

## Acute Hemorrhagic Leukoencephalitis (Hurst Disease) Secondary to H<sup>1</sup>N<sup>1</sup> in a Child - A Story of Full Recovery from Qatar, A Case Report

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### Abstract

**Background:** Hurst disease is the rarest yet the most fatal form of acute demyelinating encephalomyelitis. There around 100 cases around the world, 10 of them are pediatric patients. The disease is quite severe in course and aggressive therapy is crucial to help improving the outcome. We are reporting a rather successful story of early recognition and treatment of young toddler with using all lines of known therapies simultaneously and aggressively.

**Case report:** We are reporting 2 ½ years old girl who was previously healthy. She has some viral prodromal illness ended by severe encephalopathy. She has found to have novel H1N1 infection. Early plasma exchange and therapeutic hypothermia have been simultaneously utilized. There was obvious significant fast improvement in clinical status thereafter.

**Discussion:** Immune therapy is advised in treating Hurst disease. One trial of hypothermia has been suggested in one case report. However, Combination of early use of plasma exchange and therapeutic hypothermia has not been reported in literature up to our knowledge. Our patient showed impressive clinical progress following these rarely used procedures.

**Conclusion:** Recognition of autoimmune encephalitis especially the most severe forms is a must. If the patient shows enough clinical and radiological signs suggestive of Hurst disease, then aggressive immunotherapy and therapeutic hypothermia should be considered. A more favorable outcome might be reached using these therapies simultaneously.

**Keywords:** Hurst disease; Acute Demyelinating Encephalomyelitis (ADEM); H1N1; Autoimmune encephalitis; Immunotherapy; IVIG

### Introduction

Hurst disease is a very rare disease affecting both adults and children. The disease has many parallel names used simultaneously. The full name is acute hemorrhagic leuko-encephalitis (AHL, or AHLE). Occasionally it is called acute necrotizing encephalopathy (ANE), acute hemorrhagic encephalomyelitis (AHM), or acute necrotizing hemorrhagic leuko-encephalitis (ANHLE). The disease is often named “Hurst Disease” or “Weston-Hurst syndrome”, in regard to “E. Weston Hurst” who has been the first author describing this disease in 1941 [1].

AHLE is considered the most severe fulminant form of acute disseminated encephalomyelitis (ADEM). It is thought that it represents around 2% of cases of ADEM [2]. The disease is very rare and tends to affects adults more than children [3]. The disease has been reported in elderly patients as well [4]. There is no significant gender predominance.

### Case Report

We are reporting a 2½ years old toddler girl who has been previously healthy with no past medical history of note. She was born at term to non-consanguineous parents and required no prior medical attention. She presented to the pediatric emergency center with history of fever and flu like symptoms for 3 days. She started to be progressively sleepy then she developed a sudden generalized tonic clonic seizure for five minute. Her initial assessment showed Glasgow coma scale (GCS) of 8/15 with otherwise reactive pupils and no focalizing neurological signs. She was subsequently intubated and mechanically ventilated. The initial impression was acute meningio-encephalitis, so broad spectrum antibiotics and antiviral drugs were commenced and lumbar puncture was performed after some period of stabilization.

Her initial complete hemogram counts, inflammatory markers,

serum electrolytes, liver function tests, coagulation profiles, blood and urine cultures were all negative. Her respiratory secretions were tested positive for H1N1 PCR using direct florescent assay (DFA), thus she received a five days course of oral oseltamavir. Cerebro-Spinal Fluid (CSF) analysis was done twice showing high protein but negative for bacteria and common viruses.

After three days of pediatric intensive care unit (PICU) stay, she was progressive deteriorating and her respiratory support requirements were increasing. She needed inotropic support to maintain adequate blood pressure and perfusion. The possibility of autoimmune encephalitis was then entertained as the most likely diagnosis. Magnetic resonance imaging MRI of the brain was then arranged. The MRI showed very unique and characteristic features of micro-hemorrhages in the thalamic, hippocampi, cerebellar hemispheres, pons, and cortex, consistent with acute hemorrhagic leukoencephalitis (AHLE/ Hurst disease).

