

Extrapontine Myelinolysis: Multifactorial Etiology, About One CaseArnaud Tiafumu^{1*}, Yassir Elalami², Taoufik Abouelhassan¹¹Emergency Department - SAMU, Mohammed VI University Hospital, Marrakesh, Morocco²Radiology Department - Mohammed VI University Hospital, Marrakesh, Morocco**Case Report*****Corresponding author**

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Abstract: Osmotic demyelination syndrome (central pontine myelinolysis and extrapontine myelinolysis) is a rare condition. Although most frequently reported cause is the quick correction of hyponatremia, the osmotic demyelinating syndrome can be explained, from a physiological point of view, by two major groups of factors, specifically: factors related to under-nutrition or fasting, and factors related to the variation of osmolarity. In our case, the diagnosis of osmotic demyelination syndrome was suspected in front of both; the neurological signs (altered level of consciousness, Focal neurologic signs) and the careful correction of severe hyponatremia. The confirmation of the disorder was done by the encephalic MRI, as reported in the literature. Although occurred following a correction of severe hyponatremia, the most likely etiophysiological hypothesis was the combination of; the existence of the multiple pro-apoptotic risk factors, such as: under-nutrition, Diabetic ketoacidosis (DKA), renal failure, hypokalemia, depth of hyponatremia with minor contribution of the speed of correction of hyponatremia (considered slow and careful). The same risk factors have been reported in the literature.

Keywords: extrapontine myelinolysis, etiological factors

INTRODUCTION

Extrapontine myelinolysis (EPM) is a rare condition; in 30% of cases, it is associated with Central pontine myelinolysis (CPM) [1]. Their risk factors and physiopathology are identical; there are various clinical manifestations [1]. The causes are often subject to discussion.

We report a case of EPM in a young patient who developed during a correction, although controlled, of severe hyponatremia resulted a diabetic ketoacidosis on urinary tract and digestive infections.

CASE REPORT

Our patient is 45-year-old with type 2 diabetes who was treated by insulin for 5 years. She was admitted to resuscitation room for recurrent seizures. She was referred from a Peripheral Hospitals for persistent altered level of consciousness after the management of diabetic ketoacidosis, complicating an episode of acute enteritis and acute pyelonephritis to E. Coli (at CBEU) dating 7 days before her admission, without ionic disorder originally.

Upon arrival in emergency room, the patient had temporal and spatial disorientation disorder without any sensory nor motor deficiency, with stable hemodynamic and respiratory state. She was dehydrated (B or C), malnourished with a BMI at 16.50 Kg/m² (according to the WHO classification) [2], without fever, blood glucose level of 1.02g/L without ketonuria. The occurrence of two (2) short-

generalized tonic-clonic seizures, calmed by Diazepam in IV, motivated her admission in resuscitation room.

The biological assessment at admission showed hyponatremia at 116 mmol/L, hypokalemia at 3.05 mmol/L and hypochloremia at 73 mmol/L, with moderate functional renal failure and calculated osmolarity at 246 mOsm/L.

This was severe acute hyponatremia complicated by seizure. The management involved, among other things, rehydration and correction of hyponatremia according to the concepts and formulas of Adrogue and Madias (A and M) [3], without exceeding a correction speed of 10 to 11 mmol/L over 24 hours. The patient received during the first 24 hours: 180 cc of Hypertonic saline solution (HSS) 3% in 1 hour with the goal of gaining a rise in sodium of 3 mmol/L to stop seizures, and by 3 litres of Isotonic saline solution (ISS) 0.9% for the rest of the day; then 4 litres of ISS 0.9% on the 2nd day. Daily checks showed a serum concentration of 127 mmol/L after 24 h and 137 mmol/L after 48 h. The kalemia and

chloremia gradually corrected themselves to normalize with the natremia.

After she was transferred to the Endocrinology department, the patient showed an altered state of consciousness on the 5th day of hospitalization, while she had recovered a normal neurological state since her first hours of hospitalization. The mentioned symptomatology was combined with flaccid paralysis and partial tonic-clonic seizures of the right hemi-body with stable

hemodynamic and respiratory status. The tendons' reflexes were stretched in 4 limbs. Cerebral CT scan was performed, after treatment of seizures, and found to be normal. Encephalic MRI showed sub-cortical and bilateral periventricular white matter lesions in T1 low signal intensity, high signal intensity T2 and T2 flair. Cortical thickening at the left temporal level in T1 low signal intensity was found, T2 and T2 flair high signal intensity and on diffusion. This aspect of MRI is linked to extrapontine myelinolysis.

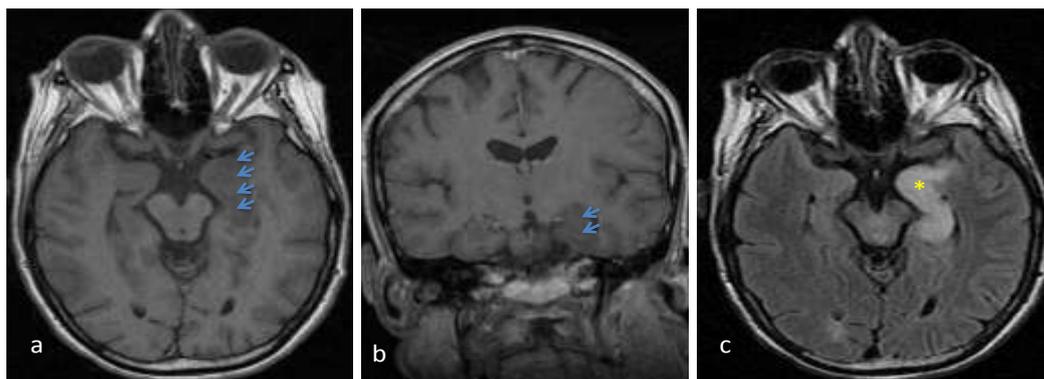


Fig-1: Encephalic MRI: Axial and coronal section in T1 (a, b) and weighting(c). Cortical thickening at the left temporal level with low signal intensity T1 (blue arrows) and high signal intensity flair (*).

