A case of AMPAR2 encephalitis with impaired cognition

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Introduction

Autoimmune encephalitis occurs when the immune system attacks intracellular neuronal antigens or neuronal surface proteins. The glutamate receptor α-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid receptor (AMPAR) is a cell-surface ionotropic receptor which is most frequently found in the hippocampus, followed by the subiculum, cerebellum, caudate-putamen, and cerebral cortex. Lai M, et al. (2009), first described anti-AMPA receptor encephalitis in their 10 patients with impaired cognition.

Abstract

Autoimmune encephalitis is a common and underdiagnosed disorder which can cause seizures, altered sensorium, impaired cognition, and alterations in consciousness. AMPAR is a cell-surface ionotropic receptor that has two main subtypes, of which encephalopathy with AMPA-1 has been well published. Here, we report a 72 yo M who presented with a sub-acute onset of episodes of confusion and fatigue, and a gradual decline in cognition. Patient was found to be positive for AMPAR-2 antibodies in both his serum and CSF. Neuropsychological evaluation showed significant improvement of alertness and relative improvement in cognition after being treated with IVIG. AMPAR2 encephalitis is rare, with a single case report describing it in the literature. This report aims to bring attention to a potentially reversible neurocognitive disorder.

Case Report

Patient is a 71yo RHM with PMH of HTN, HLD, hearing loss, RCC, melanoma. and anxiety who presented with episodes of confusion and fatigue that lasted for hours since August 2018. His neurologic exam was notable for drowsiness and cognitive tests significant for impaired verbal recall. MRI brain showed mild atrophy of the right hippocampal head and mild symmetric microvascular disease. EEG was normal. His blood and CSF came back positive for AMPA-2 antibody. Labwork was also notable for mildly elevated anti-TPO and anti-thyroglobulin.

Neuropsych evaluation

Table below shows areas of improvement in our case before and after IVIG treatment:

<table>
<thead>
<tr>
<th>Test/Measure</th>
<th>11/2018</th>
<th>1/2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE</td>
<td>24/30</td>
<td>27/30</td>
</tr>
<tr>
<td>Verbal fluency</td>
<td>S &amp;P : 19, Animals and supermarket: 34</td>
<td>S &amp;P : 21, Animals and supermarket: 42</td>
</tr>
<tr>
<td>HVLT-R/Verbal memory</td>
<td>Learning 16/36, Recognition : 7</td>
<td>Learning 15/36, Recognition : 10</td>
</tr>
</tbody>
</table>

Conclusion

Our case received a total of 5 doses of 2mg/kg IVIG. Repeat neuropsychological evaluation showed significant improvement of alertness with fair improvement in memory and cognition. Anti-AMPAR encephalitis is a new subtype of autoimmune encephalitis that was first described in the literature a decade ago. Few cases of AMPAR1 encephalitis have previously been reported in the literature. However, anti-AMPAR2 encephalitis was only once described in a case report in the setting of Hashimoto disease bu Zhu M et al. (2017). Their case despite our case was diagnosed when his disease was very progressed and was already in a coma. This case represents a rare but treatable cause of cognitive dysfunction that can often be missed in its early stages. We suggest this antibody to be tested routinely in the workup of suspected autoimmune encephalitis cases.

References