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Atypical Manifestation of Acute Hemorrhagic Leukoencephalitis (Hurst's Disease)

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Acute disseminated encephalomyelitis (ADEM) and acute hemorrhagic leukoencephalitis (Hurst's disease) are rare autoimmune demyelinating disorders, which show a monophasic illness with preceding infection. We report a 42-year-old woman presented with multiphasic and progressive neurologic deterioration without definite evidences of infection. She developed hypesthetic ataxia, followed by ipsilateral weakness after a weak, and finally encephalopathy after a month. In contrast to the first MRI showing a small longitudinal lesion, the next images revealed massive bilateral frontal lesions with hemorrhagic necrosis and biopsy unveiled inflammatory demyelination.

Key Words: Acute disseminated encephalomyelitis, Hurst's disease

Acute disseminated encephalomyelitis (ADEM) is an immune-mediated disorder, characterized by demyelination of central nervous system associated with infection or vaccination, whereas acute hemorrhagic leukoencephalitis (Hurst's disease) is recognized as a severe form of ADEM, accompanied by a fatal and fulminant course. Usually both disorders are preceded by upper respiratory or other infections and typically have a monophasic course. The rapid clinical course, imaging studies and characteristic abnormalities in CSF and brain biopsy are known to be helpful for diagnosis of Hurst's disease. We experienced an atypical case of Hurst's disease, which showed a multiphasic course, not accompanied by a definite preceding infection.

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Case report

A 42-year-old woman suddenly developed right sided-numbness and ataxia. On admission, hypesthesia with dysmetria was observed in the right side without weakness in four extremities. Recently, she had a history of a double eyelid formation 2 weeks ago, although she has not suffered from preceding infections as well as underlying disorders. There were no significant abnormal findings in her serologic test on admission. 2 days after, conventional magnetic resonance image (MRI) showed a small longitudinal lesion in the left internal capsule, thalamus and cerebral peduncle, and the lesion did not show cytotoxic edema, hemorrhages or tumorous condition (Fig 1). Spinal fluid was totally normal except increased immunoglobulin G, supported by IgG index, 0.7 and evoked potential (EP) studies including brainstem auditory, visual, posterior tibial and median nerve somatosensory EPs showed no abnormal findings. She was treated with methylprednisolone; however, she developed

right sided-weakness (MRC Gr IV+ in upper extremity, III in lower extremity, and facial weakness), 7 days after the steroid treatment. Spinal fluid showed mild pleocytosis (white cell count of 8cells/㎕, 75% lymphocytes, 12.5% neutrophils, and 12.5% macrophages) and increased IgG index (1.15) with normal opening pressure (15 cm H_2O), protein (25 mg/dl), and glucose (56 mg/dl). Gram stain, India ink, and acid-fast bacilli staining were all negative. We regarded this patient as having one of demyelinating disorders such as multiple sclerosis and maintained corticosteroid therapy.

One month after the first symptom, she suddenly developed altered mentality with fever (39.5℃), not accompanied by headache, nausea, vomiting or any focal deficits. Abulic feature with urinary incontinence progressed to drowsy mentality with neck stiffness within a few hours. She was unresponsive to voice or noxious stimuli without abnormalities of brainstem reflex and she showed paraparesis with increased deep tendon reflexes and bilateral Babinski signs. Brain MRI revealed extensive new lesions in bilateral frontal lobes, which showed small petechial hemorrhages with massive edematous swelling, but not cytotoxic edema (Fig. 2-A). Spinal fluid became turbid and whitish with relatively high opening pressure (22 cm H_2O), polymorphonuclear leukocytosis (white cell count of 2,100 cells/㎕, 88% neutrophils, 4% lymphocytes, 8% macrophages) with elevated protein (176 mg/dl), and decreased glucose (31 mg/dl, simultaneous measurement of blood glucose was 92 mg/dl). IgG index was 0.39.