On the third day of illness and the idea of autoimmune encephalitis was the most probably diagnosis, so aggressive immunotherapy course was started. She received five days of high dose pulse steroids (methylprednisilone), five sessions of plasma exchange then two days of immunoglobulins (IVIG). She also received trial of therapeutic

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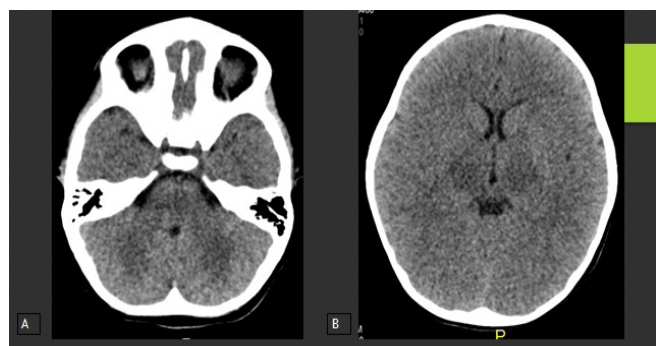
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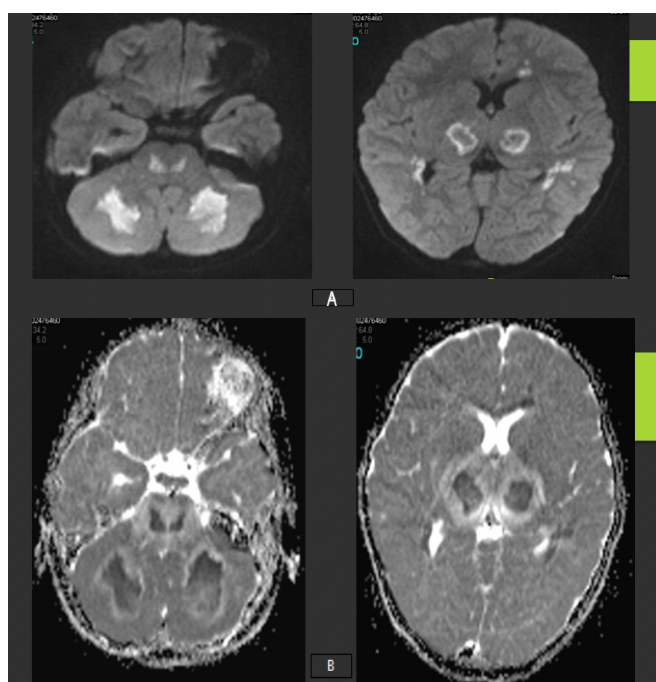
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hypothermia for five days as suggested by some literature. She is the first pediatric patient, up to our knowledge with AHLE who received this modality of aggressive treatment within short time (Figures 1-6).

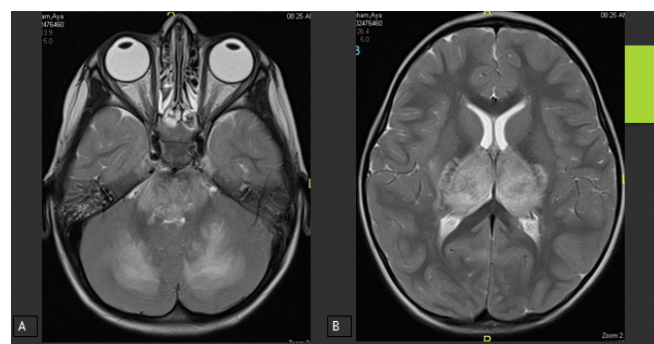
The patient thereafter started her journey of slow improvement. She was weaned quickly from respiratory support till room air. Her inotropic support was stopped. She started to open her eyes and move all her limbs equally. She could have some visual tracking and showed comfort in family presence. She began to turn to noises. She started producing some incomprehensible words though no fully understood sentences were observed. She had tolerated some oral feeding with the training aid of swallowing therapist, though she remained taking most of her feeds through feeding tubes. She was developing evolving generalized spasticity, though this had been lessened with the care of occupational therapists and physiotherapists. She did not develop any fixed contractures. A seating chair has been arranged for her with satisfactory



