Case report

Resolution of clinical and MRI abnormalities in osmotic demyelination syndrome – do corticosteroids have a potentially beneficial therapeutic effect?

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Introduction

Central pontine myelinolysis (CPM) is a rare neurological disorder defined by osmotic demyelination of the central base of the pons and extra pontine areas of the central nervous system (CNS). The most common underlying causes are chronic alcoholism and rapid correction of hyponatremia[1]. CPM has a poor prognosis and there is no specific therapy of choice. We report here a patient with CPM who improved rapidly and showed complete resolution of MRI changes following corticosteroid therapy.

Case Report

A 42-year old, previously healthy male was admitted with a history of being found collapsed at home. He was living alone and had a history of chronic alcohol use. He was drowsy, confused and disoriented on admission. There were no focal neurological signs. He subsequently developed 2 episodes of witnessed generalised tonic-clonic seizures. Seizures were controlled with phenytoin therapy with no further recurrences. However, he continued to remain drowsy.

Initial laboratory investigations revealed a hyponatraemia due to SIADH (serum sodium 124 mmol/l, serum osmolality 236 mosm/l and urine osmolality 424 mosm/l). Blood counts, C-reactive protein, renal and thyroid functions and chest radiograph were normal. Serum transaminases and ammonia levels were normal. Computed Tomography (CT) scan of the brain showed effacement of sulci suggestive of cerebral oedema. Electroencephalograph revealed polyrhythmic generalised theta wave activity. He was treated with IV Ceftriaxone, IV Acyclovir and IV Dexamethazone on the suspicion of a possible underlying meningo-encephalitis. Hyponatraemia was managed with fluid restriction and oral salt and he also received IV Thiamine. CSF analysis showed normal protein, glucose and cytology. The PCR tests in the CSF for HSV and TB were negative. The antimicrobial therapy was stopped subsequent to the CSF results, but dexamethazone continued.

Slow improvement of the level of consciousness was noted from the 2nd day since admission which was assumed to be in keeping with the correction of serum sodium level. However, the patient was found to have spastic quadriparesis and a postural tremor of upper limbs with cog-wheeling. Magnetic resonance Imaging (MRI) of the brain showed symmetrical hyperintensity on T2-weighted and FLAIR images in the caudate and putamen and, in the central pons (Figure 1). He was continued on IV Dexamethazone therapy and started on oral Levodopa + Carbidopa and Benzhexol. The pyramidal and extrapyramidal symptoms showed gradual improvement together with level of consciousness over a two week period. The steroid therapy was then tapered off and stopped at the end of 3 weeks.

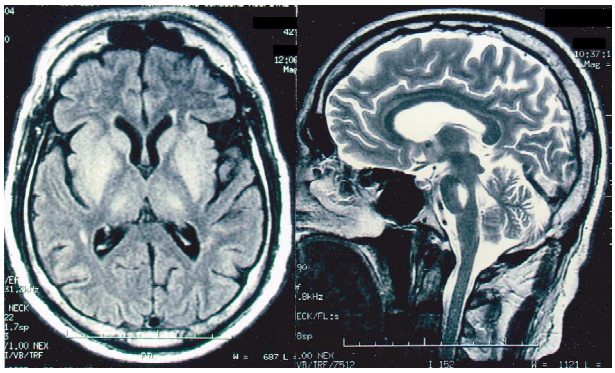

Figure 1. Axial FLAIR and sagital T_2-weighted MR images of the brain showing symmetrical hyperintense lesions in the basal ganglia, thalami and base of the pons in the acute stage.

The patient had a normal level of consciousness at 4 weeks and was mobilizing independently. There were mild extra-pyramidal symptoms and Levodopa was continued. A follow up MRI scan of the brain done at 8 weeks after admission showed resolution of the abnormalities (Figure 2).

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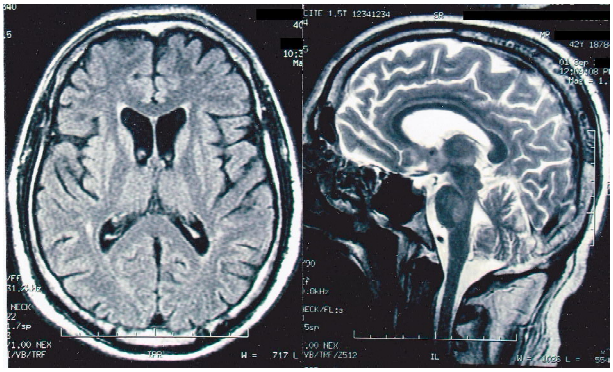

Figure 2. Follow up MRI at 8 weeks showing resolution of the abnormalities seen in Figure 1.

Discussion

The exact etiology and pathogenesis of CPM remain unclear. However, aggressive osmolar correction and in particular rapid correction of hyponatremia leading to disruption of the blood-brain barrier (BBB) caused by vascular endothelial damage is considered to play a critical role in the pathogenesis of osmotic demyelination[2]. Vasogenic oedema, release of myelinotoxic substances and damage to oligodendrocytes all contribute to the pathogenesis.

There are several publications concerning the successful use of plasmapharesis and imunoglobulin therapy in CPM suggesting a possible immune pathogenesis[3,4,5]. Bibl et al. successfully treated three young female patients with extensive therapeutic plasmapheresis soon after the diagnostic confirmation of CPM by MRI[5]. All patients had undergone correction of severe hyponatremia three to five days before the onset of neurological symptoms comprising of a rapidly evolving flaccid quadriplegia with dysphagia and dysarthria. Significant clinical improvement was obtained one month after plasmapheresis and neurological examination one year later disclosed partial recovery with total recovery in one patient. However, the pontine lesions remained unchanged in all patients even at 6 months after treatment. Grimaldi et al too report a case of CPM with clinical improvement following plasmapharesis, but persistence of MRI lesions[4].

Experience with corticosteroids in CPM is limited to the demonstration of its preventive effect on the development of the disease in animal experiments and two isolated case reports. Murase et al demonstrated severe neurological deficits with disruption of the blood brain barrier following rapid correction of induced hyponatreamia in rats, which was prevented by treatment with dexamethazone[6,7]. Hagiwara et al reported a case of CPM and extensive extra-pontine myelinolysis treated with pulsed IV methyl prednisolone resulting not only in complete recovery, but also resolution of extra-pontine MRI lesions on serial MRI[9]. Sajith et al described a patient with Addison's disease and CPM treated with hydrocortisone leading to clinical recovery and resolution of MRI lesions[10]. This patient had a similar presentation to our patient with extrapyramidal symptoms. The clinical recovery in our patient following dexamethazone therapy appear equivalent to the patients treated with steroids or plasmapharesis above. However, the unique feature following corticosteroid therapy appears to be the rapid resolution of MRI lesions in addition.

MRI appearances in the acute stage of CPM are largely due to the tissue water proton content, whereas the persistent lesions are likely due to fibrillary gliosis[11]. The resolution of MRI lesions with clinical improvement in patients treated with corticosteroids possibly indicates a potential therapeutic benefit in the acute treatment and prevention of long term severe neurological sequalae (recognized with chronic MRI lesions) in CPM.

Because of the severity of the neurological deficits, especially in the acute phase, and the possibility of a poor prognosis, treatment with corticosteroids should be further studied in CPM and extra-pontine myelinolysis. Controlled trials are needed to further assess this and other forms of immunotherapy for this condition.

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