Equal Author Contribution:

Contributions:
Amy C. Kunchok: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data; Study concept or design; Analysis or interpretation of data
Daniel Ontaneda: Drafting/revision of the manuscript for content, including medical writing for content; Analysis or interpretation of data
Jonathan Lee: Drafting/revision of the manuscript for content, including medical writing for content; Analysis or interpretation of data
Alexander Rae-Grant: Drafting/revision of the manuscript for content, including medical writing for content; Analysis or interpretation of data
Nancy Foldvary-Schaefer: Drafting/revision of the manuscript for content, including medical writing for content; Analysis or interpretation of data
Jeffrey A. Cohen: Drafting/revision of the manuscript for content, including medical writing for content; Analysis or interpretation of data
Stephen E Jones: Drafting/revision of the manuscript for content, including medical writing for content; Analysis or interpretation of data

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Anti-Ma1/Ma2 paraneoplastic neurological syndrome (PNS) is rare and often associated with testicular malignancies.\(^1\) Diencephalitis is a characteristic feature of anti-Ma1/Ma2 PNS.\(^1\) In contrast to classical limbic encephalitis,\(^2\) the clinical and radiological manifestations of diencephalitis may be initially subtle and under-recognized as PNS.

Here we show brain MRIs for seven patients with anti-Ma1/Ma2 PNS. All 7 had clinical features of diencephalitis including; hypersomnolence, narcolepsy-cataplexy, hyperphagia, syndrome of inappropriate antidiuretic hormone (Table). Other manifestations included rhombencephalitis (6), limbic encephalitis (4), limb weakness (2). All had brain MRI demonstrating symmetrical T2/FLAIR hyperintensity of the diencephalon (middle-ventral hypothalamus and posterior mammillary bodies) (Figure). Other MRI features included T2/FLAIR hyperintensity of the medial thalami, midbrain, pons and mesial temporal lobes. Several MRI were initially misinterpreted as Wernicke’s encephalopathy. These highlight the unique MRI features of anti-Ma1/Ma2 PNS paraneoplastic diencephalitis which may prompt further evaluation for Ma1/Ma2-IgGs and malignancy, in the appropriate setting.
<table>
<thead>
<tr>
<th>No., Age, Sex</th>
<th>Ab</th>
<th>Clinical syndrome</th>
<th>Oncological diagnosis/evaluation</th>
<th>Earliest Brain MRI (days from symptom onset)</th>
<th>Subsequent MRIs (summary)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1, 46, F</td>
<td>ma1, ma2</td>
<td>Diencephalitis (hypersomnolence, hyperphagia, SIADH) Limbic encephalitis (agitation, confusion, seizures, emotional lability, hallucinations) Rhombencephalitis (opsoclonus). Upper and lower limb weakness</td>
<td>Renal cell carcinoma</td>
<td>Brain: T2/FLAIR hyperintensity and Gd+ of bilateral tuber cinerum and mammillary bodies (20 days).</td>
<td>Brain: progressive T2/FLAIR hyperintensity and Gd+ of medial temporal lobes and gyrus rectus followed by atrophy. Spine: leptomeningeal Gd+ of whole spine, cauda equina and cervical nerve roots.</td>
</tr>
<tr>
<td>2, 21, M</td>
<td>ma1, ma2</td>
<td>Diencephalitis (hypersomnolence, narcolepsy-cataplexy, hyperphagia, SIADH) Rhombencephalitis (vertical gaze palsy, nystagmus)</td>
<td>Testicular germ cell</td>
<td>Brain: T2/FLAIR hyperintensity of bilateral tuber cinerum, mammillary bodies; Gd+ extending to the infundibular stalk (78 days).</td>
<td>Brain: progressive T2/FLAIR hyperintensity of bilateral periaqueductal region, supraoptic hypothalamus, anterior perforated substance, and anterior commissure. Progressive atrophy of tuber cinerum and mammillary bodies.</td>
</tr>
<tr>
<td>3, 54, M</td>
<td>ma1, ma2</td>
