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CASE REPORT

Hemolytic Uremic Syndrome Causing Multicystic Leukoencephalomalacia

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Summary

Backgrund: Hemolytic uremic syndrome is a disease characterized by hemolytic anemia, thrombocytopenia and acute renal failure with multiple organ involvement. Central nervous system involvement is detected in 20–50% of the patients and this leads to increased morbidity and mortality.

Case Report: We report the neuroimaging findings in a four-month-old male with hemolytic uremic syndrome. The cerebral cortex and white matter showed mild signal intensity on T2-weighted images. The diffusion weighted imaging demonstrated restricted diffusion in the cerebral cortex and white matter with corresponding low signal intensity on the apparent diffusion coefficient maps representing cytotoxic edema. These findings ended in multicystic leukoencephalomalacia.

Conclusions: In hemolytic uremic syndrome with brain involvement symptoms develop due to the different level of actions of factors and thus MRI protocol towards cerebral parenchyma should include DWI, especially in pediatric patients.

MeSH Keywords: Brain • Hemolytic-Uremic Syndrome • Leukoencephalopathies • Magnetic Resonance Imaging

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Background

Hemolytic uremic syndrome (HUS) is a disease characterized by hemolytic anemia, thrombocytopenia and acute renal failure with multiple organ involvement. HUS is the most common cause of acute renal failure in childhood [1]. Kidneys are primarily affected and central nervous system involvement is detected in 20–50% of the patients and this leads to increased morbidity and mortality [2]. Cerebral imaging can reveal basal ganglia [3], corpus callosum involvements, reversible posterior encephalopathy [4], subcortical and periventricular white matter involvement [5], cortical laminar and coagulative necrosis [1].

There are some studies which demonstrated basal ganglia and white matter involvements related to HUS. To our knowledge, only one case with cortical necrosis has been reported to date [1]. In our case report we aimed to present computed tomography (CT), magnetic resonance (MR) and diffusion weighted imaging (DWI) findings of a patient with multicystic leukoencephalomalacia without basal ganglia involvement.

Case Report

A four-month-old male patient, with non-bloody diarrhea for 20 days, was brought to our hospital due to a two-day history of high fever. The patient was unconsicious, his general condition was poor and he could pull his hand only with painful stimuli. Laboratory tests revealed: hemolytic anemia (haemoglobin 7 g/dL), presence of schistocytes in the peripheral smear, thrombocytopenia (platelet 39000/μL) and renal failure findings (serum creatinine 1.3 mg/dL, urea 47 mg/dL). Other laboratory tests revealed increased ALT (2399 IU/L), AST (1338 IU/L), and INR (14) levels, compatible with liver damage. Polymerase chain reaction (PCR) test was performed with stool culture for Shiga toxin detection; the test result was negative.

