H1N1 influenza virus-associated encephalitis: A case report

Encefalitis asociada al virus de la gripe H1N1: un caso clínico

Febrele respiratory symptoms represent the most common clinical manifestations of infection with 2009 H1N1 virus and are in general mild and self-limited. Since the 2009 H1N1 pandemic several neurologic complications have been described. Children and young adults are preferentially affected. We report a case of H1N1-associated encephalitis in an adult patient.

A 56-year-old male nurse, with a past medical history significant for hypertension and right-sided nephrectomy for congenital hydronephrosis, was admitted, initially to the emergency department of another hospital, with a 5-day history of influenza-like illness including lethargy, high fever and nonproductive cough. A nasopharyngeal swab was performed to test for the H1N1 virus.

On admission the patient was febrile, but otherwise his other vital signs were stable. He was conscious and orientated. The rest of the physical and neurologic examination was unremarkable.

Laboratory studies revealed normal white blood cell count, thrombocytopenia of $77 \times 10^9$/L and elevated C-reactive protein of 15.8 mg/dL. Serum electrolytes and renal and liver function tests were within normal limits. Chest radiograph demonstrated consolidation of the left lower lobe. He was diagnosed with community-acquired pneumonia and broad-spectrum antibiotic therapy consisted of intravenous ceftriaxone and azithromycin was initiated. On day 2 of hospitalization antiviral therapy with Oseltamivir 150 mg/day was associated after nasopharyngeal swab confirmed H1N1 virus infection.

Despite antibiotic and antiviral therapies, his respiratory status worsened. On day 3 he developed acute respiratory distress syndrome requiring intubation and he was transferred to the intensive care unit.

Therapy with Oseltamivir was discontinued after 9 days. Throughout his ICU-stay he remained febrile. After successful weaning from mechanical ventilation and sedation the patient was extubated on ICU-day 10. During the following day’s he was noted to have fever, fluctuating mental status and disorientation.

A computed tomography scan of the brain showed bilateral cortical and subcortical vasogenic cerebral edema with areas of hemorrhage, involving the right frontoparietal lobe, the left occipital lobe and the left cerebellar hemisphere, with mass effect on the left ventricle with midline shift and subfalcral and right-sided uncal herniation.

The patient was put on antiedemic therapy and transferred to our institution for observation by neurosurgery. Just before being transported he required reintubation for...
Figure 1  The right-hemispheric lesion area. Brain magnetic resonance images showed extensive vasogenic edema with hemorrhagic foci in the right cerebral hemisphere predominantly in the right perirolandic and fronto-temporal regions with hyperintense signal. Following intravenous gadolinium administration leptomeningeal contrast enhancement in the right temporal lobe was observed.

<table>
<thead>
<tr>
<th>Author</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Interval ILI-neurologic symptoms (days)</th>
<th>Neurologic symptoms</th>
<th>CSF</th>
<th>MRI</th>
<th>EEG</th>
<th>Antiviral therapy</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fugate et al.</td>
<td>Male</td>
<td>40</td>
<td>30</td>
<td>Acute drop on the bispectral index monitor</td>
<td>No pleocytosis</td>
<td>Subcortical lesions with hemorrhages and edema</td>
<td>Normal</td>
<td>Oseltamivir</td>
<td>Severe sequelae</td>
</tr>
<tr>
<td>Akins et al.</td>
<td>Male</td>
<td>20</td>
<td>6</td>
<td>Confusion, seizures</td>
<td>Pleocytosis</td>
<td>White matter lesions, diffuse edema</td>
<td>Bilateral diffuse continuous slow waves</td>
<td>Oseltamivir 150 mg/dia</td>
<td>Mild sequelae</td>
</tr>
<tr>
<td>Chen et al.</td>
<td>Male</td>
<td>40</td>
<td>2</td>
<td>Tremors, clumsiness, right hemiplegia</td>
<td>Elevated protein level</td>
<td>Cortical and subcortical areas of the frontal-parietal lobe</td>
<td>Diffuse slowing of cortical activity</td>
<td>Oseltamivir</td>
<td>Severe sequelae</td>
</tr>
<tr>
<td>Ito et al.</td>
<td>Male</td>
<td>26</td>
<td>Unknown</td>
<td>Memory disturbance, disorientation, drowsiness</td>
<td>Normal protein level</td>
<td>Corpus callosum</td>
<td>Normal</td>
<td>Oseltamivir 150 mg/day</td>
<td>Complete recovery</td>
</tr>
<tr>
<td>Gonzalez et al.</td>
<td>Female</td>
<td>46</td>
<td>3</td>
<td>Confusion</td>
<td>No pleocytosis</td>
<td>Normal</td>
<td>ND</td>
<td>Oseltamivir</td>
<td>Complete recovery</td>
</tr>
<tr>
<td>Tsai et al.</td>
<td>Male</td>
<td>46</td>
<td>4</td>
<td>Acute delirium</td>
<td>No pleocytosis</td>
<td>White matter lesions</td>
<td>Bilateral diffuse continuous slow waves</td>
<td>Oseltamivir 150 mg/day</td>
<td>Deceased</td>
</tr>
</tbody>
</table>

ND: not done; ILI: influenza-like illness; CSF: cerebrospinal fluid; EEG: electroencephalography.
Our patient almost always presented with influenza-like symptoms. Neurological symptoms included drowsiness, confusion and memory disturbance. CSF analysis in combination with laboratory-confirmed infection and CSF analysis in combination with laboratory-confirmed H1N1 respiratory tract infection. However, like in our patient, H1N1 RNA was not detected in CSF by RT-PCR. Other findings of CSF included elevated leukocyte counts and/ or elevated protein levels. Neuroimaging findings were variable ranging from normal to cortical and subcortical lesions, like in our patient, to involvement of deep brain structures with or without brain edema. All patients were treated with Oseltamivir. Two patients received simultaneously treatment with corticosteroids. There was a complete recovery of neurologic manifestations in two patients; in three other patients mild to severe neurologic sequelae were noted.

In conclusion, encephalitis is a rare neurological complication of influenza H1N1 virus in adults. By publishing this case report we hope to contribute by the further characterization of this group of patients. H1N1-associated encephalitis must be considered in the differential diagnosis in patients with influenza-like illness and altered mental status. Diagnosis is based on neurological and neuroimaging findings, and CSF analysis in combination with laboratory-confirmed H1N1 respiratory tract infection.

**Bibliografía**


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