Complex partial status epilepticus as a manifestation of Hashimoto’s encephalopathy

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Summary Epileptic seizures are a frequent manifestation of Hashimoto’s encephalopathy. However, status epilepticus associated with Hashimoto’s encephalopathy are not well characterized in medical literature. We described here a 16-year-old girl who presented with complex partial status epilepticus associated with elevated anti-thyroid antibodies. Ictal EEG showed lateralized high amplitude rhythmic delta waves over the right hemisphere and ictal single-photon emission computed tomography revealed regional hyperperfusion of the right parietal and temporal lobes. The patient was unresponsive to antiepileptic drug therapy but responded to intravenous steroid treatment. Screening of serum anti-thyroid antibodies for unexplained encephalopathy with epileptic seizures is suggested, as early recognition and prompt steroid treatment may lead to a favorable prognosis.

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Case report

A 16-year-old girl was admitted to the Neurology ward due to mental disturbances and prolonged confusional states. One month before admission, she developed subacute onset of impaired attention, bizarre behavior, self-talking, insomnia, and mood disturbances. After admission, she had episodic disorientation about 7–8 times/day, with confusion and acute psychotic states. The duration of attacks was from 30 to 40 min. Meaningless vocalization, laughing, chewing, and lips smacking were also noted during the attacks. Between episodes, the deteriorated consciousness occasionally did not return to the baseline. After two generalized motor convulsions, she received treatment immediately with intravenous lorazepam and subsequent intravenous phenytoin therapy (began with a loading dose of 800 mg and maintained at 300 mg/day). However, consciousness did not improve and episodic mental changes persisted, despite serum phenytoin levels were within therapeutic range. She gradually developed intermittent, semi-rhythmic clonic movement of the left arm, accompanied by alternations of consciousness.

The patient’s gestational and neonatal history was unremarkable, with normal developmental milestones. There was no history of major systemic or infectious diseases. Family history of epilepsy or febrile convulsion was also negative. Physical examination was unremarkable. Laboratory studies, including complete blood count, alanine transaminase/aspartate transaminase, blood urea nitrogen/creatinine, and serum electrolytes were all within normal limits. The cerebrospinal fluid was likewise unremarkable, as well as tests for drug screens, blood lead and copper level, porphyria screens, syphilis, anti-nuclear antibody, viral infections (herpes simplex virus, human immunodeficiency virus, hepatitis B, hepatitis C, and cytomegalovirus and Epstein-Barr virus), tumor makers, and serum electrophoresis.

Ictal electroencephalogram (EEG) revealed continuous high amplitude rhythmic lateralized delta waves over the right hemisphere (Fig. 1). Intermittent photic stimulation during EEG studies did not evoke abnormal photoparoxysmal response. Ictal brain 99mTc single-photon emission computed tomography (SPECT) revealed a hyperperfusion state over the right parietal and temporal lobes (Fig. 2A). Brain magnetic resonance imaging showed hyperintense lesions on fluid-attenuated inversion recovery-sequences image over the right medial temporal area.

Thyroid function tests showed that serum free T4 was 2.05 ng/dL (normal, 0.79–2.01 ng/dL), T3 was 97.6 ng/dL (normal, 52–175 ng/dL), and thyroid-stimulating hormone was below 0.2 μIU/mL.

Figure 1  Ictal EEG showed continuous, rhythmic, lateralized delta waves over the right hemisphere.

Figure 2  (A) Ictal SPECT revealed regional hyper-perfusion over the right parietal and temporal lobes. (B) Interictal MRI showed hyperintensity on fluid-attenuated inversion recovery-sequences image over the right medial temporal area.
The diagnosis of Hashimoto’s encephalopathy was confirmed by elevated titers of both anti-microsomal antibody and anti-thyroglobulin antibody to 1:1600 (normal, 1:100). Intravenous methylprednisolone 1000 mg for 3 days followed by oral prednisolone 60 mg/day was given. Dramatic clinical improvement of consciousness and cognitive function, as well as decreased seizure frequency, was noted. Steroid was gradually discontinued 2 months later without relapse of the encephalopathy. Thyroid function tests returned to normal and serum anti-thyroid antibody titer became negative.

**Discussion**

Because the clinical manifestations of Hashimoto’s encephalopathy are quiet variable and nonspecific, the diagnosis is often challenging. The symptoms are usually not preceded by symptoms of dysthyroidism. Therefore, this condition is easily under-recognized. Our patient had only mild hyperthyroidism at the time the neurologic symptoms manifested and the clinical neurologic presentations were nonspecific. Thus, the differential diagnosis should include viral encephalitis, Creutzfeldt-Jakob disease, central nervous system vasculitis and other autoimmune inflammatory encephalopathies. Whereas the negative sign of central nervous system (CNS) infection, a normal CSF study and the absence of viral antibodies in this patient, we excluded the possibility of infectious causes. There was also no evidence of vasculitis both in the clinical presentation and MRI study. Para-neoplastic limbic encephalitis was not suggested due to the young age of the patient and no subsequent development of neoplasm during the follow-up period. More importantly, the elevated titers of anti-thyroid antibodies eventually led to the diagnosis of Hashimoto’s encephalopathy.

