Case Report / Olgu Sunumu
doi: 10.5606/phhb.dergisi.2022.3

Pontine and extrapontine myelinolysis presenting as acute parkinsonism

Akut parkinsonizm şeklinde kendini gösteren pontin ve ekstrapontin miyelinolizis

Tuğçe Saltoğlu, Burak Geçer, Yeşim Sücüllü Karadağ

Department of Neurology, University of Health Sciences, Ankara City Hospital, Ankara, Türkiye

ABSTRACT

Osmotic demyelinating diseases of the central nervous system, appearing to be two distinct variants named central pontine myelinolysis and extrapontine myelinolysis, are rare, and the underlying cause is commonly the rapid correction of the sodium levels. The clinical features of osmotic demyelinating syndromes are usually quadriparesis, dysphagia, dysarthria, locked-in syndrome, coma, and rarely movement disorders. Herein, we present the case of a 61-year-old female who developed acute onset parkinsonism due to central pontine and extrapontine myelinolysis.

Keywords: Central pontine myelinolysis, extrapontine myelinolysis, parkinsonism.

ÖZ

İki farklı varyant olarak görülen santral pontin miyelinolizis ve extrapontin miyelinolizis olarak adlandırılan santral sinir sisteminin ozmotik demiyelinizan hastalıkları nadir görülür ve altta yatan neden sıklıkla düşük serum sodyum seviyelerinin hızlı düzeltilmesidir. Ozmotik demiyelinizan sendromların klinik özellikleri kuadriparezi, disfaji, dizartri, locked-in sendromu, koma ve nadir olarak da hareket bozukluklarıdır. Bu yazıda, santral pontin ve ekstrapontin miyelinolizis nedeniyle akut başlangıçlı parkinsonizm gelişen 61 yaşında bir kadın olgu sunuldu.

Anahtar Sözcükler: Santral pontin miyelinolizis, ekstrapontin miyelinolizis, parkinsonizm.

Osmotic demyelinating diseases of the central nervous system were described in alcoholic patients by Adams et al.[1] in 1959; however, no mention was made of an electrolyte disturbance in this description. In 1976, Tomlinson et al.[2] reported the link between central pontine myelinolysis (CPM) and electrolyte disturbance. Finally, Kleinschmidt-Demasters and Norenberg[3] determined that the highest risk of CPM occurs when hyponatremia is corrected

Correspondence: / İletişim adresi: Tuğçe Saltoğlu, MD. SBÜ, Ankara Şehir Hastanesi Nöroloji Kliniği, 06800 Çankaya, Ankara, Türkiye.
e-mail *(e-posta):* saltoglutugce@gmail.com

Received / *Geliş tarihi:* February 14, 2022 Accepted: / *Kabul tarihi:* March 05, 2022 Published online / *Online yayın tarihi*: May 12, 2022

Citation:
Saltoğlu T, Geçer B, Sücüllü Karadağ Y. Pontine and extrapontine myelinolysis presenting as acute parkinsonism. Parkinson Hast Harek Boz Derg 2021;24(1-2):10-15.

too quickly, and specific recommendations for treatment have been developed.[4] Hypertonic stress with the rapid correction of hyponatremia results in apoptosis of the astrocytes, and thus the blood-brain barrier is disrupted. Burns, sepsis, post liver transplants, psychogenic polydipsia, and malignancies, by the loss of the link between astrocytes and oligodendrocytes, eventually result in demyelination.[5] Prolonged use of diuretics is another predisposing factor.

Osmotic demyelinating syndromes (ODS) may be the cause of neurological symptoms, primarily due to brain stem and central pons involvement. If the basal ganglia structures except for the brainstem are involved, it is named extrapontine myelinolysis. Magnetic resonance imaging (MRI) is used to support the diagnosis.[6] Central pontine myelinolysis is usually associated with severe dysarthria, dysphagia, tetraparesis, bulbar palsy, coma, or locked-in syndrome. The diverse localizations of lesions in extrapontine myelinolysis (EPM) cause various different clinical symptoms, such as confusion, ataxia, tremor, myoclonus, akinetic mutism, catatonia, dysautonomia, quadriparesis, dystonia, choreoathetosis, and parkinsonism. Parkinsonism has rarely been described among these entities. Herein, we report a case of reversible parkinsonism caused by CPM and EPM after rapid correction of hyponatremia.

