video-recorded. Deep tendon reflexes were normal and plantar response was flexor. Plasma ammonia and prothrombin time were normal. Viral markers for hepatitis B, C and human immunodeficiency virus (HIV) were negative. EEG did not show any slowing or abnormal discharges. CT scan and MRI of brain were normal on 13th day of illness. Cerebrospinal fluid (CSF) study revealed normal pressure, 3 lymphocytes/cmm, sugar 52 mg/dl and protein 24 mg/dl. CSF staining for bacteria, tuberculosis and fungi, culture for tuberculosis, and antibody titer for Japanese B encephalitis were negative. Serum creatinine phosphokinase was mildly elevated (456 U/L). He was given broad-spectrum antibiotics, phenytoin sodium and general supportive treatments.

A repeat MRI of brain after one month of illness showed hypointense to isointense lesions in T1-weighted image. T2-weighted images and Flair images showed almost symmetrical hyperintense lesions in lentiform nuclei, thalami and central pontine region with peripheral sparing (Figures 1, 2). In view of temporal correlation between hyponatremia and subsequent development of extrapyramidal features with MRI evidence of pontine and extrapontine involvement, a diagnosis of osmotic demyelination syndrome was made. He was treated with levodopa/carbidopa, trihexiphenidyl, clonazepam and baclofen. Parkinsonian features and dystonia improved significantly over 2 months and he was able to return to his previous job. On follow up after one year, he had only mild residual dystonia in the fingers. No follow-up MRI was available in this patient.

CASE REPORT 2

This 62 years old hypertensive, nondiabetic, nonalcoholic man presented with gradual onset of progressive slowness of activities of daily living, unsteady gait, behavioral abnormality and forgetfulness of recent events for 2 months. He had past history of manic episodes 6 years earlier for which he was treated with sodium valproate, haloperidol, phenothiazines and benzodiazepines for one year. He had a habit of compulsive drinking



Figure 1: Showing T2 hyperintensity in the central part of the pons with normal periphery

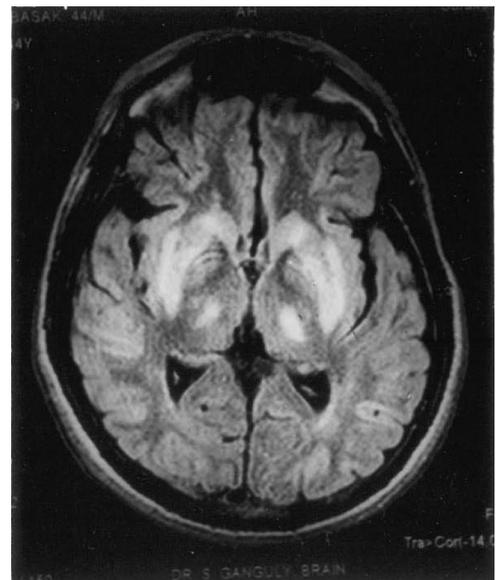


Figure 2: Showing T2 Weighted hyperintensity in the basal ganglia and thalamic region

of water. His father suffered from Parkinson disease and died at the age of 67 years.

On examination, he had stiffness of all limbs with clumsiness of hands and feet; difficulties in negotiating footwear and standing up from the squatting position; frequent falls of mostly backward direction, hesitancy of micturition with normal bladder sensation and slowing of bowel movement. He was apathetic and had impairment of recent memory but no delusion and hallucination. The Mini Mental State Examination (MMSE) score was 10/30, with gross abnormality in calculation and general information. Eye examination showed slow saccade, broken pursuit, stare look, upgaze restriction, and absent vertical optokinetic nystagmus. Muscle power was normal. There was rigidity and brisk jerks in all limbs, with bilateral extensor plantar response. He had prominent axial rigidity but no sensory loss, cerebellar signs, tremor or autonomic dysfunction. His complete blood count, plasma urea, creatinine, sugar, liver enzymes, serum creatinine kinase, thyroid hormone levels were normal. Plasma ammonia, prothrombin time, ultrasound examination of abdomen and EEG were not supportive of hepatic encephalopathy. Serum calcium, phosphate and parathyroid hormone estimation did not indicate a parathyroid hormone disorder. He was provisionally diagnosed as Parkinson plus syndrome of progressive supranuclear palsy variety. Serum sodium and potassium was 118 and 4.3 mEq/L respectively.