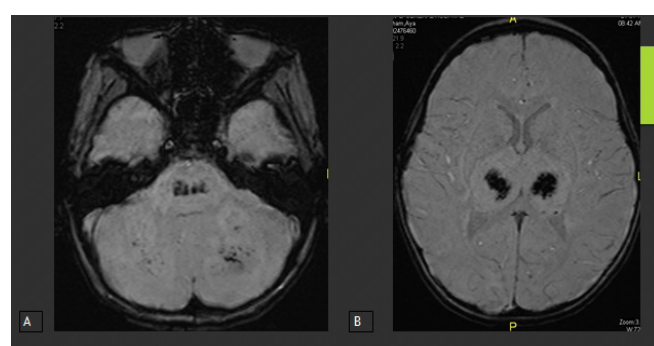
**Figure 1:** 1) Axial Non-Contrast CT examination of the brain at the level of the pons (A), Basal Ganglia and Thalami (B) showing subtle hypodensity along the thalami with no gross basal ganglia or posterior fossa changes.



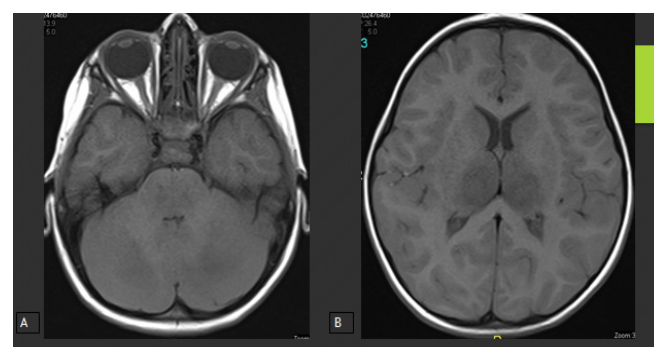
**Figure 2:** Axial DWI (A) and ADC map (B) MRI brain at the level of the Pons, Basal ganglia and thalami showing bilateral rather symmetrical parenchymal areas of bright signal in WDI and low values in ADC maps denoting some elements of restricted diffusion which is also seen involving the corpus callosum and the cerebellar white matter.



**Figure 3:** Axial T2 WI MRI of the brain at the level of the pons (A), Basal Ganglia and Thalami (B) showing swelling and bright T2 signal intensity with attenuated 3<sup>rd</sup> ventricle and basal cisterns.



**Figure 4:** Axial Susceptibility weighted images (SWI) MRI of the brain at the level of the pons (A), Basal Ganglia and Thalami (B) showing patchy dark blooming low signal intensity denoting parenchymal hemorrhages as well.

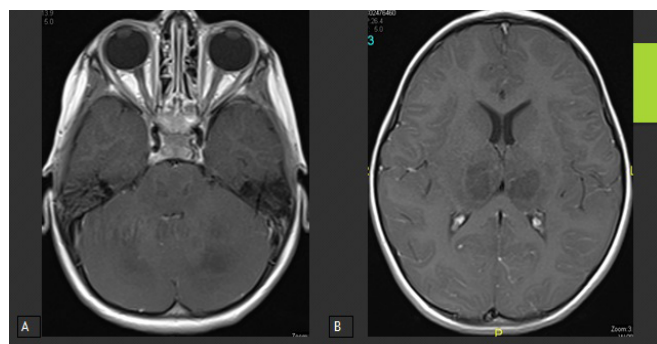


**Figure 5:** Axial non-contrast T1W1 MRI of the brain at the level of the pons (A), Basal Ganglia and Thalami (B) showing subtle hypointensity along the thalami with no gross basal ganglia or posterior fossa changes.

cooperation. She remained seizure free with one anticonvulsant drug. She has then been transferred to a specialist rehabilitation hospital to complete her recovery over there. Experienced clinicians following her have agreed that she has achieved extra-ordinary nice steps towards the maximal possible recovery. She has been discharged home in a very good condition needing only minimal assistance in performing her previous usual daily activities. She could walk reasonably balanced, talk to her family members and enjoy her toys as before.

