Acute Haemorrhagic Leukoencephalitis: Report of a Case

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Abstract - Acute haemorrhagic leukoencephalitis (AHL) usually involves the subcortical white matter but spares the cerebral cortex and subcortical U fibers. The outcome is usually fatal and very few survivors have been reported after decompressive therapy. An unusual presentation of a prolonged course of AHL in a 39-year-old man is reported. Initial brain magnetic resonance images (MRI) showed an irregular enhancing lesion in the left frontal area and another non-enhancing lesion in the right frontal subcortical white matter. A follow-up MRI 2 months later showed a remission of the right frontal lesion but a deterioration of the left frontal lesion. He received a decompressive craniotomy with left frontal lobectomy and pathological studies revealed an inflammatory reaction with haemorrhages involving the subcortical white matter. Interestingly, the haemorrhages also extended to the cortex and even to the meninges. Unfortunately, speech disturbance due to an epidural haematoma in the left fronto-parietal area was noted after the lobectomy. We conclude that AHL is unusual and the lesion may also involve the cortex and leptomeninges. Bleeding after decompression may be due to a post-operative complication or dura vessel involvement.

Key Words: Acute haemorrhagic leukoencephalitis, Epidural haematoma, MRI, Decompressive lobectomy, Pathology

INTRODUCTION

Acute haemorrhagic leukoencephalitis (AHL) was first described by Hurst¹ in 1941 with five main pathological features including 1) perivascular cellular infiltration, 2) multiple ball and ring haemorrhages, 3) perivascular demyelination, 4) fibrinoid necrosis of blood vessels and 5) perivascular or confluent edema²-⁶. The pathological changes usually involve subcortical white matter but spare cerebral cortex and subcortical U fibers. The involvement of subarachnoid vessels was not well described. The clinical course of AHL is usually characterized by an acute onset of headache, nausea, and vomiting, and then followed by a rapid progressive course of focal neurological deficits and even to deep coma. The outcome is usually fatal and very few survivors have been reported after decompressive therapy⁷-¹².

Recently, we encountered a pathologically proven case of AHL who developed a slowly progressive course after an episode of upper respiratory tract infection. Interestingly, the patient had frequent seizures and...
haemorrhages were also found in the cerebral cortex and the subarachnoid spaces. In addition, the patient developed an epidural haematoma after a decompressive lobectomy. The mechanisms and the lesion extension of AHL are also discussed.

REPORT OF A CASE

A 39-year-old man was admitted to our hospital on August 6 because of several episodes of generalized convulsion. He had enjoyed good health until one week prior to this admission. Initially he had experienced flu-like symptoms with fever, sore throat, cough and profuse sputum, and then diarrhoea in the following few days. On August 6, four episodes of generalized tonic-clonic convulsion with loss of consciousness were noted. Postictal confusion was noted for about 10 minutes. He denied any previous history of diabetes, hypertension, heart disease, head injury or strokes.

On evaluation, the blood pressure was 122/66 mmHg, body temperature 37.5 °C, pulse rate 94/min and respiratory rate 20/min. Neurological examinations revealed clear consciousness. The visual field, speech, extraocular movements, sensation, and motor function were normal. Neither frontal releasing signs such as sucking and snouting reflexes, nor palomomental sign was noted. Hemogram showed a high white count 18,200/mm³ with a predominance of neutrophils (93%). Biochemical studies disclosed normal electrolytes, and liver and renal functions. Brain computed tomography (CT) scan showed an ill-defined low density in the left frontal lobe with normal ventricular size and no midline shifting. Brain magnetic resonance images (MRI) revealed another smaller lesion in the right frontal subcortical white matter area in addition to a left frontal lesion with irregular low signal intensity on T1 weighted images (T1W) and high signal intensity on T2 weighted images (T2W) (Fig. 1A). After gadolinium (Gd) contrast medium injection, an enhancement was noted over the left frontal lesion. He was treated with phenytoin 300 mg

Figure 1. (A) Initial brain MRI revealed a high signal intensity lesion on T2W over the left frontal area and an additional lesion (arrow head) over the right frontal subcortical white matter. (TR: 5700, TE: 91.3); (B) The follow-up brain MRI 2 months later showed a deterioration of the left frontal lesion but the disappearance of the right frontal subcortical white matter lesion. (TR: 4000, TE: 99.0)
daily.

