N. Ramírez[1]
B. Arranz[1]
C. Martín[2]
L. San[1]

Course and prognosis of a case of central pontine myelinolysis in eating behavior disorder

[1] Psychiatry Department
Hospital San Rafael
Barcelona (Spain)

[2] Psychiatry Department
Hospital General de Granollers
Benito Menni CASM
Barcelona (Spain)

Central pontine myelinolysis (CPM) is a serious disorder that has been described in multiple diseases, generally involving important metabolic and hydroelectrolyte alterations. Although initially, its prognosis was usually fatal, there are a growing number of cases where the clinical symptoms begin abruptly and end after a short period, albeit with a persistence of the neuroimaging lesions. The case of a 22 year-old woman with a 6 year history of serious eating disorder with important physical deterioration and neurological and psychiatric symptoms suggestive of CPM is described. Despite the confirmation of the brain lesions through magnetic resonance imaging, neurological and psychiatric symptoms fully disappeared within a few weeks while the typical lesions of CPM remained. Although the risk of appearance of CPM exists during the course of an eating disorder, its prognosis does not seem to be as fatal as it was previously thought. Close monitoring of the clinical symptoms and neuroimaging findings should be carried out in these patients during the first months.

Key words:
Central pontine myelinolysis. Eating disorder. Neuroimaging. Electrolyte disorder.

Actas Esp Psiquiatr 2007;35(2):141-144

Evolución y pronóstico de un caso de mielinólisis central pontina en el trastorno de la conducta alimentaria

La mielinólisis central pontina (MCP) es una alteración grave cuya aparición se ha descrito en múltiples procesos patológicos que generalmente cursan con alteraciones metabólicas e hidroelectrolíticas importantes. Aunque inicialmente su pronóstico se consideró siempre grave, cada vez se describen más casos en los que la sintomatología se inicia de manera brusca y cede en poco tiempo, aunque permanezcan lesiones en las imágenes neurorradiológicas. Se describe el caso de una mujer de 22 años con historia de trastorno de la conducta alimentaria grave de 6 años de evolución, con un importante deterioro del estado general, que se inicia con síntomas neurológicos y psiquiátricos sugestivos de MCP durante el tratamiento. A pesar de la confirmación de la lesión a través de resonancia magnética, los síntomas desaparecieron totalmente a las pocas semanas, mientras que permanecieron las lesiones típicas de MCP. Aunque existe el riesgo de aparición de MCP a lo largo de la evolución de un trastorno de la conducta alimentaria, su pronóstico no parece ser tan funesto en todos los casos como se pensaba previamente, debiéndose realizar un seguimiento de la evolución de los síntomas clínicos y de la neuroimagen a lo largo de los primeros meses.

Palabras clave:
Mielinolisis central pontina. Trastorno de la conducta alimentaria. Neuroimagen. Trastorno electrolítico.

INTRODUCTION

Central pontine myelinolysis (CPM) is a recently described disorder[1] in which destruction of oligodendrocytes and myeline are characteristically observed, especially in the central zone of the pons. However, lesions may appear in other zones such as the caudate/putamen, lateral thalamus, geniculate body and cerebral cortex[2]. The onset of the symptoms is generally sudden and it is clinically manifested by neurological disorders that vary in seriousness. They go from mild neurological symptoms related with the corticospinal, corticobulbar, corticopontine and pontocerebellar tracts to progressive conditions of spastic tetraparesis, pseudobulbar paralysis and coma. Psychiatric symptoms, behavioral changes and neuropsychological deficits have also been described[3]. Diagnosis is suspected by the presence of clinical symptoms and confirmed with neuroimaging. The MRI is more sensitive to demyelinating lesion than the CT scan, showing the typical hyperintense images in the brainstem[4].

Appearance of this disorder in such different pictures as serious nutritional deficits, chronic alcoholism, transplanta-

Correspondence:
Nicolás Ramírez
Servicio de Psiquiatría
Hospital San Rafael
Paseo Valle Hebrón, 107-117
08025 Barcelona (Spain)
E-mail: 32698nrn@comb.es

tions, lung infections, hepatic disease, cerebrovascular lesions, serious burns or potomania has been described[5]. It has been associated with the presence of metabolic disorders, especially excessively rapid recovery from hyponatremia[6]. Its initial prognosis was considered fatal in all cases, however, with the introduction of neuroimaging, a growing number of cases with a better prognosis and even with total clinical and radiological recovery have been verified[7,8].

