

Myélinolyse centro-pontine liée à l'hyperglycémie chronique: Cas clinique et revue de la littérature

Chronic hyperglycemia-related central pontine myelinolysis: A case report and a literature review

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ABSTRACT

Introduction: La myélinolyse centropontine (MCP) est une affection rare et généralement associée à la correction rapide de l'hyponatrémie. L'hyperglycémie chronique est une cause extrêmement rare de MCP. Notre objectif était de décrire le cas d'un patient ayant présenté une MCP associée à une hyperglycémie chronique.

Observation: Nous rapportons le cas d'un homme de 55 ans ayant des antécédents personnels de diabète sucré qui a présenté, sur une période de deux mois, un tableau progressif de troubles de la marche, de l'élocution et une dysphagie. Les paramètres biologiques étaient sans anomalies à l'exception du taux d'hémoglobine glyquée qui était élevé à 12%. L'osmolalité sérique calculée était normale à 309,8 mOsm/kg. L'imagerie par résonance cérébrale était compatible avec le diagnostic de MCP. L'évolution clinique était favorable grâce à l'optimisation de la glycémie, à la rééducation physique et à la prise en charge orthophonique.

Conclusion: Ce cas met en évidence le lien entre l'hyperglycémie chronique et la MCP. Le mécanisme sous-jacent pourrait être la toxicité induite par les variations glycémiques sur les oligodendrocytes.

Mots-clés: Cas clinique, diabète, sodium, substance blanche, syndrome de démyélinisation osmotique

RÉSUMÉ

Introduction: Central pontine myelinolysis (CPM) is a rare condition that has been reported to occur in association with rapid correction of hyponatremia. Chronic hyperglycemia is an extremely rare cause of CPM with no other metabolic disturbances. Our aim was to describe the case of a patient who presented with CPM associated with chronic hyperglycemia.

Observation: We report the case of a 55-year-old male with a personal history of diabetes mellitus who presented, over two months, gait disorders, slurred speech, and dysphagia. All laboratory tests were within normal limits except for glycated hemoglobin level which was high at 12%. Calculated serum osmolality level was normal at 309.8 mOsm/kg. Brain magnetic resonance imaging was consistent with the diagnosis of CPM. Patient's medical condition improved by optimizing blood glucose levels, physical rehabilitation and speech therapy.

Conclusion: This case highlights the hypothesis of chronic hyperglycemia being the direct cause of CPM. The underlying mechanism might be the toxicity of varying blood glucose levels towards the oligodendrocytes.

Keywords: Case report, diabetes, osmotic demyelination syndrome, sodium, white matter

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INTRODUCTION

Central pontine myelinolysis (CPM) is a pivotal manifestation of the osmotic demyelination syndrome (ODS), along with extra pontine myelinolysis [1]. Although its exact pathogenesis is not fully understood, the most probable trigger seems to be osmolarity variation [2]. Its most known etiology is an iatrogenic effect of rapid correction of hyponatremia in intensive care units patients [1]. The clinical presentation is then usually hyperacute and severe. However, in recent years, a wide variety of medical conditions and clinical manifestations have been reported [3]. Herein, we reported a rare case of subacute onset of CPM as a result of poorly controlled diabetes mellitus.

CASE PRESENTATION

Patient information

A 55-year-old male patient was admitted to the neurology clinic in Razi University hospital-Tunisia with subacute unsteady gait, slurred speech, and dysphagia evolving for two months. His medical history was remarkable for diabetes mellitus with poor adherence to medication.

Clinical Findings

Table 1. Medical history timeline

Two months before admission	Unsteady gait, slurred speech, and difficulty swallowing.
Several weeks before symptoms	High glycated hemoglobin at 12%, with signs of polydipsia and polyuria.
On admission to the neurology clinic	Diagnosed with CPM related to chronic hyperglycemia.
During hospitalization	Diabetes management optimized, and physical rehabilitation and speech therapy initiated.
Follow-up	Improvement in gait and dysphagia

Diagnostic assessment

On laboratory investigations, fasting glycaemia was high at 194 mg/dL (normal range: 70-100) and electrolytes' levels were within normal limits: sodium 145 mmol/L (normal range: 135-145); potassium 4.0 mmol/L (normal range: 3.5-5.0); calcium 2.22 mmol/L (normal range: 2.10- 2.60). The calculated serum osmolality was 309.82 mOsm/kg (normal range: 275-295). A significantly high glycated hemoglobin level at 12% (normal range < 6.5%) was found several weeks before the symptoms' onset as well as polydipsia and polyuria.

On the brain magnetic resonance imaging (MRI) performed two weeks after symptoms' onset, symmetrical T2 and Fluid attenuated inversion recovery hyperintensities were found in the pons, the upper medulla oblongata, as well as the middle cerebellar peduncles (Figure 1). Neither mesencephalic nor supra-tentorial abnormalities were noted.

Considering all findings the patient was diagnosed with subacute CPM related to chronic hyperglycemia.



Figure 1. Hyposignal intensity on T1 weighted images on the pons (A), Hypersignals on T2 and Flair weighted images on the pons (B and C), Hypersignals on T2 weighted images on the pons and upper medulla oblongata (D).

