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Review Article

Central pontine and extrapontine myelinolysis

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ABSTRACT

Central pontine myelinolysis (CPM) was described by Adams and colleagues in 1959 as a disease affecting alcoholics and the malnourished. Also known as osmotic demyelination syndrome (ODS), PM (Pontine Myelinosis) is subdivided into central pontine myelinolysis (CPM) and extrapontine myelinolysis (EPM). Each is identified at the level of demyelination, either centered within the pons or outside the pons, respectively. Despite its relatively ambiguous pathogenesis, it is believed that rapid correction of hyponatremia plays a pivotal role in pathogenesis of ODS. Whenever a patient who is gravely ill with alcoholism and malnutrition or a systemic medical disease develops confusion, quadriplegia, pseudobulbar palsy, and pseudocoma (locked-in syndrome) over a period of several days, one is supposed to have a high index of suspicion for central pontine myelinolysis.

1. Introduction

Central pontine myelinolysis (CPM) was described by Adams and colleagues in 1959 as a disease affecting alcoholics and the malnourished.[1] The original paper described four cases with fatal outcomes, and the findings on autopsy. The etiology was not known then but the authors suspected the cause to be either a toxin or a nutritional deficiency. 'Central pontine' indicated the site of the lesion and 'myelinolysis' was used to emphasize that myelin was affected preferentially compared to the other neuronal elements. The authors intentionally avoided the term 'demyelination' to describe the condition, in order to differentiate the pathology of this condition from multiple sclerosis and other neuroinflammatory disorders in which myelin loss is associated with inflammation. In 1983, Laureno et al. suggested rapid correction of hyponatremia as the cause for the condition, based on experimental data on animal models. They suggested that the condition could be prevented by correcting hyponatremia by less than 10 mmol/L in 24 h.[2] Also known as osmotic demyelination syndrome (ODS), PM (Pontine Myelinosis) is subdivided into central pontine myelinolysis (CPM) and extrapontine myelinolysis (EPM).[3] Each is identified at the level of demyelination either centered within the pons[1] or outside the pons,[4] respectively.

2. Epidemiology

Various case reports of ODS have been published from time to time with few case series out of which the largest being studied is the one in 58 patients.[5] Though the exact incidence of ODS is

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not known, an autopsy-based study documented a prevalence rate of 0.25–0.5% in the general population[6] and 10% in patients undergoing liver transplantation.[6,7] True incidence of ODS is unknown until date. In a study of 3000 brains examined postmortem, there were 15 cases of asymptomatic central pontine myelinolysis (CPM).[8] In a recent Indian study on Osmotic demyelination syndrome in Intensive Care Unit by Rao et al., they found an ODS incidence of 2.5% over 5 years. Altered sensorium was found to be the most common symptom and hypokalemia as the most common underlying associated factor. MRI findings revealed isolated pontine involvement in 41%, and both pontine and extrapontine involvement in 23% of the cases. All the patients received supportive therapy; of these 17 patients, complete neurological recovery occurred in 24% of the patients.[9]

3. Etiology and pathogenesis

Despite its relatively ambiguous pathogenesis, it is believed that rapid correction of hyponatremia plays a pivotal role in pathogenesis of ODS.[7] Wadhwa et al. identified a case where an alcoholic patient showed signs of EPM.[10] Uchida et al. explains where a patient develops CPM secondary to liver transplant.[11] According to Wu et al., EPM can arise from primary adrenal insufficiency. This author described a 49-year-old female who presented with primary adrenal insufficiency. The patient was given an isotonic saline solution to treat for adrenal insufficiency and hyponatremia. Rapid correction showed demyelination of the bilateral basal ganglia and the thalamus, using MRI.[12] CPM can also be a rare manifestation of Wilson's disease[13] and celiac disease.[14]

Hyponatremia causes glial cells to swell via selective aquaporin channels.[15] Treatment of chronic hyponatremia, using a hypertonic saline solution, causes brain cell dehydration and the loss of vital electrolytes, in addition to organic osmolytes such as myo-inositol, taurine, glutamine, glutamate, creatine, and glycerophosphorylcholine.[16] Failure to compensate for increasing plasma tonicity within cells results in osmotic stress.[17] According to studies by Rojiani et al.,[18,19] the opening of the blood–brain barrier (BBB) and the generation of edema may play a role in the early stages of the disease. Stress on the BBB as a result of osmotic shrinkage results in the opening of tight junctions ultimately leading to demyelination and apoptosis of cells (Figs. 1 and 2).[20,21]

Some authors have emphasized the role of hypoxia in the pathogenesis of brain damage associated with hyponatremia, including the demyelinating brain lesions.[22] The genesis of this theory can be traced to a case series that included seven women who exhibited a biphasic neurologic course, typical of osmotic demyelination, following hyponatremic seizures.[23]

4. Clinical features

The patient usual presents with a biphasic clinical course, initially with encephalopathy or presenting with seizures from hyponatremia, then recovering rapidly as normonatremia is restored, only to deteriorate several days later. The initial signs of CPM, which reflect this second phase, include dysarthria and dysphagia (secondary to corticobulbar fiber involvement), as well as flaccid quadriparesis (from corticospinal tract involvement), which later becomes spastic, all from involvement of the basis pontis; if the lesion extends into the tegmentum of the pons pupillary, oculomotor abnormalities may occur. An apparent change in level of consciousness reflects the 'locked-in syndrome,' that a large lesion in this site is particularly liable to produce. If lesions of EPM are also present, the clinical picture may be very confusing, as added to

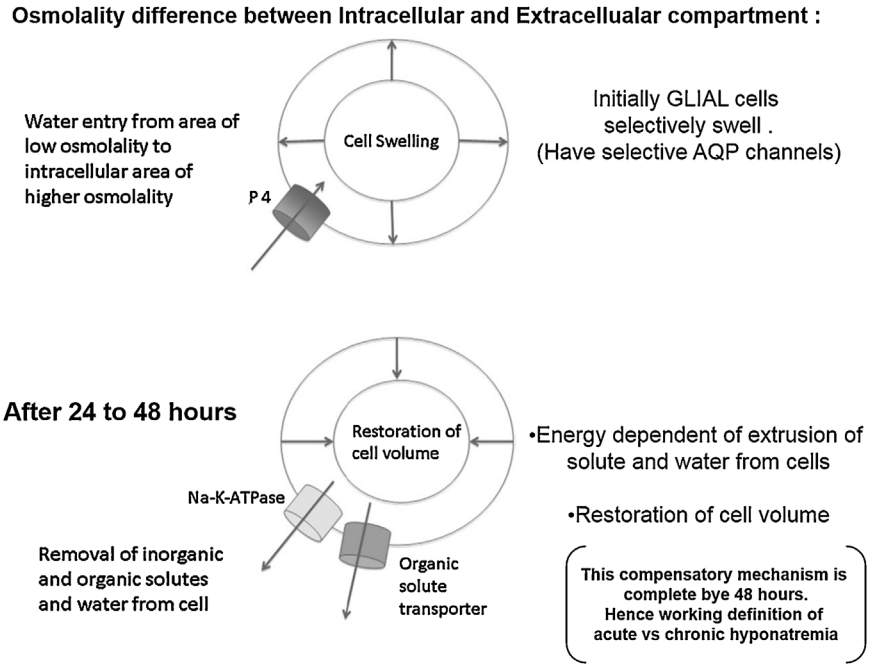

Fig. 1 – Restoration of cell volume in the setting of hyponatremia.[21]