CASE REPORT

A 61-year-old female patient was admitted to the emergency department with complaints of generalized weakness, nausea, vomiting, and shuffling gait that persisted for two days. Food poisoning was considered. The complaints did not regress after the treatment of vomiting and dehydration; on the contrary, the patient's speech worsened. With a deteriorating condition and no clear diagnosis, the patient was taken to the neurology intensive care unit. The patient had been receiving antihypertensive (valsartan/hydrochlorothiazide) and fluoxetine treatment for many years. The patient had no chronic alcohol use or exposure to toxic chemicals. In the physical examination, the patient was afebrile, and her blood pressure was normal. Cardiovascular, respiratory, and abdominal examinations were also normal. On neurological examination, the patient was lethargic and had no verbal output. Blood analyses revealed severe hyponatremia with a serum sodium level of 104 mEq/L (reference: 132-146 mEq/L) and serum potassium level of 2.74 mEq/L (reference: 3.5-5.5 mEq/L). The MRI did not show any pathology except for a few nonspecific gliotic changes in both periventricular regions (Figure 1).

Further investigations found no evidence of primary hyperaldosteronism, adrenal insufficiency, hypothyroidism, or occult malignancy. The patient was treated with 3% hypertonic saline, and potassium replacement was done. Haloperidol and quetiapine were started for delirium signs in the neurology intensive care unit. After the complaints decreased, the patient was transferred to the neurology service. During the follow-up in the neurology service, the patient had a masked face and hypophonic speech. The upper and lower limbs showed left-dominant rigidity with cogwheeling and bradykinesia. The patient also had bilateral resting tremors more prominent on the left side. Proximal muscle strength was detected as 4/5 in all extremities, and gait disturbance emerged. The patient's parkinsonian symptoms were thought to be related to haloperidol. Levodopa/benserazide 100/25 mg three times a day and rasagiline treatment were started. A week after the discharge, the patient was admitted to our neurology intensive care unit due to worsening general condition, decreased oral intake, and progression of parkinsonian symptoms. Blood tests revealed no abnormalities, and the sodium level was normal (139 mEq/L). The MRI demonstrated demyelinating lesions in the central part of the pons and peripheral parts of the basal ganglia and thalamus. Lesions were brightening in diffusion-weighted series and exhibiting hyperintensity in the simultaneous fluid-attenuated inversion recovery (FLAIR) sequence (Figure 2a, b).

Based on the clinical course and brain imaging findings, previous treatments at the other hospital were inspected. In the first neurology intensive care follow-up, the

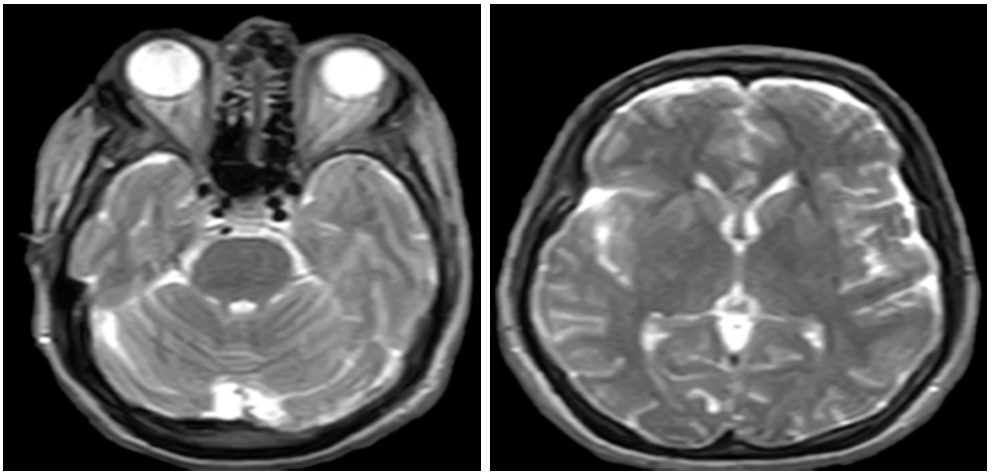

Figure 1. *Nonspecific gliotic changes at both periventricular regions in T2-weighted sequences.*