CLINICAL CASE

The case of a 22 year-old woman who came to the emergency service because of significant deterioration in her general condition as well as fever and cough in the last 24 h is presented. An eating disorder that began at age 16 stands out among her personal background. Since then, she has followed a restrictive and destructured eating regime in regards to time schedule and nutritional level as well as self-provoked vomiting. After each meal, she provokes vomiting through massive water intake, with several continuous vomiting episodes until «there was nothing left in her stomach». Her liquid intake sometimes reaches up to 8-9 liters a day. She also uses laxatives regularly. Psychopathologically, she has an intense fear of gaining weight and dissatisfaction with her body image. Her height is 166 cm and she has generally maintained her weight at about 40 kg during these years with a body mass index (BMI) close to 15. She has undergone frequent mood changes since the onset of the eating disorder. She smokes about 20 cigarettes/day and does not drink or consume addictive substances. A few months before her admission, her eating restriction behavior, water consumption and frequency of self-induced vomiting increased. External controls of her behavior were ineffective and she had lost 12 kg in 6 months, weighing 28 kg (BMI of 10.1) when admitted.

On admission, the patient had a severe condition of cachexia, with a tendency to somnolence and psychomotor retardation, was well oriented with no signs of meningism. She had mild mucose dryness, cough with expectoration, bilateral rhonchi, having a predominance on the anterior layers and isolated crackling rales in the left hemithorax. Normal heart sounds without heart failure or edemas. Psychopathologically, there was a certain level of anxiety, dysmorphophobia and fear of gaining weight. Vital signs showed blood pressure of 90/60 with heart rate of 72 and temperature of 38 ^{o}C (axillary). The main laboratory analysis data were: Hb: 15.3 g/dl; leukocytes: 1,500/mm^3; platelets: 54.000/mm^3; glucose: 78 mg/dl; urea: 26 mg/dl; creatinine: 0.7 mg/dl; sodium: 128 mmol/l; potassium: 2.8 mmol/l; calcium: 2.2 mmol/l; albumin: 4.5 g/dl; total bilirubin: 1.8 mg/dl; GPT: 177 U/l; GOT: 219 U/l; AP: 139 U/l; GGT: 28 U/l; LDH: 1.191 U/l; creatinkinase: 463 U/l; protrombin time: 62 %; fibrinogen: 479 mg/dl; pH: 7.54; pCO_2: 45.3 mmHg; bicarbonate: 38.2 mmol/l, and base excess 13.9 mmol/l. The chest X-ray showed an image of parahilium and right basal pneumonia.

The initial diagnosis was anorexia nervosa with severe cachexia, neutropenia, metabolic alkalosis, hypopotassemia and pneumonia. Treatment was initiated with antibiotics, peripheral parenteral nutrition at 1,000 kcal/day and 5 % glycosylated serum with 80 mEq/l of potassium chloride and 1,000 cc of 0.9 % saline solution the first 24 h. In the following 48 h, potassium supply was decreased to 40 mEq/l and at 72 h, electrolyte supply was stopped. At that time, the sodium and potassium concentrations in plasma were 131 mmol/l and 4.3 mmol/l, respectively.

After two weeks, normalization of the laboratory analysis alterations detected on admission was observed and the patient's infectious picture and general physical condition improved, with a 4 kg weight increase since her admission. From the psychiatric point of view, only a slight depressive mood, anxiety, asthenia, and conciliation insomnia stood out, but the patient had a good level of collaboration towards treatment and intake. Significant polyuria (5 to 6 l/day), possibly derived from excessive liquid intake, also stood out. At that time, the sudden appearance of an intense and fluctuating picture of bradypsychia, confusion and perplexity, lack of collaboration in the treatment and intake, short and coherent verbal responses and partially disorganized behavior appeared. She stated that she felt strange «as if she were dreaming», although no hallucinations or delusional ideas were observed. In the neurological examination, she had mydriatic although reactive pupils, without meningeal symptoms, mild symmetric hyperreflexia and at times, she had urinary and fecal incontinence, without other neurological symptoms. A MRI was done that showed slight global cortical atrophy and hyperintensive image in pons without other extrapontine lesions, suggestive of central pontine myelinolysis. The neurological picture improved in the first 48 h and completely disappeared in 10 days, although the same findings were found in the MRI repeated after one month. After being discharged to outpatient treatment of the eating disorder, her neurological condition was reevaluated at the end of one year, no neurological symptoms being found. A new MRI showed a slight decrease of the lesion in pons without other significant changes. A neuropsychological examination was conducted to detect cognitive functioning deficit that was totally normal. Regarding the eating disorder, behavior was more adequate, the self-induced vomiting episodes having decreased, without excessive intake of liquids, and the BMI was maintained at about 16.