MRI of brain revealed age related cortical atrophy, small central discrete area of signal intensity in T2-weighted and FLAIR images, hypointense lesions in T1-weighted images in central pons, centrum semiovale, both forceps minors and periventricular regions suggestive of demyelination. Hypointense lesions in GRE and hyperdense in CT scan in both basal ganglia were suggestive of calcification. In view of increased thirst and urine output of around 10 liters/day, he was investigated for diabetes insipidus with plasma and urine osmolality, urine Na estimation which were not indicative of the diagnosis. In view of documented hyponatremia, presence of central pontine demyelination on imaging, a diagnosis of CPM was made. Hyponatremia was corrected gradually. He also received anticholinergic and GABA-agonist drugs. The patient improved steadily over one month. On follow up 2 months after discharge, he had marked improvement in Parkinsonian features, was independent in activities of daily living and had MMSE of 25/30. No follow up MRI could be repeated.

CASE REPORT 3

This 36 years old nondiabetic, nonalcoholic man presented with moderate grade continuous fever for 3 days followed by swelling of abdomen, puffiness of face without any neurological symptom, and was admitted in a local hospital. He was diagnosed to have acute renal failure. He was transferred to another hospital after one week. The urine output improved. However, the patient developed behavioral abnormality with agitation and had one episode of generalized tonic clonic seizure. Since the seizure, the patient became mute and was unable to move his four limbs. This was 2 weeks after the onset of the fever. He was treated with phenytoin and was transferred to our institution. There was hyponatraemia (serum sodium 115 mEq/L) in one occasion, serum potassium was normal, and urine examination was suggestive of *E. coli* infection. The patient did not have any past history of seizure or renal disease.

On admission, the patient was mute, the limb power (MRC grade) was 0/5. The patient was grossly emaciated, and was admitted with Ryle's tube, indwelling urine catheter, and numerous bedsores. Gaze was restricted in all direction, especially upward gaze. The patient was unable to swallow. MRI of brain showed hyperintensity in T2-weighted and hypointense in T1-weighted lesion involving bilateral putamen, caudate nuclei and thalami and also dorsal pons and adjacent part of midbrain. Hemoglobin was 8.6 gm/dl with microcytic hypochromic anemia. Renal parameters including electrolytes were normal. CSF studies were normal with negative serology for Japanese B encephalitis virus. Two units of blood were transfused and bedsores were debrided. Physiotherapy was started. The patient slowly regained his muscle power. After two months he was able to sit with support. On discharge, his limb power was grade 4/5. Catheter and Ryle's tube were removed as improvement continued, but the patient developed spasticity, retrocollis and tremor. His speech remained slurred and extra ocular movement became full. He was diagnosed to have osmotic demyelination syndrome with both CPM and EPM, the illness precipitated by use of diuretic resulting in hyponatremia. On follow up after 2 months there was significant improvement in bulbar palsy, spasticity, retrocollis, and dystonia. He was able to walk with support of a stick. No follow up MRI could be performed.

CASE REPORT 4

This 53 year old hypertensive, nondiabetic female presented with coma. The patient was apparently well till about 3 weeks prior to admission when she developed repeated bouts of vomiting without any headache, fever or confusion. She was found to have hyponatremia of 112 mEq/L, for which she received institutional treatment for 2 days and discharged after another 2 days. She was readmitted 6 days later with confusion and status epilepticus. She was treated with phenytoin sodium and ventilatory support. After weaning from ventilator, she was found to be confused with weakness of all four limbs. She was then referred to our institute. On admission, her Glasgow Coma Scale score was 4/ 15. She had bilateral sluggishly reactive pupil. The doll's eye reflex was present. The limbs were flaccid with diminished tendon reflexes. Both plantar responses were extensor, and there was no sign of meningeal irritation.

Routine complete blood count, plasma urea, creatinine and sugar, liver function test with enzymes were all normal. Serum sodium, between admission and second week varied between 112 to 129.4 mEq/L. CSF study revealed 15 cells/cmm (polymorph:10%, lymphocyte: 90%), sugar 58 mg/dl, protein 75 mg/dl; staining for bacteria, tuberculosis and fungi, culture for tuberculosis, serology for Japanese B encephalitis, and Herpes simplex DNA polymerase chain reaction were all negative. Serology for HIV was also negative. EEG showed background activity consisting of poorly formed low amplitude alpha wave of 8-9 Hz, and no evidence of abnormal discharges or slowing. MRI brain showed changes suggestive of central and extrapontine myelinolysis.