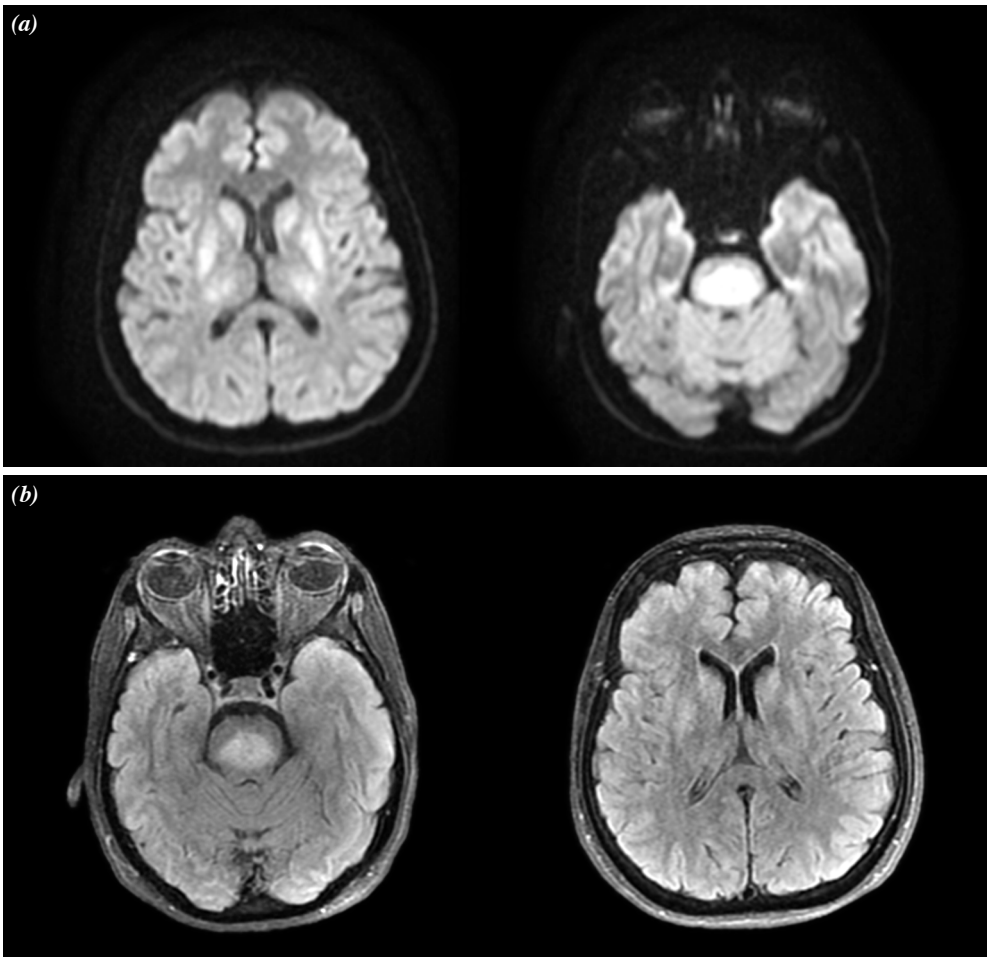

Figure 2. ***(a)*** *Diffusion-weighted series show symmetrical hyperintensity in the central pons, bilateral basal ganglia, and thalamus.* ***(b)*** *T2-FLAIR axial images demonstrate hyperintensity due to demyelination in the central pons,bilateral basal ganglia, and thalamus.*

FLAIR: Fluid-attenuated inversion recovery.

patient had been intravenously treated with hypertonic sodium, and approximately 24 h later, the serum sodium level had risen from 104 to 114 mEq/L. On the following days, sodium levels were 125, 127, and 138 mEq/L, respectively. Accordingly, we diagnosed the patient with osmotic demyelination syndrome owing to the rapid correction of hyponatremia. The patient was given symptomatic treatment in our intensive care unit and was fed via nasogastric tube. The patient's dopaminergic medication was increased. She recovered in approximately two weeks. At the follow-up MRI four months later, a significant resolution of the basal ganglia changes was observed (Figure 3). The dose of levodopa/benserazide was reduced due to significant improvement in parkinsonian symptoms.