Therapeutic intervention

The patient was referred to an endocrinologist to optimize diabetes mellitus management. Physical rehabilitation and speech therapy were also initiated.

Follow-up and outcomes

The patient showed signs of improvement in gait and dysphagia but has been lost to follow-up since.

DISCUSSION

We have described a case of CPM that is extremely original in many aspects. First, our patient presented with CPM without any ionic disturbance nor hyperosmolality, only poorly controlled diabetes mellitus. Moreover, the subacute onset with mild to moderate clinical signs constitutes another rare specificity of our case. Lastly, the benign outcome with minimal disability is an exception for a condition known for its poor prognosis.

CPM is the classical presentation of the ODS, which is a rare neurological disorder caused by damage to the myelin sheath of brain cells, with a greater susceptibility of the pons [1]. This medical condition accounts for 0.4% to 0.56% of all neurological admissions to tertiary referral hospitals and is known to be associated with severe disability and high mortality rates [2]. However, findings have proven that half of the patients diagnosed with CPM on MRI may fully recover [1]. Classically, CPM is described as a condition with a biphasic course with initial seizures or encephalopathy that may improve gradually but are

then followed by severe misleading manifestations such as dysarthria, dysphagia, oculomotor dysfunction and variable degrees of motor deficits [1]. Asymptomatic or pauci – symptomatic presentations are extremely rare [1]. CPM-associated symptoms depends on lesions topography (Table 2) [2]. The triggering factor usually precedes demyelination and its symptoms by one to fourteen days. A symptom-free interval is followed by a secondary deterioration [2].

Table 2. Central pontine myelinolysis-associated symptoms according to lesions topography

Affected regions	Symptoms
Pons, corticospinal and bulbar tracts	Frequent encephalopathies and signs of damage to the brainstem
Corticobulbar pathway	Pseudobulbar affect
Corticospinal tracts	Initial flaccid then spastic tetraparesis of varying severity
Tegmental lesions	Ocular and pupillary motility disorders

CPM can occur in cases of extreme osmotic variation and particularly in cases of unintentional overly rapid correction of hyponatremia [3]. In the central nervous system, glial cells have an important role in tissue support. They protect neurons from swelling and have a water-handling role by selectively expressing aquaporin-4 on their surface [4]. This quality comes along with a vulnerability of glial cells to excessive water shifts when adaptation mechanisms are exceeded. In a situation of hypo osmolarity, oligodendrocytes extrude ions and water molecules to keep a homeostatic state. When this state is rapidly reversed and the water flows back into the cells, hyponatremia-induced – cerebral edema is generated. The regulation process cannot follow up if the osmotic variation ensues in less than 24 hours because it is an energy-dependent – mechanism that consumes ATP [3]. As a result, the glial cell shrinkage leads to myelinolysis. With the strong concentration in descending and crossing fibers, the proximity of connected gray and white matter and the high concentration of oligodendrocytes, the pons is particularly vulnerable to ODS [2].

CPM may result from many conditions that cause an ionic disturbance. Historically, CPM's first description goes back to 1959 with the report of four patients with quadriplegia and pseudobulbar palsy presenting chronic alcoholism or malnutrition [5]. Other conditions had been also associated with CPM such as liver transplantation, cirrhosis and hypokalemia [3].

Hyperglycemia-related CPM, which had been rarely reported, is classically related to a hyperosmolar state with or without hyponatremia (Table 3) [6–19].

The clinical presentation is then often hyperacute with vigilance disturbances, which is contrasting with our case [6,8,9,13,15,18,19]. However, CPM may be also related to chronic hyperglycemia in extremely rare occasions [10,12,14]. The underlying mechanism is probably due to glycaemia variations that are toxic to oligodendrocytes. Glucose variation, as an osmotically active phenomenon, can produce water to flow out of the cells causing

shrinkage, which is the primary lesion of CPM [3]. In the case of our patient, sustained fluctuations in plasma glucose due to poor glycemic control may have contributed to an osmotic environment too unstable for normal cellular compensation, as it was suggested by Donnelly et al. [11]. Brain MRI is the current standard method of CPM diagnosis and pontine demyelination remains the hallmark of the disease. Typically, hypo-intense T1-weighted lesions and hyperintense T2-weighted lesions are described on the pons, as it was highlighted in our case [1]. Restricted diffusion can also be noted. Contrast enhancement is also inconsistently reported [20]. Extrapontine lesions can also be found, especially in the midbrain, thalami and basal ganglia [1,21]. However, none of these localizations were described in our patient. To late February 2025, there is no specific treatment for patients suffering from CPM. Yet, plasmapheresis has shown encouraging results, achieving sometimes complete recovery [22]. In the acute stage, it is used to halt disease progression. However, its effect in the chronic stage is less promising [22]. Intravenous immunoglobulin (IVIG) has also proven its efficacy. The underlying mechanism comprises promoting remyelination by inhibiting the proliferation of Th17 cells and reducing pro-inflammatory mediators. It is also possible that IVIG accelerates the spontaneous recovery of patients presenting ODS [23]. In the particular case of hyperglycemia-related CPM, clinicians should consider the efficacy of glycemic control and optimizing insulin therapy [6–19]. In addition, supportive care performed by a multidisciplinary team is compulsory to alleviate sequelae. Speech and physical therapies are the cornerstones of the rehabilitation process [2]. It is noteworthy that no correlation has been observed between symptoms' severity or initial clinical presentation and clinical outcome, as patients with severe deficits at presentation can achieve good recovery [24]. Our case in this regard is interesting as minimal sequelae and benign outcomes were noticed despite the severity of lesions on MRI.