<td>Diencephalitis (hypersomnolence, hyperphagia, sexual dysfunction) Rhombencephalitis (opsoclonus, pseudobulbar palsy) Cerebellitis (gait ataxia)</td>
<td>Testicular germ cell</td>
<td>Brain: T2/FLAIR hyperintensity of bilateral medial thalami, tuber cinerum and mammillary bodies (51 days).</td>
<td>Brain: progressive T2/FLAIR hyperintensity of bilateral mesial temporal lobes.</td>
</tr>
<tr>
<td>4, 60, F</td>
<td>ma1, ma2</td>
<td>Diencephalitis (narcolepsy-cataplexy) Rhombencephalitis (vertical gaze palsy, nystagmus)</td>
<td>Initial cancer screen (CT C/A/P, FDG-PET body) negative</td>
<td>Brain*: T2/FLAIR hyperintensity of bilateral tuber cinerum and mammillary bodies. Patchy T2/FLAIR in midbrain and pons along decussation of superior cerebellar peduncles (12 days).</td>
<td>Brain: progressive atrophy of tuber cinerum and mammillary bodies.</td>
</tr>
<tr>
<td>5, 57, M</td>
<td>ma1, ma2</td>
<td>Diencephalitis (hypersomnolence, sexual dysfunction) Limbic encephalitis (agitation, confusion, emotional lability, hallucinations)</td>
<td>Testicular germ cell</td>
<td>Brain: T2/FLAIR hyperintensity of bilateral tuber cinerum, mammillary bodies, supraoptic hypothalamus, medial thalami, ventral midbrain, and mesial temporal lobes. Bilateral patchy Gd+ of mesial temporal lobes (373 days).</td>
<td>Brain: progressive atrophy of bilateral tuber cinerum, mammillary bodies, supraoptic hypothalamus, medial thalami, ventral midbrain, and mesial temporal lobes.</td>
</tr>
<tr>
<td>6, 48, M</td>
<td>ma2</td>
<td>Diencephalitis (hypersomnolence, narcolepsy-cataplexy, hyperphagia, SIADH, hyperthermia, sexual dysfunction) Limbic encephalitis (agitation, confusion, seizures, emotional lability, hallucinations)</td>
<td>Testicular microcalcifications, pathology negative for</td>
<td>Brain: T2/FLAIR hyperintensity and Gd+ of bilateral supraoptic hypothalamus, tuber cinerum, and mammillary bodies (50 days)</td>
<td>Brain: progressive atrophy of bilateral supraoptic hypothalamus, tuber cinerum, and mammillary bodies. Spine: leptomeningeal Gd+ of distal conus and cauda equina.</td>
</tr>
<tr>
<td>ID</td>
<td>Age</td>
<td>Gender</td>
<td>Symptoms</td>
<td>Diagnosis</td>
<td>Findings</td>
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<tr>
<td>7, 32, M</td>
<td>ma2</td>
<td></td>
<td>Rhombencephalitis (pseudobulbar palsy) Lower limb weakness</td>
<td>neoplasm</td>
<td>Brain: T2/FLAIR hyperintensity and Gd+ of bilateral tuber cinerum, mammillary bodies and temporal lobes (381 days)</td>
</tr>
</tbody>
</table>
Title: Clinical-radiological features of anti-Ma1/Ma2 paraneoplastic syndrome

Table legend:

Notes:

Patients #1-6 brain MRI were completed prior to immunotherapy.

Patient #7 had initial imaging externally and this was not available for review. He had received steroids and plasmapheresis 6 m prior to the earliest available brain MRI presented here.

Patient #4 had an initial non-contrast brain MRI.

All patients were treated with immunotherapy prior to subsequent MRI.

Abbreviations:

Gadolinium enhancement (Gd+)
Syndrome of inappropriate antidiuretic hormone (SIADH)
Fluorodeoxyglucose (FDG)-positron emission tomography (FDG-PET)
Computed tomography (CT)
Chest, abdomen, pelvis (C/A/P)
Fluid-attenuated inversion recovery (FLAIR)
Male (M)
Female (F)
Antibody (Ab)
Figure: MRI brain of anti-Ma1/Ma2 patients demonstrating hypothalamic involvement

(A): FLAIR axial images demonstrating symmetrical T2/FLAIR hyperintensity of the bilateral hypothalamus (supraoptic hypothalamus, tuber cinereum, mammillary bodies) and anteromedial thalamus (red arrows).

B: Post-contrast T1-weighted coronal images demonstrating gadolinium-enhancement of the bilateral tuber cinereum and mammillary bodies in four patients (red arrows).

References


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