Patient slowly started responding to verbal stimulus and over the subsequent days, began to recover his horizontal and vertical eye movements. She developed rest tremor, stiffness and rigidity of all four limbs. She was given levo-dopa, other antidystonic drugs, botulinum toxin (200 units) and physiotherapy to which she showed moderate improvement. On follow up after 2 months, she had minimal dystonia and spasticity, but still needed assistance in activities of daily living.

CASE REPORT 5

A 55 years old physician, nonhypertensive and nondiabetic presented with generalized convulsion preceded by refusal to take food, insomnia and depressed mood for one month. He had depression and was treated with antidepressant for 5 years.

He stopped the drugs for one year. He was found to have hyponatremia (serum sodium 118 mEq/L) and was treated with intravenous fluid and oral common salt replacement. He gradually improved and was referred to our institute for further evaluation. He had no past or family history of seizure disorder.

On examination, he had mild masked-like facies, normal jaw jerk, absence of any facial paresis, and no other systemic or neurological abnormalities. His blood biochemistry including serum sodium and potassium, ECG, EEG and CT brain scan were all normal. MRI brain revealed T2-weighted hyperintensity in the central pons. He was put on phenytoin and remained seizure free since then. On follow up he had no cognitive or any neurological dysfunction

DISCUSSION

Bangur Institute of Neurosciences and Psychiatry (BINP), previously known as Bangur Institute of Neurology, is a tertiary care teaching hospital in Eastern India located in the heart of the metropolitan city of Kolkata. This hospital serves patients from the local community, adjoining districts, states and also neighboring countries like Nepal, Bhutan and Bangladesh. It also receives some of the very sick patients referred from the rural areas. Diagnostically difficult cases and referred patients are given preference for admission. There is also regular out-patient service. Emergency patients are admitted to adjacent multidisciplinary Seth Sukhlal Karnani Memorial (SSKM) Hospital. Both the institutes are affiliated to The Institute of Post Graduate Medical Education and Research, Kolkata. BINP has a capacity of 46, 53 and 36 beds in Neurology, Neurosurgery, and Psychiatry departments and an eight bedded intensive care unit with a provision of 15% free beds. Number of neurology outpatient and admission in last one year (2006) were 29,930 and 611 respectively. There are 2 CT scans (one in SSKM and another in BINP) and one MRI scan. Most of the patients with Parkinson's disease are evaluated in Movement Disorders Clinic on out patient basis, held once in a week. A total of 653 patients including both new and old attended the Movement Disorder Clinic in last one year. Idiopathic Parkinson's disease consists of 59 patients comprising 46% of the new cases seen in the clinic. This compares to 5 cases of CPM and EPM seen in our institute in the last 2 years. CPM and EPM is thus not uncommon in neurology practice in India.

CPM has been reported to be resulting from rapid correction of hyponatraemia and generally patients present with various brain stem dysfunctions such as tetraparesis, pseudobulbar palsy and, occasionally locked-in syndrome.⁵ EPM can occur concomitantly with CPM in 10% of cases⁸ and may occur as an isolated event too. Diagnostic confusion occurs when the typical feature of CPM is overshadowed by the presence of clinical feature of EPM in which extra pyramidal features are dominant and involvement of pyramidal tract may be absent. Our patients had features of extrapyramidal disturbances, biochemical documentation of hyponatremia and the typical imaging characteristics of CPM and evidence of EPM in 4 out of 5 patients (Table 2). The causes of hyponatraemia were different in all the patients. Case 1 and 4 had an acute onset due to vomiting and possibly predisposed by excessive alcohol intake in the Case 1. Case 2 had a more gradual onset of hyponatremia possibly precipitated by compulsive water drinking. Overuse of diuretic was present in Case 3 and diminished intake of food secondary to depression in Case 5.

