# Extra-Pontine Myelinolysis in a Patient with Diabetes Insipidus Secondary to Disgerminoma of the Central Nervous System: Case Report

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*Mielinólise Extrapontina em Adolescente com Diabetes Insípidus Secundário a Disgerminoma do Sistema Nervoso Central: Relato de Caso*

Mielinólise Extrapontina en Paciente con Diabetes Insípida Secundário a Disgerminoma del Sistema Nervioso Central: Relato de Caso

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***Abstract***
**Introduction:** Osmotic demyelination syndrome is a rare neurological condition caused by damage to the myelin sheath of neurons, involving difficulty in the management of sodium imbalance in patients with diabetes insipidus. **Case report:** Patient was a 14-year-old female with diabetes insipidus secondary to dysgerminoma of the central nervous system, with severe hyponatremia (sodium 103 mEq/L). Five days after rapid correction of the sodium imbalance, the patient presented coma (Glasgow scale:11), dysphagia, mutism, and quadriparesis. Cranial MRI findings were consistent with a diagnosis of extrapontine myelinolysis. Twenty-five days after admission to the ICU, the patient was alert, oriented, walking without difficulty, eating an oral diet without choking, although with slightly diminished strength in the upper limbs and slightly sluggish verbal communication. Three-month follow-up MRI showed atrophy of the basal nuclei, confirming severe cellular injury. **Conclusion:** Presentation of osmotic demyelination may range from mild or asymptomatic clinical forms to severe motor sequelae and death. There is no specific treatment, which highlights the importance of early diagnosis and adequate management of the sodium imbalance, as well as rigorous control of serum sodium levels.
***Key words:*** Myelinolysis, Central Pontine; Central Nervous System; Diabetes Insipidus; Hyponatremia.

Resumo
**Introdução:** A síndrome de desmielinização osmótica é uma condição neurológica rara causada pelo dano à bainha de mielina dos neurônios, com difícil manejo do distúrbio do sódio em paciente com *diabetes insípidus*. **Relato do caso:** Adolescente do sexo feminino, 14 anos, com *diabetes insípidus* secundária a disgerminoma do sistema nervoso central, com hiponatremia grave (sódio 103 mEq/L). Cinco dias após a correção rápida do sódio, apresentou coma (Escala de Glasgow:11), disfagia, mutismo e tetraparesia. Os achados na ressonância nuclear magnética craniana foram compatíveis com diagnóstico de mielinólise extrapontina. Vinte e cinco dias após a internação no Centro de Tratamento Intensivo, a paciente encontrava-se lúcida, orientada, deambulando sem dificuldade, alimentando-se por via oral, sem engasgos, ainda com discreta diminuição de força nos membros superiores e comunicação verbal pouco lentificada. A ressonância nuclear magnética após três meses mostrou atrofia dos núcleos da base, comprovando lesão celular grave. **Conclusão:** A desmielinização osmótica pode apresentar-se com formas clínicas leves ou assintomáticas, até sequelas motoras graves e morte. Não existe tratamento específico, o que ressalta a importância do diagnóstico precoce e do manejo adequado do distúrbio do sódio, assim como controle rigoroso dos seus níveis séricos.
**Palavras-chave:** Mielinólise Central da Ponte; Sistema Nervoso Central; Diabetes Insípido; Hiponatremia.

Resumen
**Introducción:** La síndrome de desmielinización osmótica es una condición neurológica rara causada por el daño en lãs vainas de mielina de las neuronas, con difícil manejo del trastorno de los niveles de sódio en los pacientes con diabetes insípida. **Relato del caso:** Adolescente do sexo feminino, 14 anos, com diabetes insípida secundária a disgerminoma del sistema nervioso central, con hiponatriemia grave (sódio103mEq/L). Cinco días después de la corrección rápida del sódio, presentó coma (Escala de Glasgow: 11), disfagia, mutismo y tetraparesia. Los hallazgos en la resonancia magnética del cráneo fueron compatibles con diagnosis de mielinólise extra-pontina. Veinticinco días después de la internaciónen el Centro de Tratamiento Intensivo la paciente se encontraba lúcida, orientada, deambulando sin dificultad, alimentándose por vía oral sin atorarse, aúncon discreta disminución de fuerza en los miembros superiores y comunicación verbal poco lentificada. Una resonancia nuclear magnética después de tres meses mostró atrofia de los núcleos de la base del cráneo, comprobando lesión celular grave. **Conclusión:** Una síndrome de desmielinización osmótica puede presentarse con formas clínicas ligeras o asintomáticas, hasta secuelas motoras graves y muerte. No existe tratamiento específico, lo que resaltala importancia del diagnóstico precoz y del manejo adecuado del disturbio del sodio, así como control riguroso de sus niveles séricos.
**Palabras clave:** Mielinólisis Pontino Central; Sistema Nervioso Central; Diabetes Insípida; Hiponatremia.

