Bilateral Thalamic Lesions Associated With Atezolizumab-Induced Encephalitis: A Follow-up Report With Autopsy Findings

Author(s):
Haruo Nishijima, MD, PhD1,2; Tomoya Kon, MD, PhD1; Yusuke Seino, MD, PhD3; Norito Yagihashi, MD, PhD4; Chieko Suzuki, MD, PhD1; Takashi Nakamura, MD1,2; Hisashi Tanaka, MD, PhD5; Yui Sakamoto, MD5; Koichi Wakabayashi, MD, PhD7; Masahiko Tomiyama, MD, PhD1

Corresponding Author:
Haruo Nishijima
haruonishijima@gmail.com

Neurology® Published Ahead of Print articles have been peer reviewed and accepted for publication. This manuscript will be published in its final form after copyediting, page composition, and review of proofs. Errors that could affect the content may be corrected during these processes.
Affiliation Information for All Authors: 1. Department of Neurology, Institute of Brain Science, Hirosaki University Graduate School of Medicine, Hirosaki City, Aomori, Japan; 2. Department of Neurology, Hirosaki University Hospital, Hirosaki City, Aomori, Japan; 3. Department of Neurology, Hirosaki National Hospital, Hirosaki City, Aomori, Japan; 4. Division of Pathology and Clinical Laboratory, Hirosaki National Hospital, Hirosaki City, Aomori, Japan; 5. Department of Respiratory Medicine, Hirosaki University Graduate School of Medicine, Hirosaki City, Aomori, Japan; 6. Department of Neuropsychiatry, Hirosaki University Graduate School of Medicine, Hirosaki City, Aomori, Japan; 7. Department of Neuropathology, Institute of Brain Science, Hirosaki University Graduate School of Medicine, Hirosaki City, Aomori, Japan.

Contributions:
Haruo Nishijima: 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
Tomoya Kon: 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
Yusuke Seino: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data
Norito Yagihashi: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data; Analysis or interpretation of data
Chieko Suzuki: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data
Takashi Nakamura: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data
Hisashi Tanaka: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data
Yui Sakamoto: Drafting/revision of the manuscript for content, including medical writing for content; Major role in the acquisition of data
Koichi Wakabayashi: Drafting/revision of the manuscript for content, including medical writing for content; Study concept or design; Analysis or interpretation of data
Masahiko Tomiyama: Drafting/revision of the manuscript for content, including medical writing for content; Study concept or design; Analysis or interpretation of data

Number of characters in title: 118
Abstract Word count: 0
Word count of main text: 155
References: 2
Figures: 1
Supplemental: Patient consent


Acknowledgements: We would like to thank Editage (www.editage.com) for English language editing.

Study Funding: The authors report no targeted funding

Disclosures: All the authors report no disclosures relevant to the manuscript.
Case Summary:

A 72-year-old woman was clinically diagnosed with atezolizumab-induced encephalitis.\(^1\)

