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Osmotic Demyelinating Syndrome

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ABSTRACT This article discusses the clinical cases of rare and difficult to diagnose brain damage — osmotic demyelinating syndrome (ODS). ODS is a life-threatening condition, manifested by acute demyelination of the headbrain on the background of water-electrolyte disturbances,usually associated with fast management of hyponatremia. Within the framework of ODS, central pontine myelinolysis (CPM) and extra-pontine myelinolysis (EPM) are observed, which are accompanied by acute demyelination in the pons and white matter of the cerebral hemispheres, respectively. In 60%, CPM combine with EPM. The main reason for the development of ODS is a violation of water-electrolyte metabolism associated with alcohol abuse, chronic hepatic and/or renal failure, diabetes mellitus, Sheehan syndrome, polydipsia, condition after the removal of pituitary adenoma, bulimia, immunodeficiency syndrome. Today, the diagnosis of ODS is based on magnetic resonance imaging of the brain. The article indicates the main causes of the disease, clinical features, methods of diagnosis and treatment, as well as the outcomes of the disease.

Keywords: central pontine myelinolysis, extrapontine myelinolysis, osmotic demyelinating syndrome
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ALV — artificial lung ventilation
CT — computed tomography
CPM — central pontine myelinolysis
DWI — diffusion-weighted image
EPM — extrapontine myelinolysis
GCS — Glasgow Coma Scale
MRI — magnetic resonance imaging
ODS — osmotic demyelinating syndrome
WI — weighted images

INTRODUCTION

Osmotic demyelinating syndrome (ODS) is a life-threatening condition manifested by acute demyelination of the brain against the background of water-electrolyte disturbances, usually associated with rapid correction of hyponatremia [1, 2]. This condition was first described by R. Adams et al. in 1959 in patients with alcoholism and malnutrition [3]. Currently, central pontine myelinolysis (CPM) and extrapontine myelinolysis (EPM), which are accompanied by acute demyelination in the area of the pons and white matter of the cerebral hemispheres, are distinguished within the ODS, respectively. In 60% ODS combines CPM and EPM.

The main reason for the development of ODS is disorders of water and electrolyte metabolism that occur due to alcohol abuse, chronic liver and/or renal failure, diabetes mellitus, Sheehan's syndrome, polydipsia, conditions after removal of the pituitary adenoma, bulimia, and immunodeficiency syndrome [3–7].

In 1994 Rojiani et al. found that sodium deficiency leads to intracellular cerebral edema [7]. The development of ODS is based on intracellular edema of cerebral tissue, which occurs during the rapid replenishment of sodium deficiency, which passes into the extracellular space and leads to the death of neuroglial cells and destruction of myelin [1, 4].

Clinical manifestations of ODS are intermittent. Thus, CPM is characterized by clinical improvement after rapid correction of hyponatremia, followed by the development of a neurological picture of acute myelinolysis in a few days, manifested by impaired swallowing, tetraparesis, oculomotor disorders, ataxia, depression of the level of consciousness to coma, or the development of the locked-in syndrome [8-10].

Currently, the diagnosis of ODS is based on the data of magnetic resonance imaging (MRI) of the brain. In CPM, early changes such as hyperintense signal are detected in the diffusion-weighted imaging (DWI) mode in the lower pons within 24 hours from the onset of clinical symptoms [11]. In the same area, an increase in the signal intensity on T2-FLAIR images is noted, which corresponds to a low signal in T1-weighted images (WI). The appearance of characteristic changes on T1 and T2-WI can take up to two weeks from the clinical onset of the disease. The area of increased signal on T2 and T2-FLAIR images can have the form of a “trident” [12-15] (Fig. 1B) or a “snout” [16] (Fig. 2A). EPM is characterized by the appearance of symmetric areas of hyperintense signal on T2 and T2-FLAIR images in the area of the ventrolateral nuclei of the thalamus, basal ganglia, caudate nucleus, internal capsule, at the border of the gray and white matter of the brain, less often the corpus callosum [17].

Currently, there is no specific treatment for ODS [1, 4]. However, early diagnosis of this condition is extremely important due to the high incidence of respiratory disorders and the need for artificial lung ventilation (ALV).