Under the impression of multicentric glioma, a stereotactic brain biopsy was performed from the left frontal area on August 10 and revealed perivascular cellular infiltraions with edema and haemorrhages. The perivascular infiltration cells included eosinophils, neutrophils and mononuclear cells. There were reactive astrocytes with positive stain for glial fibrillary acidic protein. Therefore, a diagnosis of acute necrotizing vasculitis was tentatively made. However the studies for rheumatoid factor, antinuclear antibody, and anti-double-stranded DNA antibody were all negative or within normal limits. After the operation, the condition was stationary and he was treated with phenytoin and dexamethasone or prednisolone 30 mg daily for about one month. During the follow-up period, he developed aphasia. The follow-up brain MRI scan on Oct. 10 disclosed an ill-defined heterogeneous mass lesion over the left frontal area with an enhancement after Gd administration. A mid-line shifting and compression of the left frontal horn were noted. However the right frontal subcortical lesion disappeared (Fig. 1B). He developed one episode of generalized seizures of about 5 min in duration on Oct. 10 and 17 respectively. He could not speak very well and dizziness was noted. He was placed on methylprednisolone and admitted again.

During the second admission on Oct. 29, his consciousness was clear. Mild weakness with a pronator sign was found on the right upper extremity. Deep tendon reflexes were generally increased. However the plantar reflex was flexion. One day after admission, headache, nausea, and vomiting with a deterioration of Glasgow coma scale from 15 to 10 (E3V1M6) were

Figure 2. The lobectomy specimen revealed an involvement of the subcortical white matter (arrow heads) and a slight sparing of subcortical white matter U fibers. In addition, the haemorrhages were found in the cerebral cortex (arrows) and the subarachnoid spaces (small arrow heads).

Figure 3. The pathological study of the frontal lobectomy disclosed (A) perivascular cuffings with lymphocytes and PMNs (H & E stain, 200X), (B) perivascular demyelination and edema (Luxol fast blue stain, 100X), (C) multiple ball haemorrhages in the subcortical white matter (H & E stain, 40X).
noted. After exclusion of metabolic and electrolyte abnormalities, emergent craniotomy and frontal lobectomy were performed under the impression of impending herniation. The excised gross specimen exhibited cystic and necrotic lesions predominantly located in the subcortical white matter and sparing of the subcortical U fibers. In addition to focal petechial haemorrhages in the white matter, the haemorrhages were also found in the cerebral cortex and subarachnoid space (Fig. 2). Microscopically, there were marked perivascular lymphocytic cuffings, aggregations of foamy histiocytes, petechial haemorrhages, and perivenous demyelination (Fig. 3). The serological study for herpes simplex virus type I and type II (IgM), cytomegalovirus (CMV) IgM, and hepatitis B surface antigen were negative, but a relatively high CMV IgG (190 AU/mL) was noted. After the operation, the patient developed aphasia in the following day. A follow-up brain CT scan on Nov. 10 showed an epidural haematoma over the left fronto-parietal area. (Fig. 4) Emergent operation was performed to remove the epidural haematoma. The condition got better, and he could speak more fluently although impairment of naming was still infrequently found. A follow-up brain MRI scan in January, 2000 revealed that the lesions disappeared and no new lesions developed. He remained stationary and steroid was tapered off in the following 3 months.

FIGURE 4. A follow-up brain CT scan 10 days after decompressive frontal lobectomy disclosed an epidural haematoma over the left fronto-parietal area after enhancement.