DISCUSSION

Our patient presented with features of parkinsonism, which had developed acutely following rapid correction of severe hyponatremia leading to osmotic demyelination syndrome. The ODS is an acute neurological emergency. It specifically involves the central pontine area, which is abundant with oligodendrocytes producing myelin. These cells are very susceptible to changes in serum osmolality.[7] Extrapontine myelinolysis has been identified in 10% of CPM cases, which include extrapontine regions, such as the basal ganglia, thalamus, midbrain, cerebellum, and cerebral hemisphere.[6] The exact pathogenesis of myelinolysis is not completely understood, but it is believed to be caused by a disbalance between brain electrolytes and organic brain osmolytes, such as creatine, taurine, and glutamate.[8] Taurine transfer to astrocytes protects the neurons from osmotic stress.[4] Rapid correction of hyponatremia leads to hypertonic stress and prevents taurine transfer. Afterward, astrocyte apoptosis occurs, followed by the loss of communication between astrocytes and oligodendrocytes, which is critical for the myelination processes.[5] Oligodendroglial cells appear to be vulnerable to physical stress, leading to myelinolysis in the typical sites of CPM and EPM.[7]

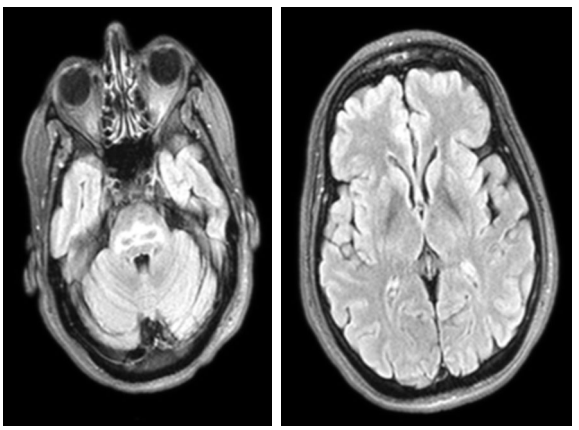

Figure 3. T2-FLAIR axial images display symmetrical hyperintensity in the chronic phase due to demyelination in the central pons, bilateral basal ganglia, and thalamus.

FLAIR: Fluid-attenuated inversion recovery.

Rapid correction of severe acute hyponatremia, beyond 10-12 mEq/L sodium change over a 24-h period, is the most common trigger of ODS. It is also known that the recommendation is not to exceed 8 mEq/L/day of sodium correction in chronic hyponatremia.[7,8] Our patient's hyponatremia was probably multifactorial, with the contribution of fluoxetine, antihypertensive treatment, and a salt-free diet; nevertheless, the sodium correction with hypertonic saline was 10-11 mEq in the first 24 h.

Clinical symptoms of neurological damage due to ODS begin as early as one day and at the latest 16 days after osmotic shifts occur. Central pontine myelinolysis is generally associated with paresis, bulbar palsy, coma, or locked-in syndrome, and less likely dysarthria, dysphagia, and ophthalmoplegia. Lesions in EPM can cause many different clinical symptoms: altered consciousness, confusion, ataxia, tremor, myoclonus, akinetic mutism, catatonia, dystonia, choreoathetosis, or parkinsonism. Both hypokinetic and hyperkinetic movement disorders can manifest due to the influence on direct and indirect pathways of striatal lesions.