HER CLINICAL FEATURES WERE PREVIOUSLY DESCRIBED IN THIS JOURNAL AND HERE WE PRESENT THE AUTOPSY FINDINGS. She had been treated with atezolizumab, an immune check-point inhibitor (ICPI), due to a metastatic non-small cell lung cancer diagnosis. She received her final atezolizumab injection three weeks after encephalitis onset, and cancer therapy ceased. Although the bilateral thalamic lesions shrank after steroid pulse, intravenous immunoglobulin, and long-term oral steroid, the patient died due to aspiration pneumonia seven months after encephalitis onset. An autopsy revealed no evidence of cancer recurrence. Brain histological analyses revealed lymphocytic infiltration only into the thalamus, without infection or metastasis (Figure). Both B and T cell infiltration was identified accompanied by neuronal loss and thalamic gliosis. The T-cell infiltration was in-agreement with previous work describing ICPI-induced encephalitis,\(^2\) suggesting mechanistic-overlap with encephalitis/encephalopathy caused by paraneoplastic syndromes. Additionally, this case indicates that B-cells also contribute to inflammatory process.
<table>
<thead>
<tr>
<th>Name</th>
<th>Location</th>
<th>Contribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haruo Nishijima, MD, PhD</td>
<td>Hirosaki University Graduate School of Medicine, Hirosaki, Japan</td>
<td>Design and conceptualized study; patient care and acquisition of data; analyzed the data; drafted the manuscript for intellectual content</td>
</tr>
<tr>
<td>Tomoya Kon, MD, PhD</td>
<td>Hirosaki University Graduate School of Medicine, Hirosaki, Japan</td>
<td>Design and conceptualized study; patient care and acquisition of data; analyzed the data; revised the manuscript for intellectual content</td>
</tr>
<tr>
<td>Yusuke Seino, MD, PhD</td>
<td>Hirosaki National Hospital, Hirosaki, Japan</td>
<td>Patient care and acquisition of data; revised the manuscript for intellectual content</td>
</tr>
<tr>
<td>Norito Yagihashi, MD, PhD</td>
<td>Hirosaki National Hospital, Hirosaki, Japan</td>
<td>Acquisition of data; analyzed the data; interpreted the data; revised the manuscript for intellectual content</td>
</tr>
<tr>
<td>Chieko Suzuki, MD, PhD</td>
<td>Hirosaki University Graduate School of Medicine, Hirosaki, Japan</td>
<td>Patient care and acquisition of data; interpreted the data; revised the manuscript for intellectual content</td>
</tr>
<tr>
<td>Takashi Nakamura, MD</td>
<td>Hirosaki University Graduate School of Medicine, Hirosaki, Japan</td>
<td>Patient care and acquisition of data</td>
</tr>
<tr>
<td>Hisashi Tanaka, MD, PhD</td>
<td>Hirosaki University Graduate School of Medicine, Hirosaki, Japan</td>
<td>Patient care and acquisition of data; revised the manuscript for intellectual content</td>
</tr>
<tr>
<td>Name</td>
<td>Affiliation</td>
<td>Contributions</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>--------------------------------------------------</td>
<td>-------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Yui Sakamoto, MD</td>
<td>Hirosaki University Graduate School of Medicine, Hirosaki, Japan</td>
<td>Patient care and acquisition of data; revised the manuscript for intellectual content</td>
</tr>
<tr>
<td>Koishi Wakabayashi, MD, PhD</td>
<td>Hirosaki University Graduate School of Medicine, Hirosaki, Japan</td>
<td>Acquisition of data; analyzed the data; interpreted the data; revised the manuscript for intellectual content</td>
</tr>
<tr>
<td>Masahiko Tomiyama, MD, PhD</td>
<td>Hirosaki University Graduate School of Medicine, Hirosaki, Japan</td>
<td>Interpreted the data; revised the manuscript for intellectual content</td>
</tr>
</tbody>
</table>
Figure Legend:

Histological brain findings

(A) Atrophy with myelin pallor in the right thalamus (arrows; Klüver–Barrera stain). (B) Perivascular lymphocyte infiltration (arrowhead) and marked neuronal loss and gliosis (asterisk; Hematoxylin stain). (C,D) Infiltrating lymphocytes were immune-positive for CD3 (C) and CD20 (D). Bars = 5 mm (A), 100 µm (B-D).
References


Bilateral Thalamic Lesions Associated With Atezolizumab-Induced Encephalitis: A Follow-up Report With Autopsy Findings
Haruo Nishijima, Tomoya Kon, Yusuke Seino, et al.
Neurology published online November 19, 2021
DOI 10.1212/WNL.0000000000013091

This information is current as of November 19, 2021

Updated Information & Services
including high resolution figures, can be found at:
http://n.neurology.org/content/early/2021/11/18/WNL.0000000000013091.citation.full

Subspecialty Collections
This article, along with others on similar topics, appears in the following collection(s):
All Epilepsy/Seizures
http://n.neurology.org/cgi/collection/all_epilepsy_seizures
Status epilepticus
http://n.neurology.org/cgi/collection/status_epilepticus

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
http://www.neurology.org/about/about_the_journal#permissions

Reprints
Information about ordering reprints can be found online:
http://n.neurology.org/subscribers/advertise