Hyponatremia is a decrease in serum sodium levels below 135 mmol/L. Hyponatremia is considered acute if it develops less than within 48 hours. According to the Clinical Practice Guideline on Diagnosis and Treatment of Hyponatraemia, developed jointly by the European Society of Intensive Care Medicine (ESICM), the European Society of Endocrinology (ESE) and the European Association of Nephrologists (ERA-EDTA), an algorithm for the relief of acute sodium deficiency is as follows:

1. In a hospital within the first hour after diagnosing sodium deficiency, 150 ml of 3% sodium chloride solution or its equivalent should be administered intravenously within 20 minutes. After 20 minutes, it is necessary to check the sodium level and, if necessary, re-enter the same amount of 3% sodium chloride solution within 20 minutes. Repeated injections of 3% sodium chloride solution should be continued until the blood sodium level increases by 5 mmol/L.

2. When the sodium level rises by 5 mmol/L within an hour, it is necessary to stop the administration of a 3% sodium chloride solution and continue the intravenous administration of a small volume of 0.9% sodium chloride solution until the beginning of etiotropic treatment. The sodium level should not be increased by more than 10 mmol/L on the first day and by more than 8 mmol/L on each subsequent day, until the sodium level reaches 130 mmol/L. The sodium level should be monitored every 6 hours daily until it stabilizes.

3. If the symptoms of hyponatremia persist after a rise in the level of sodium in the blood serum by 5 mmol/L for an hour, in order to increase its level by another 1 mmol/L per hour, it is necessary to continue the intravenous administration of a 3% sodium chloride solution. After regression of clinical signs: if the blood sodium level rises by 10 mmol/L or when the sodium level reaches 130 mmol/L, the administration of sodium chloride solution should be stopped. It is necessary to exclude another pathology similar to the clinic with hyponatremia. It is recommended to monitor the serum sodium level every 4 hours during the infusion of 3% sodium chloride solution or its equivalent.

4. Patients with a low volume of circulating blood need the introduction of 0.9% sodium chloride solution or balanced crystalloid saline solution at a dose of 0.5–1.0 ml/kg/h. In patients with unstable hemodynamics, the effectiveness of the performed rehydration is higher than the risk of a possible rapid correction of the sodium level.

In the case of excessively rapid replenishment of sodium deficiency when it increases by more than 10 mmol/L in the first day or by more than 8 mmol/L for every next 24 hours, its level should be reduced by intravenous administration of 5% glucose solution at the rate of 10 ml per 1 kg of body weight for 1 hour with careful monitoring of urine output. Intravenous administration of 2 mg of desmopressin is possible, but not more often than once in 8 hours [18].

The purpose of this article is to increase the awareness of doctors of multidisciplinary hospitals about the clinical manifestations and methods of diagnosing ODS, as well as ways to prevent it.

MATERIAL AND METHODS

From January 2015 to January 2019 at the N.V. Sklifosovsky Research Institute for Emergency Medicine, 4 cases of ODS were registered. The examined patients included 3 women (80%) and one man (20%) aged 36 to 63 years (mean age 44.5 ± 12.5 years).

RESULTS

Clinical example 1

A 38-year-old female patient A. was admitted to the intensive care unit for emergency patients with a diagnosis of "Unspecified coma". From the anamnesis of the disease, collected from the words of relatives, it is known that within 10 days before hospitalization, the patient noted repeated vomiting. Due to severe dehydration, the patient received massive intravenous infusion therapy at home - up to 4 liters of crystalloid solutions per day. The day before hospitalization, the patient had an episode of psychomotor agitation, which was managed by phenobarbital. The next day, the patient was found unconscious by relatives. Upon admission in a neurological status, a decrease in the level of consciousness to deep stupor, on the Glasgow coma scale (GCS) score 11, psychomotor agitation, oculomotor disorders (divergent squint), spastic tetraparesis (muscle strength 1 point). Spontaneous breathing, blood pressure (BP) 100/70 mm Hg, heart rate (HR) 98 beats/min. Given the psychomotor agitation and the need for sedative therapy, the patient underwent tracheal intubation and artificial respiration was initiated. Barbiturates were found in the patient's biological media. Blood tests: leukocytosis (21.5 x 10^9/L), hyponatremia (114.0 mmol/L), hypokalemia (2.4 mmol/L), hypochloremia (76.2 mmol/L), hypoproteinemia (30.9 g/L), hypoalbuminemia (15.7 g/L), hyperglycemia (11.19 mmol/L). Computed tomography (CT) of the brain did not reveal areas of abnormal X-ray density. Analysis of cerebrospinal fluid showed an increase in the level of lactate in it to 4.8 mmol/L with a normal cellular composition (5 cells). On the 5th day, bilateral lower lobe pneumonia and bilateral hydrothorax developed, leukocytosis remained in the clinical blood test (17.4 x 10^9/L), sodium within normal limits (133.3 mmol/L), hypoalbuminemia (19.5 g/L). On the 7th day, the patient underwent lower puncture dilatation tracheostomy. Considering the anamnestic information about massive infusion therapy with crystalloid solutions at the prehospital stage, hyponatremia upon admission to 114.0 mmol/L, as well as clinical manifestations in the form of a decrease in the level of consciousness to deep stupor, oculomotor disorders (divergent squint), spastic tetraparesis, ODS was suspected. In order to verify the diagnosis, MRI of the brain was indicated, which revealed changes characteristic of the CPM - a high signal zone was revealed on T2-FLAIR and DWI in the area of the cerebral pons (Fig. 1).