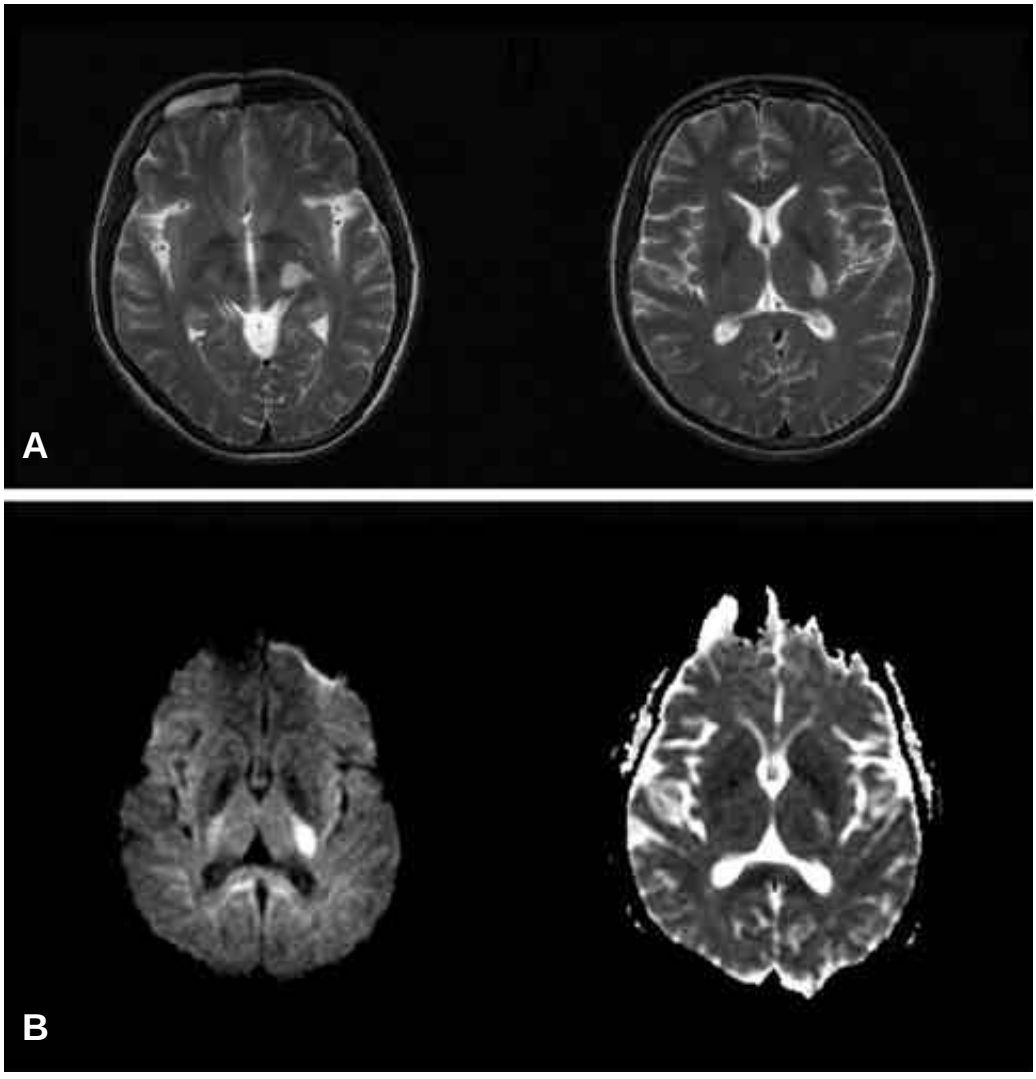

Figure 1. (**A**) Two days after the first symptom, T2-weighted image showed high signal intensity from internal capsule, thalamus to cerebral peduncle in the left side, longitudinally. (**B**) These longitudinal lesions were detected as high signal intensity in diffusion MR imaging with increased apparent diffusion coefficient (ADC).

Serum pleocytosis (white cell count of 13,740 cells/㎕) was detected, but there were no evidences to suggest infection of bacteria, tuberculosis, cryptococcus, and other fungi in spinal fluid. Polymerase-chain-reaction (PCR) testing of cerebrospinal fluid for HSV-1 was negative and serology for Epstein-Barr virus, cytomegalovirus, human immunodeficiency virus, Brucella and Borrelia were all negative. Cold-agglutinins and PCR tests for M. pneumoniae in both serum and CSF were negative. Myelin basic protein in spinal fluid was measured at 1 ㎍/L (normal, 0-0.5 ㎍/L) and oligoclonal bands were observed.

We diagnosed this patient as a fulminant form of ADEM, Hurst's disease and continued to treat her with high dose corticosteroid. With treatment, she did not improved, although spinal fluid nearly normalized (white cell count of 9 cells/㎕, red blood cell 24/㎕, protein 14mg/dl and normal glucose level). In rechecked MRI, the extent of previous frontal lesions increased with necrosis and multiple irregular enhancing lesions newly developed (Fig. 2-B). Therefore, we performed a stereotactic brain biopsy, which showed reactive gliosis with relatively preserved axons in demyelinating areas and microscopically, perivascular mononuclear inflammatory cells with macrophages and hemorrhage with demyelination (Fig. 3). We continued steroid therapy and she improved very slowly. A few months after her neurologic deterioration, she could walk with cane without recurrences, although mild abulic feature remained and follow-up images showed mild reactive hydrocephalus.