Akinetic-rigid state and postural dysfunction are the common movement disorder symptoms of patients; however, secondary parkinsonism seen in our patient is rare, and the pathogenesis is not completely clarified. It is thought to

be EPM that induces secondary parkinsonism owing to deficiency of dopamine in myelinated fibers in the striatum receptors and presynaptic dopamine transporters.[6]

Diagnosis of ODS should be based on the presence of risk factors and a compatible clinical course. Demyelination sites in MRI, typically localized in the pons, cerebellum, lateral geniculate body, thalamus, and external and extreme capsules, confirm the diagnosis. T2-weighted and T2-FLAIR sequences, as well as T1-weighted sequences, are used for diagnosis. Demyelination lesions show hyperintensity in T2 sequences.[9]

The ODS has better outcomes compared to 50 years ago due to early recognition with imaging techniques, better knowledge of the pathophysiology of electrolyte disorders, and experience in the management of the syndrome. Most patients survive if aspiration, sepsis, and pulmonary embolism are prevented, and successful management is generally achieved as a result of the advanced facilities in today's intensive care units.[6] Treatment of EPM and CPM is symptomatic. Some clinical trials and case reports determined that the use of steroids, intravenous immunoglobulins, and thyrotropin-releasing hormones can be beneficial; nonetheless, they are insufficient, and other treatment options are required. The movement disorders in EPM are well-responsive to dopaminergic treatment. Response to levodopa and dopamine agonists trigger the activation of undamaged dopamine receptors. The dopaminergic treatment also provides the replacement of dopamine deficiency in the presynaptic nigrostriatal pathway.[10]

In conclusion, we present a rare case of osmotic demyelination syndrome, particularly CPM and EPM, presenting as acute parkinsonism treated with dopaminergic medication. Although CPM and EPM have a wide range of clinical presentations, the onset of symptoms may be delayed. It should be kept in mind that these syndromes are acute neurological emergencies, and it is better to prevent them rather than treat them. Correction of serum sodium should not exceed 8 mEq/L per day to prevent the occurrence of osmotic demyelinating syndromes.

Patient Consent for Publication: A written informed consent was obtained from the patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: All authors contributed equally to the article.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Adams RD, Victor M, Mancall EL. Central pontine myelinolysis: A hitherto undescribed disease occurring in alcoholic and malnourished patients. AMA Arch Neurol Psychiatry 1959;81:154-72.
2. Tomlinson BE, Pierides AM, Bradley WG. Central pontine myelinolysis. Two cases with associated electrolyte disturbance. Q J Med 1976;45:373-86.
3. Kleinschmidt-DeMasters BK, Norenberg MD. Rapid correction of hyponatremia causes demyelination: Relation to central pontine myelinolysis. Science 1981;211:1068-70.
4. Brown WD. Osmotic demyelination disorders: Central pontine and extrapontine myelinolysis. Curr Opin Neurol 2000;13:691-7.
5. Kheetan M, Ogu I, Shapiro JI, Khitan ZJ. Acute and chronic hyponatremia. Front Med (Lausanne) 2021;8:693738.
6. de Souza A. Movement disorders and the osmotic demyelination syndrome. Parkinsonism Relat Disord 2013;19:709-16.
7. Abdul Halim S, Mohd Amin NA. Treatment response in osmotic demyelination syndrome presenting as severe parkinsonism, ptosis and gaze palsy. BMJ Case Rep 2018;2018:bcr2018225751.
8. Perikal PJ, Jagannatha AT, Khanapure KS, Furtado SV, Joshi KC, Hegde AS. Extrapontine myelinolysis and reversible parkinsonism after hyponatremia correction in a case of pituitary adenoma: Hypopituitarism as a predisposition for osmotic demyelination. World Neurosurg 2018;118:304-10.

9. Lambeck J, Hieber M, Dreßing A, Niesen WD. Central pontine myelinosis and osmotic demyelination syndrome. Dtsch Arztebl Int 2019;116:600-6.

10. Rizvi I, Ahmad M, Gupta A, Zaidi N. Isolated extra pontine myelinolysis presenting as acute onset parkinsonism. BMJ Case Rep 2012;2012:bcr2012007140.