Epileptic seizures are a common clinical symptom of Hashimoto’s encephalopathy. However, status epilepticus rarely occurs in patients with Hashimoto’s encephalopathy. Our patient exhibited fluctuating clinical presentations, including memory deficits, bizarre behavior, psychosis, and confusion. Ictal EEG demonstrated right lateralized high amplitude rhythmic delta waves associated with episodic altered mental status suggestive of complex partial status epileptics.

Intriguingly, the SPECT revealed regional hyperperfusion in the right parietal and temporal lobes, which correlated with the lateralized high amplitude rhythmic delta waves on the EEG. We are aware that most reported cases of Hashimoto’s encephalopathy showed reversible diffuse or focal hypoperfusion on SPECT during the interictal stage. Vascular insufficiency caused by vasculitis had been proposed as the underlying pathogenesis. In this patient, the ictal seizure activities might contribute to the hyperperfusion change in regional cerebral cortex that further supports the diagnosis of complex partial status epileptics.

A Medline research conducted to identify published papers regarding status epilepticus associated with Hashimoto’s encephalopathy between 1967 and February 2007 showed only six patients (Table 1). With our patient, there were five females and two males. The age ranged from 16 to 61 years. Except for our patient (Patient 7), four (Patients 1—4) had generalized convulsive status epilepticus, one (Patient 5) had generalized absence status epilepticus, and one (Patient 6) had epilepsy partialis continua.

The prognosis of status epilepticus remains poor, with prompt seizure control and treatment of the underlying etiology as the principal management considerations in clinical practice. In our patient and the six reported cases of Hashimoto’s encephalopathy that had status epilepticus, antiepileptic drug therapy was ineffective. Among the seven patients, five (Patients 1, 3 and 5—7) had good response to intravenous steroid therapy. Two patients (Patients 2 and 4) did not response to steroid therapy and had an unfavorable outcome. Accordingly, poor response to steroid ther-

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age/sex</th>
<th>Seizure type</th>
<th>AED response</th>
<th>Steroid response</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 [Ref. 8]</td>
<td>42/F</td>
<td>GCSE</td>
<td>Poor</td>
<td>Good</td>
<td>Recovery</td>
</tr>
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<td>Poor</td>
<td>Poor</td>
<td>Death</td>
</tr>
<tr>
<td>3 [Ref. 7]</td>
<td>41/M</td>
<td>GCSE</td>
<td>Poor</td>
<td>Good</td>
<td>Recovery</td>
</tr>
<tr>
<td>4 [Ref. 10]</td>
<td>27/F</td>
<td>GCSE</td>
<td>Poor</td>
<td>Poor</td>
<td>Death</td>
</tr>
<tr>
<td>5 [Ref. 9]</td>
<td>61/F</td>
<td>GASE</td>
<td>–</td>
<td>Good</td>
<td>Recovery</td>
</tr>
<tr>
<td>6 [Ref. 5]</td>
<td>37/F</td>
<td>EPC</td>
<td>Poor</td>
<td>Good</td>
<td>Recovery</td>
</tr>
<tr>
<td>7 [present]</td>
<td>16/F</td>
<td>CPSE</td>
<td>Poor</td>
<td>Good</td>
<td>Recovery</td>
</tr>
</tbody>
</table>

M: male; F: female; GCSE: generalized convulsive status epilepticus; GASE: generalized absence status epilepticus; CPSE: complex partial status epilepticus; –: not available; AED: antiepileptic drug; EPC: epilepsy partialis continua.
apy, general convulsive status epilepticus, and extended involvement of brain structures might be associated with poor prognosis in Hashimoto’s encephalopathy. Therefore, Hashimoto’s encephalopathy might be a treatable etiology for status epilepticus and aside from antiepileptic drugs, intravenous steroid therapy should be started as soon as possible to prevent the unfavorable results. For those unresponsive to steroid therapy, plasmapheresis and intravenous immunoglobulin had been suggested. But whether plasmapheresis, immuno-suppressants, or intravenous immunoglobulins are effective for steroid-resistant cases need further study.

The pathogenesis of Hashimoto’s encephalopathy is unclear. Proposed mechanisms include autoimmune CNS vasculitis, anti-neuronal antibody-mediated reaction, and an autoimmune reaction to antigens shared by the thyroid and CNS. Although anti-thyroid antibodies are essential in the diagnosis of Hashimoto’s encephalopathy, their levels do not correlate with the severity of neurologic deficits. The role of anti-thyroid antibodies in epileptic seizures in Hashimoto’s encephalopathy is unknown. Recent studies have suggested that auto-antibodies, such as anti-glutamic acid decarboxylase antibody or anti-voltage gated channel antibody, may contribute to certain forms of epilepsy or seizure-associated disorders. Whether the anti-thyroid antibodies themselves harbor effects on neurons, which lead to epileptogenesis in Hashimoto’s encephalopathy, needs further research.

In conclusion, complex partial status epilepticus can occur in Hashimoto’s encephalopathy. Although Hashimoto’s encephalopathy is a treatable condition, the associated status epilepticus is often refractory to antiepileptic drug therapy. Screening of serum anti-thyroid antibodies for unexplained encephalopathy with epileptic seizures should be suggested. Early recognition of this disease and prompt steroid treatment may lead to a favorable prognosis.

References