CT images of that unconscious patient revealed diffuse white matter hypodensity compatible with cerebral oedema, lateral ventricle compression, sulcal effacement and dense cerebellum (Figure 1). Cranial MRI showed normal basal ganglia, thalamus and cerebellum, whereas mild hyperintensity
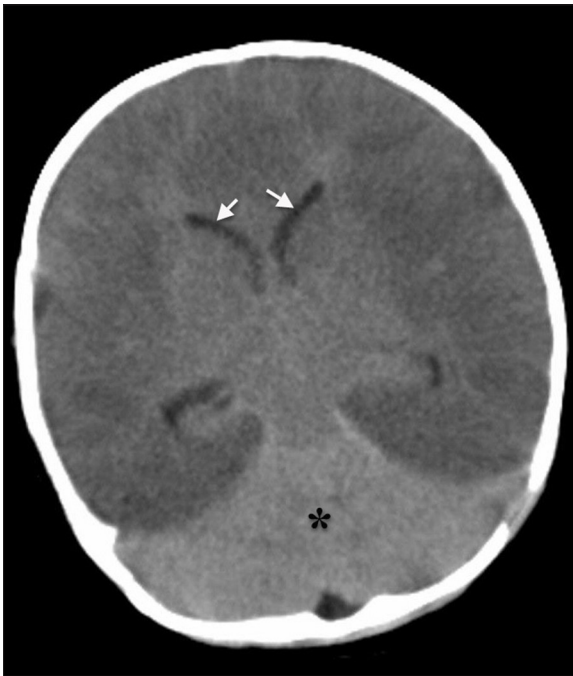
Figure 1. Axial non-enhanced CT demonstrates diffuse white matter hypodensity compatible with cerebral oedema, lateral ventricle compression (arrows), sulcal effacement and dense cerebellum (asterix).
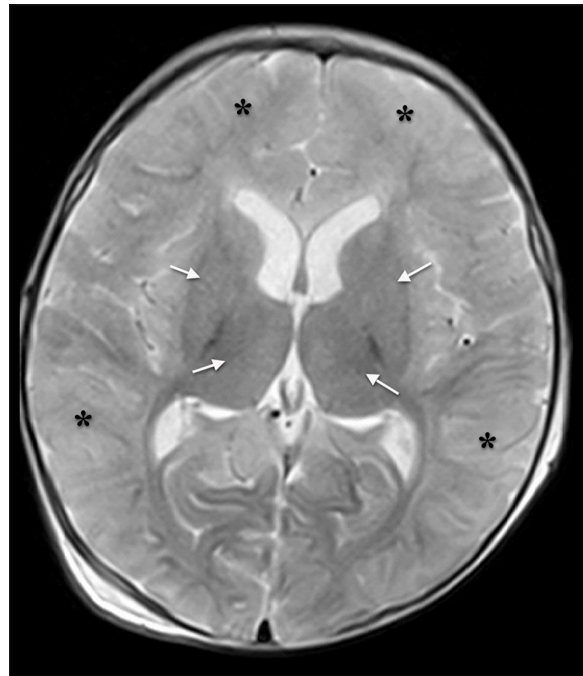

Figure 2. Axial T2-weighted MRI demonstrates normal basal ganglia, thalamus and cerebellum (arrows) with mild hyperintensity of the cerebral cortex and white matter (asterix).

of the cerebral cortex and white matter was revealed on T2/FLAIR sequences (Figure 2). The diffusion weighted imaging revealed restricted diffusion in the cerebral cortex and white matter with corresponding low signal intensity on the apparent diffusion coefficient maps (Figure 3A, 3B). Intracranial carotid arteries and their branches appeared signal void on T2-weighted images. No sign of hemorrhage was present on CT, T1 or SWI images. One month after control MRI, multicystic leukoencephalomalacia was detected (Figure 4A). MRI images of the next month showed development of bilateral subdural effusion (Figure 4B).

Discussion

The central nervous system (CNS) is the most common extrarenal involvement site of hemolytic uremic syndrome (HUS) [6]. Multi-organ involvement occurs when thrombotic microangiopathy (TMA) develops in HUS. TMA arises secondary to the coagulation cascade, which is caused by Shiga toxin-induced endothelial damage [7]. We suspected that the kidney and liver damage in our case was caused by this mechanism. However, along with TMA, metabolic damage (uremia, hyponatremia, hypocalcemia), hypertension, or toxin damage may also play a role in the physiopathology of CNS involvement [1,5,6].

Findings of HUS on CNS imaging usually include general symmetrical edema in the basal ganglia or changes related with infarct or hemorrhaging. Less frequently, cortical edema, infarct, or changes related to posterior reversible encephalopathy syndrome (PRES) are discovered [1]. The pathogenesis of CNS involvement is controversial despite the fact that TMA has been shown to play a primary role in the physiopathology of cerebral damage in the reported

cases [6] and performed similarly in *in vitro* tests [8]. Studies conducted by Bos et al. [9] reported that TMA was the cause of generalized cerebral edema in only 2 out of 5 cases with generalized cerebral edema. Gallo et al. [10] reported TMA in the pathophysiology of 11 autopsy cases out of 32 autopsy cases with cerebral edema related with HUS and/or intracranial hemorrhage.