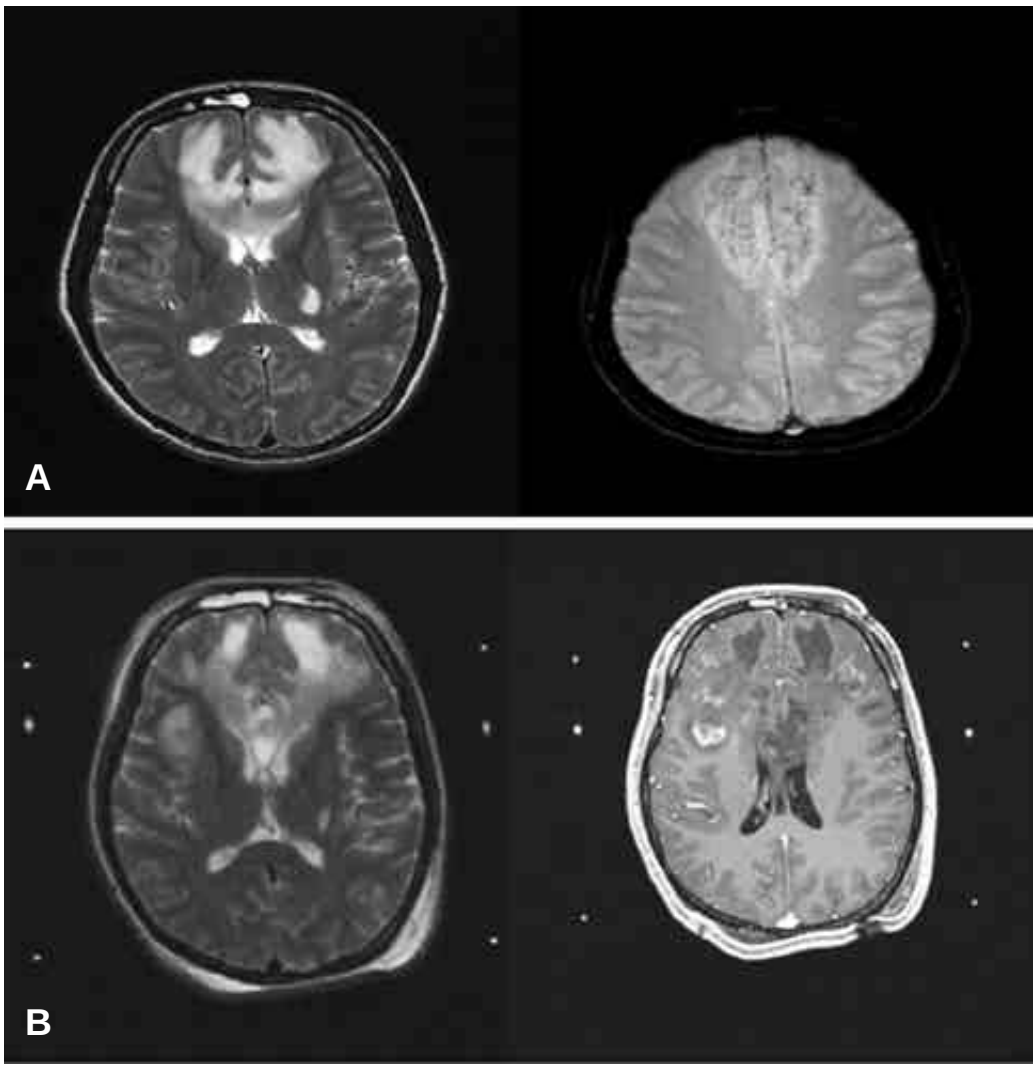

Figure 2. (**A**) One month after the first symptom, MRI revealed new lesions in bilateral frontal lobes with genu of corpus callosum and Gradient echo image disclosed multiple small dark signals suggesting of petechial hemorrhages in these lesions. (**B**) At the time of symptom aggravation though extensive steroid therapy, MRI showed increased extent of bilateral frontal lesions with necrosis and newly developed multiple irregular enhancing lesions.