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## INTRODUCTION

Osmotic demyelination syndrome is a rare neurological condition caused by injury to the myelin sheath of neurons[1], related to a sudden change in plasma osmolarity, especially in serum sodium. The classic clinical presentation is central pontine myelinolysis with involvement of the white matter in this area and extrapontine myelinolysis which can involve broad areas of the brain such as the cerebellar peduncles, basal ganglia, frontal and temporal white matter, external and internal capsule, thalamus, subthalamic nucleus, deep layers of the cerebral cortex, hippocampus, and corpus callosum[2]. It occurs sporadically in all age brackets and in both sexes, and the exact incidence is unknown[3].

This report describes a case of osmotic demyelination and highlights the difficulty in management of the sodium disorder in a patient with diabetes insipidus, as well as the importance of rigorous control of natremia in these patients.

The current study was approved by the Institutional Review Board of the Brazilian National Cancer Institute José Alencar Gomes da Silva (INCA), under protocol number CAAE: 54322015.7.0000.5274. Authorization for publication was provided by the patient's parents/guardians by signing the free and informed consent form.

## CASE REPORT

The case was a 14-year-old female patient with diagnosis of dysgerminoma of the central nervous system with suprasellar location, pan-hypopituitarism, in regular use of levothyroxine, prednisone, and desmopressin acetate (DDAVP). She had been in chemotherapy for seven months, with the last cycle 13 days previously. Patient sought medical attention with a complaint of fever, vomiting, and decreased liquid intake and was diagnosed with febrile neutropenia and hypernatremia (serum sodium 160 mEq/L). She was admitted to the ward for antimicrobial treatment and correction of the sodium imbalance with free water replacement. The sodium was corrected and the patient completed her antibiotic regimen.

On day 11 in hospital, patient presented altered level of consciousness, with diagnosis of severe hyponatremia (sodium 103 mEq/L), and was transferred to the pediatric intensive care unit (PICU), where correction of the fluid-electrolyte imbalance was initiated with 3% saline solution.

Upon physical examination on admission to the pediatric ICU, patient was somnolent, responding to questions, with mobility of all four limbs preserved, pupils isochoric and reactive to light, hemodynamically stable, and with no abnormal lung sounds. Patient was started on correction of hyponatremia with 3% saline solution, calculated to correct 10 mEq in 24 hours, and assessed by serial collection of serum sodium every three hours.

Several hours after initial correction, the patient showed improved level of consciousness, remaining alert, moving all four limbs, and with adequate verbal response. However, even with the assessment of serum levels every three hours, sodium increased by 18 mEq/L (to 121 mEq/L) in 12 hours. At this point the sodium replacement was suspended, and intranasal desmopressin acetate was started. In the following hours the patient received free water replacement and administration of desmopressin acetate. Nevertheless, the sodium continued to increase, reaching 138 mEq/L, with an increase of 35mEq/L in 24 hours and 54 mEq/L in 48 hours (Figure 1).

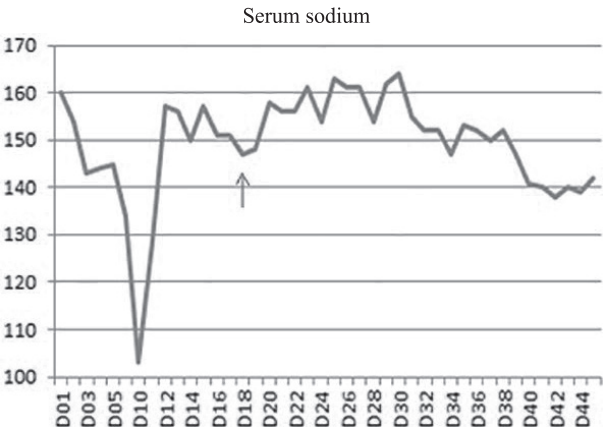


**Figure 1**. Serum sodium levels in the first 44 days of admission to the pediatric ICU, with arrow indicating the worst clinical stage