In a different study, Gitraux et al. identified reversible ADC restrictions at parenchymal involvement sites. Despite those restrictions, the reversibility suggested that instead of TMA, cerebral vasculitis is likely the major pathogenesis [7]. The same study detected that the basal ganglia and the white matter were the sites of primary involvement both in HUS-related and vasculitic conditions. The basal ganglia were determined to be the characteristic involvement site of HUS in CNS by Steinbern et al. They suggested that infarct site or PRES-related changes were complications rather than specific signs [5]. Donnerstag et al. reported that basal ganglia and thalamus involvements were mostly seen along with cerebral white matter involvement, and those involvements could be caused by a direct effect of the Shiga toxin [4]. In contrast to other studies, Schmidt et al. reported a HUS case with coagulative necrosis secondary to microthrombosis in the basal ganglia and cortical laminar necrosis without hemorrhage [1]. Wengennoth et al. concluded that the most common finding of CNS involvement was a DWI signal increase due to vasogenic edema. According to their study, cases with cerebral infarct have not been reported in the literature, while cases with a hemorrhagic component had been previously studied [3].

In contrast to the data presented in the literature, in our study, the basal ganglia and thalamus were completely normal. Marked pathologic signals were not detected in
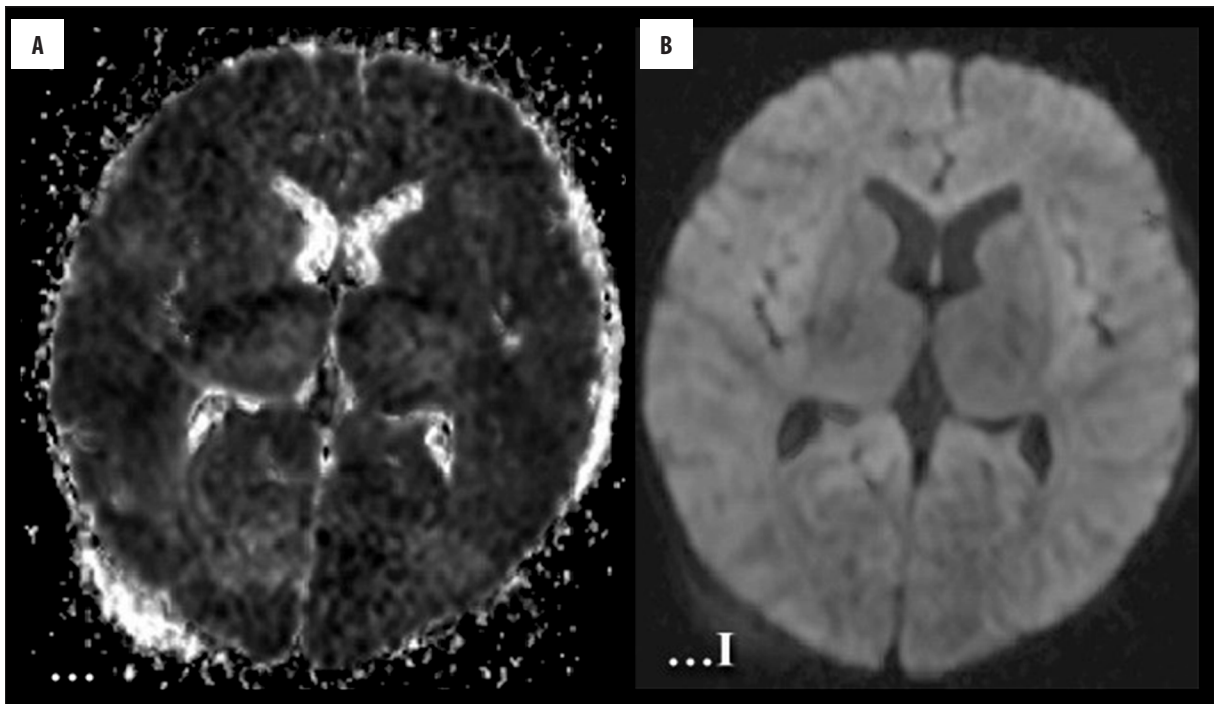