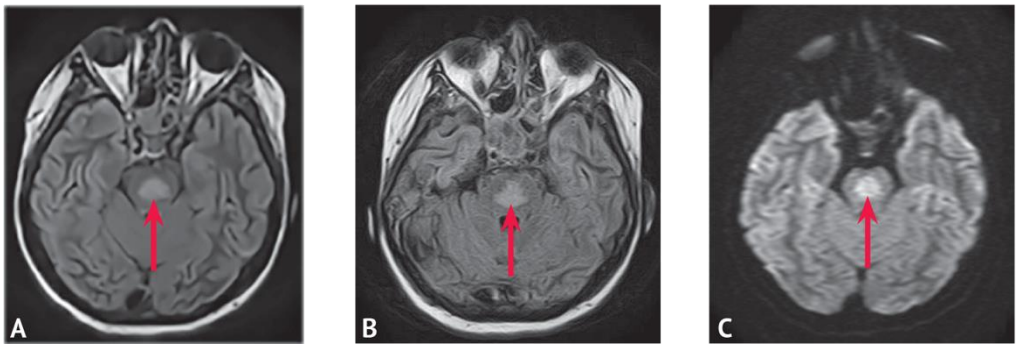

Fig. 1. Magnetic resonance imaging of the brain in patient A. T2-FLAIR, axial sections: A — the arrow indicates the high signal area in the area of the brain pons, B — the region of the increased signal in the form of a «trident» characteristic of the CPM is indicated, C — DWI, axial section, the arrow indicates the high signal in the area of the brain pons

Clinical example 2

A 41 year-old-female patient I. was admitted to the Research Institute for Emergency Medicine with a diagnosis: "Rupture of the mucous membrane of the cardiac section of the stomach (Mallory-Weiss syndrome), fractures of the V, VII ribs on the right, IX-XII ribs on the left of unspecified date, bilateral pneumothorax, pneumomediastinum, soft tissue emphysema of the chest wall and neck ". On the day of hospitalization, the sodium level was within the normal range (135 mmol/L), hypokalemia (2.8 mmol/L) was noted. The patient underwent urgent surgical intervention: laparotomy, diaphragmotomy, fundoplication, splenectomy, suturing of the esophageal defect, gastrostomy, mediastinal drainage. In the early postoperative period, the patient was on a ventilator. During the first days after surgery, she was extubated and transferred to independent breathing. On the 2nd day, psychomotor agitation, visual and auditory hallucinations developed. Considering the need for sedative therapy, the patient underwent repeated tracheal intubation and was put on a ventilator. On the 3rd day of hospitalization, an increase in body temperature up to 39°C was noted, a depression of the level of consciousness to moderate coma (GCS score 6). The neurological status revealed anisocoria, ophthalmoplegia, meningeal syndrome, spastic tetraplegia. Lab tests: hypernatremia (178 mmol/L). No abnormalities were revealed on CT of the brain. There were no specific changes in the cerebrospinal fluid either. On the 10th day, a lower tracheostomy was performed. Considering the rapid increase in the level of sodium in the blood from 135 mmol/L upon admission to 178 mmol/L on the 3rd day of inpatient treatment, the clinical picture (depression of the level of consciousness to moderate coma, oculomotor disorders, spastic tetraplegia), ODS was suspected. In order to verify the diagnosis, MRI of the brain was performed, which showed changes specific to the CPM and EPM - symmetric zones of increased signal intensity on T2-FLAIR and DWI were revealed in the middle cerebellar peduncles, cerebellar peduncles and the inner capsule (Fig. 2).