Five days after the hyponatremia (sodium 103 mEq/L), the patient's neurological status worsened, with a drop in her level of consciousness, Glasgow 11 (opening eyes on command, incomprehensible speech, and obeying commands), dysphagia, paresthesia in the four limbs, hypoventilation with descending tongue, and need for non-invasive ventilatory support (on this day, sodium 149 mEq/L). Two days later, magnetic resonance imaging (MRI) showed uptake in the bilateral lentiform nuclei and subcortical white matter diffusely, suggestive of severe extrapontine myelinolysis (Figure 2).

On the subsequent days, patient presented fluctuating level of consciousness, quadriparesis, attempts to communicate with the examiner, uttering incomprehensible sounds, communicating via eye movements, suggestive of locked-in syndrome.

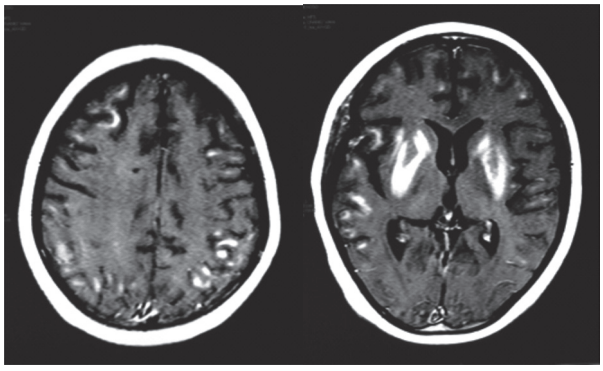

**Figure 2.** Axial MRI in T1 with contrast. Uptake in the bilateral lentiform nuclei and diffusely in the subcortical white matter

Twenty-five days after admission to the PICU, patient showed progressive neurological improvement, with mobilization of the four limbs, but with muscle weakness, responding to simple requests with single words, with coherence and improvement in the dysphagia, and initiation of an oral diet. She was transferred to the ward on the thirtieth day of follow-up in our department.

Three months after the initial symptoms, a new MRI was performed (Figure 3) which did not show uptake, with atrophy of the basal ganglia, formation of cavitation and expansion of the Sylvian fissure bilaterally. On clinical examination, patient was lucid, oriented, walking without difficulty, eating by mouth without choking, with slightly diminished strength in the upper limbs and persistently sluggish verbal communication.

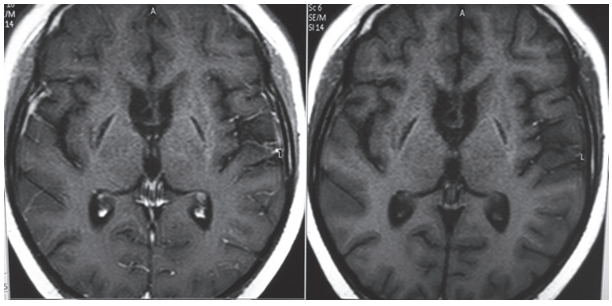

**Figure 3.** Cranial MRI, axial slice, T1 with and without contrast, respectively

## DISCUSSION

Osmotic demyelination syndrome is traditionally associated with rapid changes in serum osmolarity, particularly rapid correction of hyponatremia. However, various other associations have been reported, such as severe hypophosphatemia, hypokalemia, diabetes mellitus, renal failure, hemodialysis, gestational hyperemesis, anorexia nervosa, Wilson's disease, severe burns, and systemic lupus erythematosus, among othes[1].

Hyponatremia is defined as serum sodium less than 135 mEq/L and is considered severe when less than 120-125mEq/L[3,4]. Osmotic demyelination is related to a rapid correction of hyponatremia greater than 10-12 mEq/L in 24 hours; that is, greater than a rate of 0.5 to 1 mEq/L/h or 25 mEq/L in 48 hours[4].