The subsequent management was mainly symptomatic with corticotherapy, nursing, enteral feeding with prevention of seizures and rehabilitation. Monitoring of biological parameters didn't show any disturbances until the 8th day of hospitalization. The patient was discharged on the 10th day after stopping seizures, but she kept a clouding of consciousness and deficit of the right hemi-body.

DISCUSSION

Described in 1959 by Adams *et al.*, [4] in alcoholic, malnourished and chronically ill patients, Central pontine myelinolysis (CPM) corresponds to the destruction of oligodendrocytes and myelin in the central part of the protuberance without affecting neurons and axons. The same histological lesions were later found in the thalamus, putamen, globus pallidus, lateral geniculate ganglia and the white matter of the cerebellum, defining Extrapontine myelinolysis (EPM). These two entities (CPM and EPM) are often grouped under the name of Osmotic demyelination syndrome (ODS).

Osmotic demyelination syndrome (pontine myelinolysis and extrapontine myelinolysis) is a rare condition. Although most frequently reported cause is the quick correction of hyponatremia [5-8] which, would be combined with extracellular osmotic high pressure leading to cellular dehydration; There are two main groups of factors already described:

- Factors related to malnutrition or fasting: chronic alcoholism, amyotrophic lateral sclerosis, burns,

liver failure (acute or chronic), liver transplantation, pancreatitis, vitamin PP deficiency.

- Factors related to osmolarity variation: burns, polydipsia, renal failure, sickle cell disease, hypothalamic tumor, dyskalemia, dysnatremia, diabetic decompensation (Diabetic ketoacidosis and hyperosmolar hyperglycemic state).

It was in 1976 that Tomlison *et al.*, [9] discussed the relationship between osmotic demyelinating syndrome and hyponatremia; hypothesis confirmed by Lauren R. in 1981 [4] with highlighting the speed of correction of hyponatremia.

A rare disease, CPM is often associated with EPM in 30% of cases [1]. Although both have same risk factors and pathophysiology, the CPM and the EPM are of variable clinical manifestations (1). Spastic quadriplegia, pseudobulbar effect, dysphonia, dysarthria, apraxia, and neuropsychiatric disorders are the most common symptoms. The diagnosis is confirmed by encephalic magnetic resonance imaging (MRI), which shows a T1-weighted low signal intensity and a high signal intensity on the T2 - weighted and flair sequences [10]. To date, there is no coded treatment and only symptomatic treatment can be offered.

In our case, the diagnosis of osmotic demyelinating syndrome was suggested in front of the found risk factors and confirmed by MRI. The

hypothesis of myelinolysis following osmotic aggression caused by quick correction of hyponatremia was considered unlikely, since this correction was careful and spread over time, not exceeding 11 mmol/L/24h, below current recommendations described by several authors (1 mmol/h in average over 24 hours) [2, 11-14]. According to the same authors, the speed can be faster at the very beginning when the clinical signs are disturbing (seizures, deep coma): for example 3 mmol in 1 hour then 1 mmol/h and 0.5 mmol/h to stay below the limit of 24 mmol/L in 24 hours. Also, Brahim LF [15] reports the controversial

effect of the speed of correction of dysnatremias in the occurrence of CPM.

Formulas that have become classical make it possible to plan the treatment of dysnatremias, as used in our case, especially those of Adrogué and Madias (A and M) [11, 12]. Calculation by this formula predicts, for 1 liter of perfused fluid (and depending on the type of liquid chosen), the variation of the expected natremia, as a function of body weight and initial natremia level [2, 10, 12, 16].

$\text{Change in plasma Na}^+ = \frac{\text{Infusate Na}^+ - \text{plasma Na}^+}{\text{Total body water} + 1}$	eqn. 1
$\text{Change in plasma Na}^+ = \frac{(\text{Infusate Na}^+ + \text{infusate Na}^+) - \text{plasma Na}^+}{\text{Total body water} + 1}$	eqn. 2
<p>Note:</p> <ul style="list-style-type: none"> • Equation 1 estimates the effect of one litre of a sodium containing fluid on plasma Na⁺ and equation 2 the effect of replacement of one litre of fluid containing sodium and potassium. • Total body water is estimated as a fraction of body weight, being 0.6 and 0.5 in adult men and women respectively. • Na⁺: sodium concentration. 	

Fig-2: Formulas of Adrogué and Madias [16]

The most likely etiophysiological hypothesis would be the combination of; the existence of multiple pro-apoptotic risk factors, such as: under-nutrition, Diabetic ketoacidosis (DKA), renal failure, hypokalemia, depth of hyponatremia with minor contribution of the speed of correction of hyponatremia as described by several authors [17-19].

CONCLUSION

EPM is a rare and serious condition, its main cause is osmotic stress on the brain caused by quick rise in osmolarity; this is the case in the rapid correction of hyponatremia. The latter is far from being the only determining factor, because there are other risk factors whose their combination increases the risk of occurrence of CPM or EPM such as undernutrition, chronic alcoholism, hyponatremia .

Diagnosis is based primarily on encephalic MRI to visualize the pontine lesion. The treatment remains symptomatic and no curative treatment is currently validated. Corticotherapy remains controversial. The only treatment is preventive with a careful correction of hyponatremia. The prognosis unfortunately stays dark with a heavy morbidity and mortality.

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