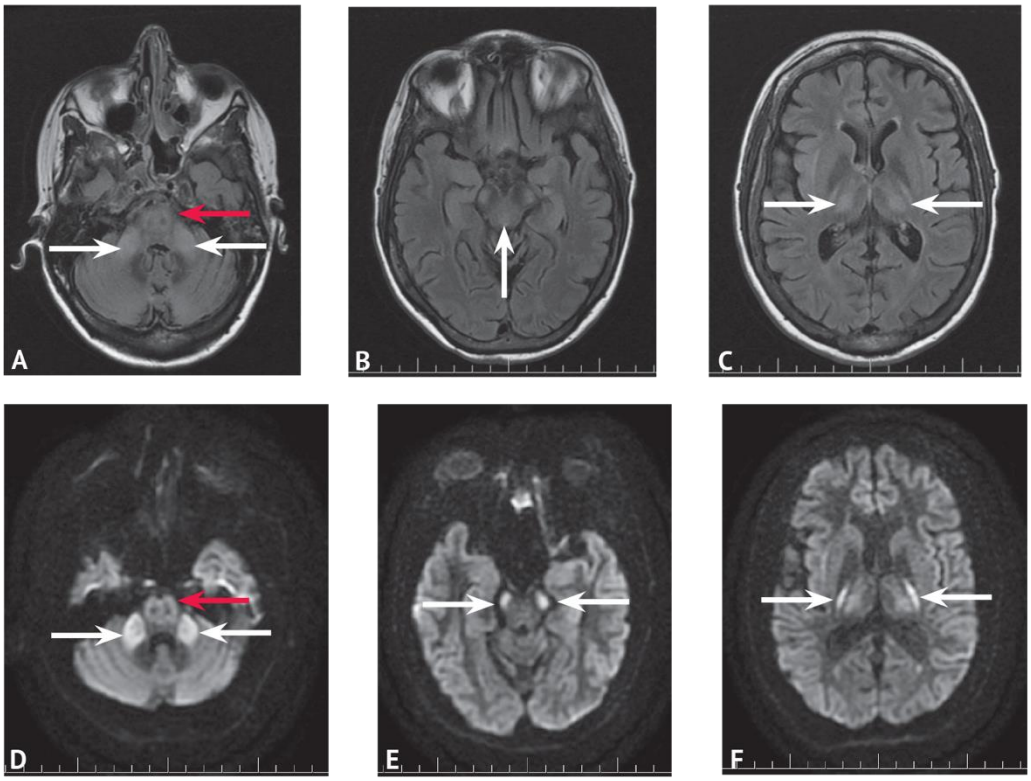

Fig. 2. Magnetic resonance imaging of the brain in patient I. T2-FLAIR, axial sections: A — red arrow indicates the characteristic of the CPM region of altered MR signal — «swine snout» symptom, white arrows show symmetric zones of high signal in the middle cerebellar peduncles (EPM); B — area of increased signal in the area of the brain pons (CPM) is noted; C — arrows show high signal areas in the symmetrical parts of the inner capsule's, specific for EPM. DWI, axial sections: D — red arrow indicate the characteristic of the CPM region of increased signal in the form of «snout», white arrows show symmetrical high signal in the middle cerebellar peduncles (EPM); E — arrows show symmetric zones of high signal in brain peduncles (EPM); F — arrows indicate areas of high signal in the symmetrical parts of the internal capsule specific for EPM

Given the absence of pathogenetic therapy, the patient underwent prophylaxis of venous thrombotic and trophic complications, symptomatic, infusion and antibacterial therapy. In the course of the correction of hypernatremia (Fig. 3) on the 11th day, there was a positive trend such as an increase in the level of consciousness to sopor (GCS score 8.)

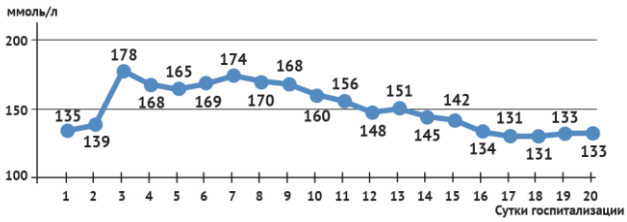

Fig. 3. The dynamics of the concentration of sodium in the blood (mmol/l)

On the 32nd day, in the course of intensive therapy and stabilization of the sodium level in the blood (133–139 mmol/L) - restoration of the level of consciousness to mild stupor (GCS score 14), complete regression of meningeal syndrome, anisocoria and partial regression of oculomotor disorders. On the 42nd day there was clear consciousness (GCS score 15), the patient lay with her eyes open, trying to follow the examination, didn't follow the instructions; sodium level within normal limits (136 mmol/L). On the 62nd day after "respiratory training", she was transferred to spontaneous breathing through a tracheostomy tube. Due to the low rehabilitation potential (gross cognitive deficit and spastic tetraplegia), on the 63rd day of hospitalization, the patient was discharged to the palliative care center.