Figure 3. The diffusion weighted imaging demonstrates restricted diffusion in the cerebral cortex (**A**) and white matter (**B**) with corresponding low signal intensity on the apparent diffusion coefficient maps.
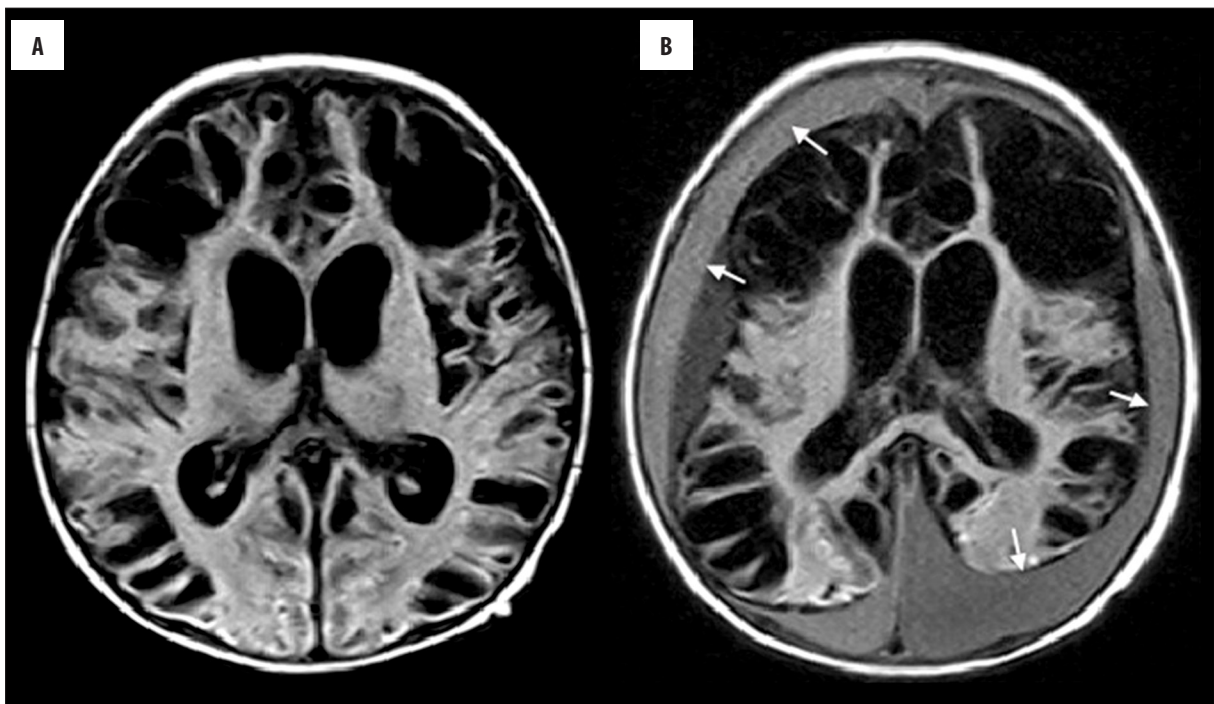

Figure 4. Axial FLAIR image demonstrates multicystic leukoencephalomalacia (**A**) and bilateral subdural effusion obtained on the next month (**B**).

the cortex or white matter in non-DWI. Diffusion restriction compatible with cytotoxic edema was present at these sites and in the cerebral peduncles bilaterally. Multicystic leukoencephalomalacia development was detected 1 month after the control images were obtained. In light of these findings and previous study data, we suggest the following: Hypertension due to ADC restriction and irreversibility; Shiga toxin as a result of diffuse cortical involvement distinct from white matter involvement; TMA due to diffuse and homogenous involvement of the cortex excluding the basal ganglia and thalamus do not play a role in the pathogenesis of cases with cerebral cortex involvement. Instead, symptoms may develop due to the different level of actions of factors, which we mentioned above. Therefore, magnetic resonance imaging protocol towards cerebral parenchyma should include DWI, especially in pediatric patients.

Conclusions

In hemolytic uremic syndrome with brain involvement symptoms develop due to the different level of actions of factors, and the MRI protocol towards cerebral parenchyma should include DWI, especially in pediatric patients.

Conflict of interest

None.

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