DISCUSSION

We present a pathologically proved case of AHL who run an unusually prolonged course and improved after a surgical decompression. In addition, the pathological study also showed haemorrhages in the cerebral cortex and subarachnoid spaces. Furthermore, the development of an epidural haematoma after frontal lobectomy suggests a risk of bleeding in AHL.

AHL was first described by Hurst(1) with perivascular polymorphonuclear leukocyte infiltration, multiple haemorrhages, perivascular demyelination with edema, and fibrinoid necrosis of small veins and arteries. In addition, a sparing of the cerebral cortex and subcortical U fibers was noted2-6. Our case fulfilled all the main pathological features. Intriguingly, in our patient, the haemorrhages extended to the cerebral cortex and meninges, particularly the arachnoid membranes. The involvement of meninges or cerebral cortex had been neglected. However, in the original case of Hurst(1), in few places, the lesions might spread into the cerebral cortex or other gray matter and polymorphonuclear leukocytes were present in parts of the leptomeninges. In some other reports, meningeal vessels were hyperemic, congested, or inflamed2,3,5. In a report by Michaud et al.(13), they found a small amount of meningeal haemorrhages. Kristiansen et al.(11) also reported extravasation of red blood cells into the subarachnoid space. Rothstein et al.(14) noted the cerebral cortex over the lesion was well preserved except for occasional small foci of ischemic neuronal changes and edema. Therefore, focal infiltration of the leptomeninges with inflammatory cells is not uncommon. In addition, congestion in some cortical areas is very pronounced, and occasionally focal haematogenic infiltration extends into the deeper layers of the cortex2. Although the pathological lesions may appear in the cortex and/or arachnoid vessels, this feature has not been emphasized in most of the studies11-13.

Surgical decompression had been suggested to be one of the life saving procedures7-12,18-17. However, an epidural haematoma after decompressive lobectomy developed in our case. Although the epidural haematoma may be directly related with the surgical operation, it may also indicate that the risk of bleeding may increase...
in AHL while performing a craniotomy. AHL usually has a rapid progressive course leading to death. However it occasionally has a fluctuant or chronic course. Our patient had a chronic progressive course for about 2 months. In a follow-up MRI scan, the right frontal subcortical white matter lesion had a spontaneous remission while the left frontal lesion deteriorated. The progression on MRI appeared to correlate with the clinical deterioration. In a case reported by Michaud and Helle(13), the evolution was biphasic with an acute onset on the second day, followed by an improvement in the following three days, and eventually fulminant leading to death. Kristiansen et al. reported two patients who had survived following decompressive craniotomy. Coxe and Luse(7) showed two biopsy-proven cases with a long survival of 2.5 years and 1 year, respectively, following surgical decompression. The first case survived with some sequelae but the second case eventually expired. The patient of Lamarche et al. survived 9 months after a partial frontal lobectomy. In our previous report, one patient died 3 months from the onset and another survived 1.5 months with recovery(12). The data suggest that some patients may have a prolonged clinical course and surgical decompression may be helpful in prevention of herniation.

The etiology and pathogenesis of AHL remain obscure. However an allergic reaction may play an important role. From some clinical and histopathological studies, acute brain purpura, AHL and acute disseminated encephalitis (ADL) may share the same mechanisms and can be considered as a triad of organ specific allergic conditions(2,4,18). The speed of deterioration may correlate with the spreading of multiple discrete small ring and ball hematomas. In hyperacute state such as brain purpura, cellular infiltration is rarely found. In AHL, the perivascular cellular infiltrations are usually polymorphonuclear cells. In ADL, the infiltrations are usually mononuclear cells or lymphocytes(2). In our case, the presence of both of the lymphocytes and polymorphonuclear cells possibly indicated an intermediate type between AHL and ADL.

We conclude that AHL is rare, and the pathological lesions may also involve the cortex and leptomeninges. In addition, the procedure of lobectomy should be very careful because that epidural haematomas may occur due to post-operative complication or dura vessel involvement.

**REFERENCES**

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