Clinical case 3

A 63 year-old female patient S. was hospitalized with a diagnosis of "Closed pertrochanteric-subtrochanteric fracture of the right femur with displacement of fragments." On the 2nd day of inpatient treatment, acute disorientation in time and place developed, which was accompanied by psychomotor agitation. CT scan of the brain revealed no pathology. Upon admission, the level of sodium in the blood was 132.7 mmol/L, potassium - 3.29 mmol/L. On the second day, the patient had hyponatremia (121 mmol/L) and hypokalaemia (2.2 mmol/L). Despite the lack of data for the rapid correction of hyponatremia, MRI of the brain revealed changes specific to the CPM and EPM - an increase in the signal on T2 and T2-FLAIR images in the left regions of the medulla oblongata, in the region of the pons and pedicles, as well as in the white matter of the cerebellar hemispheres (Fig. 4).

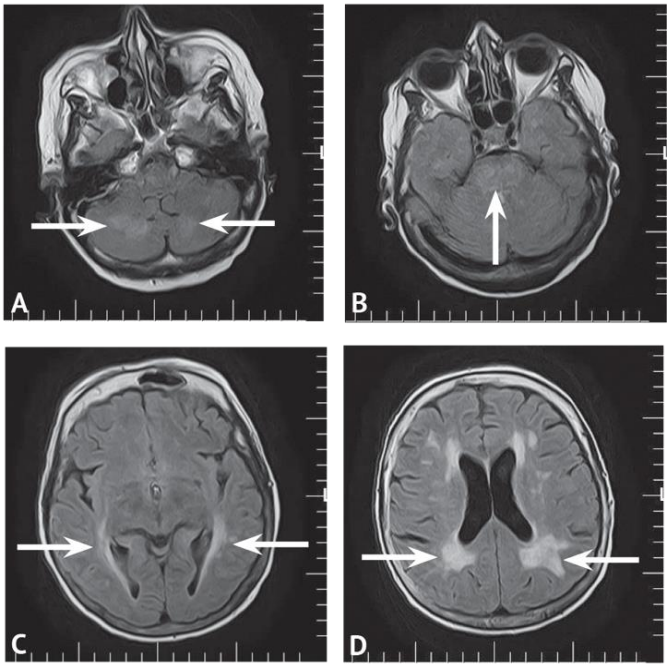

Fig. 4. Magnetic resonance imaging of the brain in patient C. T2-FLAIR, axial sections: A — arrows indicate areas of increased signal in the white matter of the cerebellar hemispheres, specific for EPM; B — the arrow shows the high signal area in the brain pons (CPM); C, D — designated areas of high signal in the brain peduncles (EPM)

Based on the data of MRI of the brain, clinical presentation (disorientation, psychomotor agitation), hyponatremia up to 121.0 mmol/L, the diagnosis of ODS was made. Given the absence of pathogenetic therapy, the patient underwent prevention of thrombotic and trophic lesions of the veins, symptomatic, infusion therapy. On the 3rd day of hospitalization, the patient showed positive dynamics: the patient was oriented to person, place and time. Lab tests: an increase in the level of sodium (135 mmol/L) and potassium (2.9 mmol/L). On the 4th day, the patient underwent osteosynthesis of the right femur. On the 10th day, the patient was discharged without neurological symptoms for the next stage of rehabilitation.

Clinical case 4

A 36-year-old male patient R. was transferred to the intensive care unit of the Center for the Treatment of Acute Poisoning of the N.V. Sklifosovsky Research Institute with a diagnosis of "Ethylene glycol poisoning, coma, complicated by mixed breathing disorders" from another hospital, where he was taken 7 hours ago in a coma (GCS score 8). Ethylene glycol was found in the patient's biological media. Upon admission to the Institute, the consciousness was depressed to a deep coma (GCS score 4), focal neurological symptoms were not revealed. In the clinical analysis of blood, leukocytosis was noted (20.5 x 10^9/L), in the biochemical analysis of blood, no abnormalities were found (sodium 142.8 mmol/L, potassium 4.36 mmol/L). In the course of the therapy, on the 5th day, the patient had clear consciousness, inhibited, there were no focal neurological symptoms. On the 6th day of hospitalization, the patient underwent lower puncture-dilatation tracheostomy. On the 58th day, intense headache developed. Neurological status: clear consciousness (GCS score 15), simple instructions were followed, there were positive meningeal syndrome and reflexes of oral automatism. Analysis of cerebrospinal fluid revealed an increase in cellular composition (9 cells per μL), erythrocytes (1000 in 1 μL), lactate levels (25 mmol/L), glucose (11.9 mmol/L) and protein (0.3 g/L) no signs of xanthochromia. MRI of the brain revealed CPM-specific changes: hyperintense signal on T2-FLAIR and DWI in the pons, which corresponded to hypointense signal on T1-WI (Fig. 5).