Some limitations need to be highlighted such as the absence of a long-term follow-up to demonstrate whether the patient had sustained recovery or experienced relapses. The single imaging time point did not allow us to assess the presence of residual damage in our patient, even though the majority of case studies have not conducted a radiological follow-up, and clinical improvement was usually considered sufficient to evaluate the outcome of CPM. Moreover, while interventions like glycemic control, supportive care, and rehabilitation have been reported to improve previously published cases, their efficacy remains a pathophysiological hypothesis due to the small sample of patients and the rarity of the condition.

Table 3. Reported cases of Central pontine myelinolysis associated to hyperglycemia.

Study [reference] Year	Age Sex	Alcoholism Onset	Symptoms	Osmolality (mOsm/kg) Sodium level (mmol/L)	Acute complications of diabetes mellitus	Glycated hemoglobin levels (%)	Lesions location	Proposed treatment	Clinical outcome	Radiological outcome
Hattori et al. [6] 1989	53 F	No 1 day	Altered consciousness	390 Not provided	HS	Poor control	Posterior central pons	IVHI	Death at 11 months	
Burns et al. [7] 2009	93 M	No 1 day	CS	343 137	HS	Poor control	Rostral Pons	IVHI	Marked improvement within 1 month Mild Ataxia	Progressive improvement
Hegazi et al. [8] 2012	43 F	- 15 days	Behavioral changes Disorientation PS	428 181	HS	Poor control	Posterior central pons	IVHI	Total recovery within 4 weeks	-
Rodríguez al. [9] 2014	47 M	No 1 day	Seizures Coma	320 133	HS	10.1	Medulla and central pons	IVHI	Regained consciousness within 3 weeks Asymptomatic within 6 months	No residual damage
Saini et al. [10] 2015	45 F	No 15 Days	CS PS Pseudobulbar affect	307 138	No	18	Pons and upper midbrain	IVHI	Gradual improvement over the ensuing week	-
Donnelly al. [11] 2016	22 M	- 15 days	CS Pseudobulbar affect Bilateral ptosis Dysphagia	326 135	Ketoacidosis	Poor control	Pons	IVHI	Improvement within 2 weeks Relapse caused by ketoacidosis 7 months later	Resolution within three months
Herráiz et al. [12] 2017	55 M	Yes 15 Days	CS PS Pseudobulbar affect Dysphagia	300 140	No	15.8	Pons	IVHI	Improvement within 3 months Moderate persistent dysarthria	-
Hirosawa al. [13] 2018	55 M	- 3 days	Abdominal discomfort Altered consciousness CS	324 126	HS	17.8	Pons and both cerebral hemispheres	IVHI	Total recovery over several months	Unchanged
Marsili et al. [14] 2018	45 M	No 1 day	Muscle spasms	305 Normal	HS	14	Central pons	IVHI	Total recovery within one week	-
Pliquett et al. [15] 2018	55 M	Yes 9 days	CS PS Altered consciousness	300 115	HS	17.6	Central pons	IVHI	Total recovery within 3 months	-
Mir et al. [16] 2021	34 F	No 30 days	PS	291 138	Ketoacidosis	12.3	Central pons	IVHI	Partial improvement within one week	-
Olowoporoku et al. [17] 2022	48 M	No 30 days	PS	299 133	Chronic hyperglycemia	14.7	Central pons	IVHI	Total recovery within 7 days	-
Qu et al. [18] 2023	46 M	No 20 days	Altered consciousness Pseudobulbar affect PS	327 128	HS	16.34	Central pons	IVHI	Total recovery over 6 months	-
Shrestha et al. [19] 2023	44 M	Yes 45 days	Altered consciousness CS PS	275 130	HS	15.5	Central Both cerebellar hemispheres	IVHI	Total recovery within 18 days	-

CS: Cerebellar syndrome. F: Female. HS: Hyperosmolar state. IVHI: Intravenous hydration insulin. M: Male. PS: Pyramidal syndrome.

CONCLUSION

This case report illustrated that CPM, with moderately severe symptoms, may occur subacutely. Chronic hyperglycemia may be the leading cause of this condition. Therefore, optimal and long-lasting control of blood glucose levels is a crucial preventive measure to avoid this disabling complication.

Patient informed and written consent was obtained

Patient perspective

"I ignored my diabetes for years, never thinking it could affect my brain and my work as a sports coach. After being diagnosed with central pontine myelinolysis from poorly managed diabetes, I understood the importance of managing my condition and prioritizing my health."

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