Discussion

Hurst's disease is characterized by a hyperacute and fulminant inflammatory demyelination of white matter accompanying hemorrhagic necrosis, with a grave prognosis associated with death or fatal morbidity within several days [1-4]. Hurst first described this disorder as a pathological entity in 1941[5] and then several cases have been reported about characteristic clinical and CT findings. Hurst's disease is now generally recognized as a severe form of ADEM[3-5], both of which share the common features; the autoimmunity to CNS myelin, a monophasic disease course, preceding upper respiratory infection and periventricular demyelination with inflammation restricted to white matter. However, ADEM and Hurst's disease have different characteristic findings in respect of clinical, MRI, laboratory and pathologic findings.

As above commented, Hurst's disease develops hyperacutely to progress rapidly and has a fatal course comparing with ADEM. MRI of Hurst's disease shows extensive lesions with edema, mass effect and hemorrhages, while ADEM does not reveal neither involvement of basal ganglia or evidences of hemorrhagic necrosis. In spinal fluids, Hurst's disease has mostly polymorphonuclear pleocytosis with some red blood cells, whereas ADEM shows predominantly lymphocytic pleocytosis[3]. In addition, the pathologic finding of Hurst's disease shows neutrophilic infiltration with pericapillary ball and ring hemorrhage, while ADEM does usually lymphocytic infiltration.

Our case is regarded, as one of demyelinating disorders to white matter, such as ADEM or Hurst's disease; however she showed recurrent