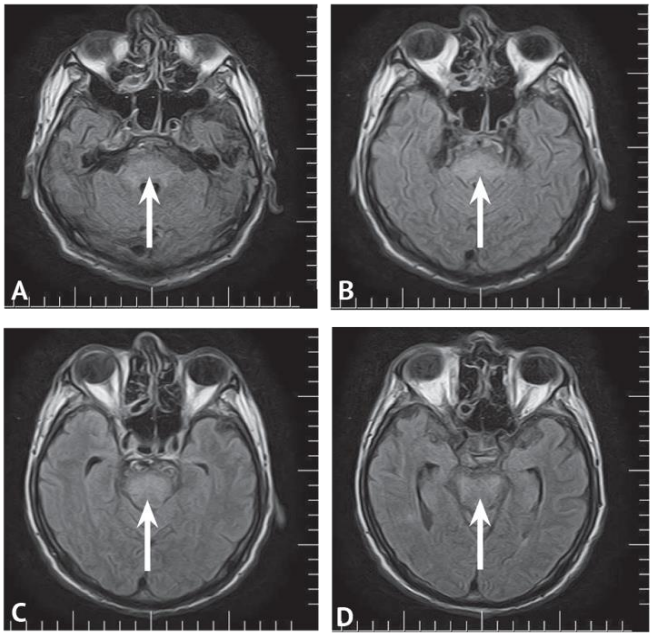

Fig. 5. Magnetic resonance Tomo graphy patient brain P . On MRI of the brain, specific signs of CPM were revealed. A–D – T2-FLAIR, axial sections, arrows indicate high signal areas in the area of the brain bridge

During inpatient treatment, the sodium level was within 124.6-143.9 mmol/L, potassium 2.73-4.36 mmol/L. Due to the absence of pathogenetic therapy for ODS, the patient underwent prophylaxis of thrombotic and trophic lesions of the veins, symptomatic, and infusion therapy. On the 73rd day, against the background of purulent-septic complications, the patient's condition had negative dynamics: depression of the level of consciousness to a shallow coma (GCS score 7), followed by hemodynamic instability, arterial hypotension, cardiac arrest and biological death.

DISCUSSION

Osmotic demyelinating syndrome is a life-threatening condition in which the immediate cause of neurological symptoms is edema of the trunk and/or white matter of the cerebral hemispheres and/or cerebellum. In most patients with ODS disorders of consciousness and breathing develop that require mechanical ventilation. Despite the absence of pathogenetic treatment for this condition, urgent diagnosis helps avoid the development of aspiration syndrome associated with disorders of consciousness and breathing. To make a diagnosis, a thorough analysis of anamnestic information, radiological picture and laboratory diagnostic methods is required, which avoids overdiagnosis of acute disorders of cerebral circulation. It should be remembered that a patient with ODS is a patient with limited mobility, therefore, measures are needed to prevent thrombotic complications. In our series of observations, we encountered ODS due to the rapid correction of hyponatremia, as well as caused by both direct toxic and mediated hyperosmolar effects of ethylene glycol. Early diagnosis and timely initiation of mechanical ventilation is the only correct decision if this disease is suspected.

CONCLUSION

In our series of observations, it was once again shown that the acute onset of cerebral and/or focal neurological symptoms is characteristic not only of acute disorders of cerebral circulation. The characteristic magnetic resonance imaging features of osmotic demyelinating syndrome are an increase in signal intensity on diffusely weighted images and T2-FLAIR, which manifest as "trident" and "snout" symptoms. The main clinical signs that suggest osmotic demyelinating syndrome are oculomotor disorders, dysphagia, tetraparesis, and impaired consciousness. The rate of correction of hyponatremia by no more than 10 mmol per day is the main method for preventing the development of osmotic demyelinating syndrome.

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