## Discussion

Acute hemorrhagic leukoencephalitis belongs to the spectrum of



**Figure 6:** Axial contrast-enhanced T1W1 MRI of the brain at the level of the pons (A), Basal Ganglia and Thalami (B) showing no evident post-contrast enhancement.

autoimmune demyelinating encephalopathy disorders. Being quite rare with many non-specific clinical features put an extra challenge in diagnosing the disease early enough to have window of successful treatment. Lack of defined medical knowledge regarding the disease mechanisms and suboptimal disease management might have resulted in many cases being diagnosed retrospectively via autopsy histopathological specimens.

The disease often presents clinically like other varieties of encephalitis with febrile prodromal illness associated with progressive decreasing level of consciousness and interaction with or without seizures. The presentation however is usually more subacute. Symptoms of increased intracranial pressure might be apparent including headache, vomiting and blurred vision. Oro-facial dyskinesic movements are seen often, as in other autoimmune encephalitis group members. Signs of meningeal irritation might be elicited.

Similar to other autoimmune encephalopathy syndromes the disease has been linked to prior viral illness in almost half of the cases [5]. List of such viruses includes Human Herpes Virus (HSV), Epstein Barr Virus (EBV), influenza A virus, measles, mumps as well other organism like mycoplasma and malaria. There are theories in regard to possible association with inflammatory bowel disease, overwhelming septicemia and methanol poisoning (5). Post-vaccination AHLE has been suggested as well (5).

After the epidemic of novel H1N1 in 2009, there has been a lot of research emphasis on the possible neurological sequelae of H1N1. The cases reported in the literature linking AHLE to H1N1 were mostly among adult population [6-8]. Our case has been proved to have novel H1N1 infection confirmed by PCR testing of her respiratory secretions. Testing for H1N1 in CSF however was not feasible.

Trial of organism isolation after extensive infection work-up is usually unsuccessful. There is no diagnostic test for AHLE, though CSF anti-neuronal panel might be occasionally positive. The whole mark of the disease is widespread necrotizing venulitis, perivascular multifocal hemorrhages, diffuse CNS ischemic lesions and myelin destruction [5]. Demonstration of punctuate hemorrhages in brain magnetic resonance images (MRI) especially in susceptibility weighted images (SWI) is a good distinguishing feature from the classical ADEM. Rarely, AHLE may present as a solitary brainstem lesion with gross hemorrhage and should be considered in patients with isolated enhancing brainstem lesions [9].

The disease is often fatal and only few patients survived the acute phase. For survivors, most have lived with some long term neurological

sequel. Aggressive immunotherapy with immune globulins, high dose steroids and plasma exchange is warranted [10]. Prognosis is usually guarded. Interestingly, very few patients might have near normal recovery out of proportion to their illness severity and radiological findings [11].

Only little is known about favorable prognostic factors in children diagnosed with AHLE. Given the proposed immune nature of disease, use of early plasma exchange has shown some beneficial outcome in terms of less hospital stay and final neurological status in some cases [12]. Some authors have reported reasonable outcomes with high doses of pulse steroids for 3-5 days, followed by maintenance therapy for weeks [13,14]. A very recent study has reported use of mild therapeutic hypothermia as a major treatment modality for a child with severe symptomatic AHLE [15]. This is assumed to improve the final neurological outcome in children [16]. The rationale of such therapy might have relied on the assumption that low temperature is known to slow the immune response as well reducing the associated brain edema.

## Conclusion

Hurst disease is the hyper-acute, most severe form of ADEM & autoimmune encephalopathy. High index of suspicion is inevitably needed to get a prompt and fast diagnosis. Our case has thrown a light on importance of utilizing all lines of immune-modulating therapies, a practice that is highly advisable without delay. Early administration of high dose methylprednisolone, 3-5 cycles of plasma exchange, followed by IVIG seems to be a sense and rational approach. Adjuvant use of mild cooling is advised helping in decreasing secondary edema and slowing the pathological immune response. Early involvement of rehabilitative therapy is a cornerstone in restoring the maximal possible function. Complete or near complete recovery seems feasible.

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