In the current case, the patient underwent rapid correction of the hyponatremia, with an increase of 34 mEq/l in 24 hours and 54 mEq/l in 48 hours, evolving with hypernatremia despite rigorous control of serum sodium and numerous attempts at free water replacement and the use of desmopressin acetate, which highlights the difficult management due to the close relationship between diabetes insipidus and intracranial dysgerminoma, even after surgical treatment and chemotherapy[5].

Classically, osmotic demyelination presents a biphasic course, with an initial phase of seizures or encephalopathy, with progressive improvement of the neurological symptoms with the correction of hyponatremia, and a late phase, two to eight days later, with severe deterioration expressed as fluctuating level of consciousness, behavior changes, dysarthria, mutism, dysphagia, oculomotor disfunction, and various degrees of quadriparesis. The quadriparesis is initially flaccid due to the injury to the corticospinal tract and progresses to a spastic phase with injury to the pontine base. More severe cases can present locked-in syndrome, with the patients awake, but unable to move or communicate, only with preservation of vertical ocular movements and blinking[1,6].

The patient in this case displayed the classic clinical presentation, with diminished level of consciousness, dysphagia, dysarthria, and decreased strength on the fifth day after the disorder of sodium balance. Diagnosis of osmotic demyelination syndrome was confirmed by MRI, with severe extrapontine lesions. On the subsequent days she continued to show progressive clinical deterioration with mutism and quadriparesis. Clinical improvement began on day 25 after admission to the pediatric ICU.

MRI of the brain is sensitive for the detection of myelinolysis with recognition of mild to asymptomatic cases, besides determining the extent of demyelination. Typical radiological findings are symmetric hypointense lesions in T1 images, in the pons, sparing the periphery; and other extrapontine structures and hyperintense lesions on T2 and fluid acquisition inversion recovery (FLAIR)[6]. In the case reported here, MRI showed uptake in the basal ganglia and diffusely in the subcortical white matter in T1, T2, and FLAIR, characterizing severe lesion with cell death.

Some studies have reported that the typical radiological findings of pontine myelinolysis are not usually seen on MRI in the first week after the onset of clinical symptoms[7].

Diffusion-weighted imaging is currently the most widely used modality, due to early detection of myelinolysis findings, 24 hours after the onset of quadriplegia[2,6]. However, in the current case MRI was performed on day 7 and did not reveal restriction in the diffusion-weighted sequence, possibly indicating that besides demyelination there was also cell death.

In the subacute and chronic phases, the pontine and particularly the extrapontine lesions may become smaller and better defined. In some cases, MRI can show a typical batwing lesion in the pontine base[2]. Follow-up MRI showed atrophy of the basal ganglia, proving severe cellular lesion.

The medical literature reports varied evolution in osmotic demyelination, ranging from complete recovery to death. Recovery tends to be slow and gradual. Mortality associated with severe hyponatremia ranges from 40% to 50%[8,9]. In 2006, our service reported a case of extrapontine myelinolysis in an adolescent with an unfavorable outcome[2]. A literature review in 2014 found that half of the cases of osmotic demyelination syndrome can experience good recovery, even in patients with severe initial neurological deficits. Post-liver transplant patients showed worse prognosis[1].

Despite the severity of initial neurological impairment, our patient showed good clinical evolution, with partial recovery of strength and improvement of the dysphagia and dysarthria.

## CONCLUSION

Osmotic demyelination syndrome is a rare neurological condition, with clinical involvement ranging from mild or asymptomatic to severe motor sequelae and death. There is no specific treatment, highlighting the importance of early diagnosis of the sodium imbalance and adequate management, as well as rigorous serial control of serum sodium levels.

Studies in pediatrics are necessary to establish safer protocols for control and management of patients with critical serum sodium levels.

### CONTRIBUTIONS

Bruno Espírito Santo de Araújo, Daniela Capuzzo Dias Castiglione, and Sandra Helena dos Santos Victal participated substantially in the study's conception and planning, data analysis and interpretation, and writing, critical revision, and approval of the final version for publication. Fernanda Lobo Rascão, Sima Esther Ferman, Fernanda Ferreira da Silva Lima, and Fernanda Costa Capela participated substantially in the data analysis and interpretation and writing, critical revision, and approval of the final version for publication.

### CONFLICT OF INTEREST

None.

### FUNDING SOURCES

None.

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