DISCUSSION

CPM has been described in several disorders that occur with the metabolic alteration. Standing out among these are patients with an eating behavior disorder that are generally of long evolution, in whom there are generally episodes of bulimia or alterations in liquid intake, laxative and diuretic abuse or self-provoked vomiting that leads to hydroelectrolytic disorders, among them hyponatremia,

hypopotassemia or hypokalemia[9,10]. These ion disorders have been associated with the demyelinating process[11]. Other alterations in the laboratory analyses generally observed in eating disorders are elevated serum concentrations of CO_2, calcium, alanine transaminase, cholesterol, and decreased concentrations of potassium, chloride and phosphate[12]. In any event, the onset of symptoms suggestive of CPM has coincided with an excessively rapid correction of serum sodium[13]. However, although it has been suggested that an increase of plasma sodium less than 10 mml/l/24 h is associated with low risk of the appearance of CPM, there does not seem to be a direct relationship between sodium concentration or its plasma recovery and the risk of CPM[14]. In fact, the appearance of CPM with normal concentrations of serum sodium or with a correction rhythm of the adequate hyponatremia seems to confirm this hypothesis[8,15]. In postmortem studies conducted in 20 patients with severe symptomatic hyponatremia and a clinical picture suggestive of CPM, Tien et al.[16] observed the presence of diffuse cerebral demyelination, possibly consistent with hypoxic damage, while only a minority of the patients had a lesion in the pons. In every case, it is recommended to keep sodium concentrations below 135 in the first 48 h and to avoid hypernatremia[17].

Up to a few years ago, the prognosis of CPM was considered to be serious in every case with irreversible symptom consequences. The diagnosis of CPM was essentially derived from the clinical symptoms, the serious cases or those whose course could be more negative standing out more. This prognosis has been varying in the last decades due to the developing of neuroimaging techniques that allow for a more reliable and rapid detection of the specific lesions of CPM. Confirmation diagnosis of CPM is made through neuroimaging findings, although these also lack a well-defined prognostic value. Thus, it has been observed that the size of the lesion in the pons does not correlate with the seriousness of the neurological disorders or the clinical picture course of CPM[7]. Furthermore, in the initial phases, it is possible that no lesions will appear in the neuroimaging. Thus, when CPM is suspected, neuroimaging should be repeated after a few weeks[2]. Menger and Jörg[18] made a review of 44 patients with CPM, 32 of whom totally or almost totally recovered from the neurological symptoms in spite of the persistence of lesions in the pons. Lilje et al[19] describe a patient with anorexia nervosa and alcohol abuse in a stage of cachexia complicated by a respiratory infectious conduction who developed an acute picture of CPM confirmed by neuroimaging. It was verified that the visual, acoustic and motor evoked potentials as well as the functioning of the corticospinal and corticonuclear tracts were within normality. There was total recovery after 18 months, the CPM disappearing from the X-ray image. Other authors have also observed complete disappearance of the MRI lesions a few months after diagnosing CPM without previous hyponatremia[8].

Another case of anorexia nervosa described with rapid correction of hyponatremia and hypocalcemia derived from aqueous intoxication due to polydipsia that caused MRI confirmed CPM was characterized by an acute confusional episode with affective lability and incoherence but without serious neurological symptoms[20]. In this case, recovery of the psychiatric and neurological symptoms was also total, although the pathological images in the MRI remained at 6 weeks. The symptoms typically described in CPM are spastic tetraparesis, pseudobulbar paralysis and coma, although other lesser neurological symptoms may appear, such as deficits in attention and concentration, short term memory and consolidation, learning capacity and tremor at rest[3]. The most frequently mentioned psychiatric signs in CPM are awareness level and cognitive function alterations although disorders in behavior having a longer-term course have also been described and may be due to corticobulbar lesions[3]. These psychiatric symptoms may be similar to the presence of a delirium picture and be clearer than the neurological symptoms. Thus, the clinical picture that is generally observed may be due to an acute water intoxication condition or hydroelectrolytic metabolism disorder than to the specific lesion in the CNS that characterizes CPM. Changes in awareness level could be attributed to a lesion in the pons due to hyponatremia or to a rapid increase in sodium concentrations. This would explain the remission of the clinical symptoms while the neuroimaging lesions remain. Better knowledge of the CPM pathophysiology would make it possible to define not only the prognosis but also especially its treatment more accurately.