CPM and EPM are basically the same disease, sharing the same pathology, associations, and time course but differing in clinical manifestations.⁹ In severe cases of CPM, additional demyelination may occur in extrapontine locations, giving rise to extra pyramidal features which is often obscured by the concomitant pyramidal tract lesions. EPM present with features of Parkinsonism and dystonia.¹⁰ In our series, however we noticed higher frequency of combined CPM and EPM. Presence of CPM with EPM may mask the clinical features of the latter causing diagnostic confusion. Brain MRI discloses hyperintense lesions in the striatum, especially in the putamen and the caudate nuclei. Typically the globus pallidus is spared.¹¹

Case 1 had features of parkinsonism with dystonia that have been reported earlier in the literature.^{5,10,12} In addition, it is remarkable that CPM developed despite the relatively slow and delayed correction of hyponatraemia. It seems feasible that the rather low initial serum electrolyte concentrations, particularly in Case 1, as well as pre-existing alcoholism increased the risk of myelin damage.¹³ Although initially described as occurring among alcoholics (3 out of 4 of Adams' original patients) and the undernourished, CPM and EPM has also been reported in adults with a variety of serious illnesses including immunodeficiency states^{2,4}, certain

surgical procedures and even in toddlers with psychogenic polydipsia. Case 2 is an example of psychogenic polydipsia in an adult, which has not been previously reported. Hyponatraemia is the most common biochemical abnormality. Though the association with alcoholism has been noted in early report, other factors such as hypokalaemia, hypoglycemia and azotaemia have also been identified as trigger factors.^{13,15} It has been pointed out that alcohol itself interferes with sodium and water regulation by suppression of antidiuretic hormone. Case 1 had alcoholism as well as hypokalaemia and Case 3 had azotemia.

The localization of the pontine lesion within this basal region sparing tegmentum has long been one of the most puzzling features of the condition. The lesion may extend up to the midbrain, but only very rarely down to the medulla. It has been hypothesized that this is a region of maximal admixture of gray and white matter elements. In support of this, lesions of EPM also are rich in gray white apposition. In a necropsy study of the brain, apoptosis of oligodendrocytes were prominent.^{16,17}

MRI is the imaging technique of choice having greater sensitivity for CPM than CT, and also superior in demonstrating the lesions of EPM. Lesions are hyperintense on T2, hypointense on T1-weighted images, and are non-enhancing. The timing of the appearance of lesions on MRI may be delayed. As demonstrated in Case 1, when the initial imaging was negative, if the clinical indication is strong, MRI should be repeated after 10-14 days. MRI changes usually have no prognostic value.¹⁸ There is no consistent correlation between the clinical improvement and persistence of MRI abnormalities. Though we could not perform follow-up MRI due to financial reason and reluctance of the patients as they have improved clinically, previous report has shown that there may be total reversal of abnormalities within two years.¹⁹ However, in one of our patients not reported here, the imaging abnormality persisted in spite of clinical improvement even after two years, and the patient had residual extrapyramidal and behavioral changes. Diffusion weighted imaging (DWI) has been recently undertaken to improve the sensitivity of demonstrating lesions, which were undetectable on conventional sequences.

The MRI appearance of CPM is so characteristic that one feels justified in making the diagnosis based on imaging alone. This has the potential for misdiagnosis and may account for cases without characteristic shifts in sodium. It has been argued that large symptomatic pontine lesions

Table 2: Summary of patients with central pontine myelinolysis and extrapontine myelinolysis

Case no.	Age in years/sex	Precipitating factors	Clinical presentation	Rate of sodium correction	MRI brain	Treatment	Recovery and residual deficit	Follow-up
1	44 Male	Alcoholism, recurrent vomiting following a binge drink	Acute onset, convulsion, behavior disorder, parkinsonism with dystonia	4 mEq/day over 9 days	CPM, EPM	Phenytoin, Levo-dopa/carbidopa, trihexiphenidyl, clonazepam, baclofen	Parkinsonism and behavioral problem recovered completely with minimal dystonia in fingers	2 years
2	62 Male	Compulsive water drinking	Gradual onset, behavior abnormality, forgetful, progressive supranuclear palsy	5 mEq/day over 4 days	CPM, EPM	Levo-dopa/carbidopa	Marked improvement in recent memory and parkinsonism	2 years
3	36 Male	Overuse of diuretics for acute renal failure	Acute onset, convulsion, behavioral disorder, flaccid quadriplegia	Not known* (Treated in another hospital and no record was sent regarding treatment)	CPM, EPM	Phenytoin, baclofen, trihexiphenidyl, clonazepam	Significant improvement in bulbar palsy, spasticity, retrocollis, dystonia and was able to walk with support of a stick.	Did not come turn up follow up
4	53 Female	Recurrent vomiting	Acute onset, status epilepticus, flaccid quadriplegia	12 mEq/day over 2 days	CPM, EPM	Phenytoin, levo-dopa/ carbidopa, trihexiphenidyl, clonazepam, Baclofen, botulinum toxin	Minimal dystonia and spasticity-still dependent	one and half year
5	55 Male	Refusal to take food secondary to depression	Acute onset, convulsion, apathy, masked-like facies	Not known* (Treated in a nursing home)	CPM	Phenytoin	Improvement in depression	Fully