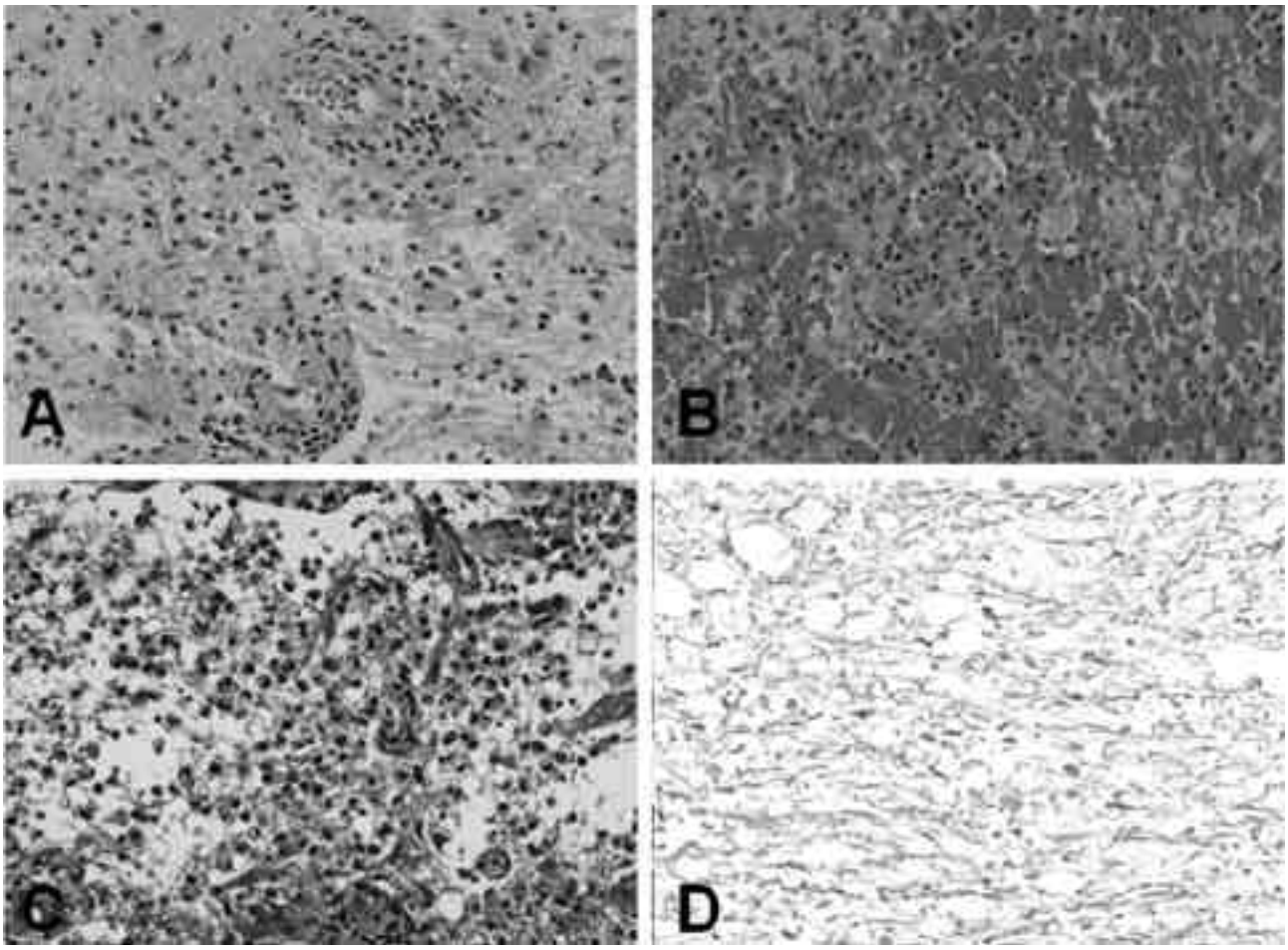

Figure 3. (**A**) Light microscopically, the lesion shows perivascular mononuclear inflammatory cell cuffing and diffusely inifltration of macrophages. (H&E, ×200) (**B**) Central blood vessel with perivascular hemorrhage is noted, which separate infiltration of macrophages. (H&E, ×200) (**C**) Luxol fast blue (LFB) staining shows the demyelination with blue myelin debris-laden macrophages is seen. (LFB staining, ×200) (**D**) Bodian staining reveal relatively preserved linear black axons in the demyelinating area. (Bodian staining, ×400)

neurological deficits with rapid progression, which were ataxic hypesthesia, ipsilateral weakness after a week, and encephalopathy after 1 month. This multiphasic course from mild neurologic deficit to progressive encephalopathy is quite unusual in both disorders, although a few ADEM cases with recurrent events have been reported. And ADEM and Hurst 's disease have triggering factors such as infectious antigens and usually prodromal symptoms are preceded before neurologic deterioration. However, our patient did not have any symptoms suggesting upper respiratory infection, instead, she had the history of a double eyelid formation two weeks before the neurological symptoms. Though there were no evidences, this procedure might be a triggering factor of a fulminant form of ADEM as described in a previous report[6].

In Hurst 's disease, MRI shows extensive lesions involving unilateral or bilateral white matter of the posterior frontal and parietal lobes 1,3,7 and these lesions occasionally extend to the gray-white matter junction, but not to the cortex. According to previous reports, Hurst 's disease show bilateral, confluent, multifocal and extensive white matter lesions observed as hyperintensity and hypointense punctate hemorrhages on T2 weighted image (T2WI)[4,7]. The first MRI study in our patient showed a small and longitudinal lesion involving from internal capsule to cerebral peduncle like multiple sclerosis and the followed MR revealed bilateral and relatively symmetric white matter involvement of the frontal areas with corpus callosum, later with enhancement. With MRI findings, spinal fluids and serologic findings of two disorders show different abnormal findings; ADEM has predominantly lymphocytic pleocytosis and Hurst 's disease has mostly polymorphonuclear pleocytosis with some red blood cells, although both disorders show elevated protein and normal glucose. And in contrast to ADEM, Hurst 's disease usually has been known to have leukocytosis in the serum.

Brain biopsy shows microscopic several features in Hurst 's disease: perivascular ring and ball hemorrhage; serous exudates; perivascular neutrophilic leukocytic infiltration; focal areas of demyelination; degeneration of small blood vessels with fibrinoid replacement of vessel walls; and glial nodules. These pathological features have been known to be somewhat different in not only findings of autopsy or biopsy but also experimental animal models. ADEM and experimentally induced acute allergic encephalomyelitis show the predominant lymphocytic perivascular infiltrates without hemorrhage or necrosis[8]. However, Hurst 's disease and experimentally induced hyperacute allergic encephalomyelitis, the perivascular infiltrates consist mainly of polymorphonuclear cells; the distinctive feature is a necrotizing vasculitis of venules with pericapillary ball and ring hemorrhages[4,9].

This case was a fulminant ADEM (Hurst 's disease), which showed a multiphasic neurologic deterioration with rapid progression, supported by peripheral leukocytosis and predominant polymorphonuclear pleocytosis in CSF. MRI of this patient revealed relatively symmetric bilateral extensive lesions with petechial hemorrhages and necrosis, although the pathology showed perivascular mononuclear inflammatory cell cuffing and diffusely infiltration of macrophages with demyelinating changes without necrotizing vasculitis of venules.

In general, Hurst 's disease results in death or severe neurological deficit within a few days, but sometimes, the treatment with corticosteroid, immunoglobulin and cyclophosphamide results in successful recovery of this disastrous disorder 2,10. Our patient was also treated with high-dose glucocorticoids and showed a relatively favorable recovery. We report an atypical fulminant ADEM (Hurst's disease) case, which showed favorable outcome after high-dose steroid treatment.

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