CONCLUSION

CPM is a disease that may appear in patients with eating behavior disorder, probably derived from hydroelectrolytic and metabolic disorders that are caused by the malnutrition condition, frequent induction of vomiting, abuse of laxatives or diuretics and potomania behavior characteristic of these patients. The possible appearance of this complication, especially when there is rapid correction of the hydroelectrolytic disorders such as hyponatremia, must be taken into account.

Prognosis when CPM demonstrated with neuroimaging exists does not seem to be as fatal as previously thought in all the cases. In order to establish prognosis with greater certainty, a follow-up of the evolution of the clinical symptoms and of the neuroimaging should be done during the first months, as a dissociation between the seriousness of both is frequently found.

REFERENCES

1. Adams RD, Victor M, Mancall EL. Central pontine myelinolysis: a hitherto undescribed disease occurring in alcoholic and malnourished patients. Arch Neurol Psychiatry 1959;81:154-72.
2. Kumar SR, Mone AP, Gray LC, Troost BT. Central pontine myelinolysis: delayed changes on neuroimaging. J Neuroimag 2000; 10:169-72.

3. Vermetten E, Rutten SJ, Boon PJ, Hofman PA, Leentjens AF. Neuropsychiatric and neuropsychological manifestations of central pontine myelinolysis. Gen Hosp Psychiatry 1999;21:296-302.
4. Brunner JE, Redmond JM, Haggar AM. Central pontine myelinolysis after rapid correction of hyponatremia: a magnetic resonance imaging study. Ann Neurol 1988;23:389-91.
5. McColl P, Kelly C. A misleading case of central pontine myelinolysis: risk factors for psychiatric patients. Br J Psychiatry 1992; 160:550-2.
6. Sterns RH, Riggs JE, Schochet SS. Osmotic demyelination syndrome following correction of hyponatremia. N Eng J Med 1986; 314:1535-42.
7. Laubenberger J, Scheneider B, Ansorge O, Götz F, Häussinger D, Volk B, et al. Central pontine myelinolysis: clinical presentation and radiologic findings. Eur Radiol 1996;6:177-83.
8. Killinç M, Benli US, Can U. Osmotic myelinolysis in a normonatremic patient. Acta Neurol Belg 2002;102:87-9.
9. Greenberg WM. Anorexia nervosa/bulimia and central pontine myelinolysis. Gen Hosp Psychiatry 1992;14:357-8.
10. Sugimoto T, Murata T, Omori M, Wada Y. Central pontine myelinolysis associated with hypokalemia in anorexia nervosa. J Neurol Neurosurg Psychiatry 2003;74:353-5.
11. Lohr JW. Osmotic demyelination syndrome following correction of hyponatremia: association with hypokalemia. Am J Med 1994;96:408-13.
12. Mira M, Stewart PM, Abraham S. Hormonal and biochemical abnormalities in women suffering from eating disorders. Pediatrician 1983;12:148-56.
13. Copeland PM. Diuretic abuse and central pontine myelinolysis. Psychoter Psychosom 1989;52:101-5.
14. Kelly J, Wassif W, Mitchard J, Gardner WN. Severe hyponatremia secondary to beer potomania complicated by central pontine myelinolysis. Int J Clin Pract 1998;52:585-7.
15. Karp BI, Laureano R. Pontine and extrapontine myelinolysis: a neurologic disorder following rapid correction of hyponatremia. Medicine 1993;72:359-73.
16. Tien R, Arieff AI, Kucharczyk W, Wasik A, Kucharczyk J. Hyponatremic encephalopathy: is central pontine myelinolysis a component? Am J Med 1992;92:513-22.
17. Ayus JC, Krothapalli R, Arieff AI. Treatment of symptomatic hyponatremia and its relation to brain damage: a prospective study. N Eng J Med 1987;317:1190-5.
18. Menger H, Jörg J. Outcome of central pontine and extrapontine myelinolysis. J Neurol 1999;246:700-5.
19. Lilje CG, Heinen F, Laubenberberg J, Krug I, Brandis M. Benign course of central pontine myelinolysis in a patient with anorexia nervosa. Pediat Neurol 2002;27:132-5.
20. Amann B, Schäfer M, Sterr A, Arnold S, Grunze H. Central pontine myelinolysis in a patient with anorexia nervosa. Int J Eat Disord 2001;30:462-6.