*Patient was admitted in a local hospital, rate of sodium correction not documented.

encroaching the periphery are unlikely to be CPM.¹⁹ Pontine and concomitant basal ganglion involvement is fairly specific for osmotic pontine and extrapontine myelinolysis. Confusion may arise when a patient develops only extrapontine lesion on imaging without pontine lesion.¹⁰ Bilateral signal changes confined to the putamen, globus pallidi or thalami may be seen in hypoxic-ischemic injury and in Wilson's disease. In EPM, characteristically, globus pallidus is spared. There is predominant pallidal involvement in carbon monoxide poisoning and metabolic disorders such as Leigh disease. Patchy multifocal signal changes may be seen in the basal ganglia in acute disseminated encephalomyelitis, Japanese B encephalitis, Creutzfeldt-Jakob disease, lupus vasculitis, or indeed any vascular disease involving deep perforators, deep venous occlusion (typically thalamic) and the mitochondrial cytopathies.²⁰ Precipitating factors, biochemical parameters and clinical course will help in coming to a specific diagnosis. A note of caution is that in asymptomatic alcoholic subjects, MRI abnormalities may be seen.²¹

As for treatment, most authors agree that the correction of acute hyponatraemia can be rapid. For chronic hyponatraemia, the most recent recommendation is not in excess of 8 mEq/L/day.²² Only 2 cases of CPM occurred after rapid correction of serum sodium among 200 patients with acute hyponatremia. Our first two cases had developed CPM and EPM even after slower correction.²³ For symptomatic control of the extrapyramidal features, from our experience, dopamine agonists and other antidystonic drugs are helpful.^{24,25} Whether it is the natural resolution of the disease process, or transient dysfunction of nigrostriatal pathway which has been ameliorated by dopaminergic therapy, is controversial. EPM may involve the basal ganglia, thalamus, cerebellum and subcortical white matter. Within the zone of demyelination, blood vessels, neurons and axis cylinders are largely spared and inflammation is absent.¹⁵ But it is also possible that during the stages of recovery, disorganized synaptic connections or ephatic transmissions may be responsible for development of neurological sequel.

Previously CPM and EPM was considered to have high mortality of up to 40-50%, which was possibly based on post mortem diagnosis. Since the advent of modern neuroimaging, diagnosis has become simpler and consequently, the asymptomatic cases and better survival rate are being increasingly reported. With the

intensive care facility, the mortality has been reduced remarkably.^{22,23,26} In a recent series of 34 cases, only 2 died. Out of the rest, one-third recovered completely, another third was independent with mild residual deficit, and one third was significantly dependent.¹⁸ Few anecdotal reports of treatments with steroids, intravenous immunoglobulin and thyrotrophin releasing hormone have shown good outcome but are difficult to interpret due to small number of cases and lack of controlled trial.²⁷ The follow-up period for most of the patients is relatively short and long term follow up with neuroimaging may provide the natural history of this condition .

In summary, we documented 5 patients of CPM over a span of 2 years from a center in Eastern India. All of the patients had hyponatraemia, imaging evidence of CPM, and additional evidence of EPM in 4 patients. The clinical features were predominating extrapyramidal either from onset or during recovery, and evidence of pyramidal involvement was seen in only 2 patients. The CPM was associated with acute illness as well as chronic conditions (Case 5). One of our patients manifested progressive supranuclear palsy from compulsive water drinking that has not been previously documented in adult. The reason of improvement following levo-dopa and antidystonic therapy may be related to potential reversibility of the condition and minimal cell damage.

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