Adaptive B-cell and T-cell responses to SARS-CoV-2 vaccination in patients with Multiple Sclerosis on disease modifying immunotherapies

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Introduction

- Immunomodulatory therapies prescribed for patients with Multiple Sclerosis (MS) have been associated with decreased or absent anti-SARS-CoV-2 immunoglobulin production following COVID-19 vaccination.1,2
- While disease modifying treatments (DMTs) are deemed to have an acceptable safety profile during the COVID-19 pandemic, anti-CD20 therapy has been associated with increased risk of severe COVID-19 infection.3
- The risk of attenuated immunity to COVID-19 vaccines may differ according to DMT class and mechanism of action.4
- Antibody testing does not assess the post-vaccination cellular immune response by which T cell immunity may contribute to humoral immunity.
- We investigated humoral and cell-mediated responses to SARS-CoV-2 vaccination in patients with MS on DMTs, including anti-CD20 and S1P therapies.

Methods

- Using the Stanford Research Repository database, we identified 79 MS patients – based on the 2017 McDonald Criteria5 and IC19 code – who were on a stable DMT regimen for MS and were tested for humoral and cellular reactivity against the SARS-CoV-2 spike protein post-COVID vaccination.
- B-cell and T-cell responses were tested using SARS-CoV-2-IgG and SARS-CoV-2 Interferon Gamma Release Assay (IGRA), respectively.
- The following groups were analyzed: patients on anti-CD20 therapy (alemtuzumab, ofatumumab, rituximab) (n=37), patients on S1P modulators (fingolimod, dimethyl fumarate, monomethyl fumarate, glatiramer acetate, natalizumab, and daclizumab) (n=26).
- Differences among groups were assessed using Chi-Square Test for categorical variables and T-test for continuous variables. Results significant if p<0.05.
- All vaccinated patients were assessed between 4 weeks and 10 months after receiving at least one dose of the COVID-19 vaccine. Assessments were completed between December 2020 and February 2022.

Table 1: Baseline demographics and clinical characteristics according to DMT. SD: Standard Deviation, CI: Clinically Isolated Syndrome, PPND: Primary progressive MS, S1P: S1P modulators, MS: Multiple Sclerosis, B19: Transverse Myelitis, ALC: Absolute Lymphocyte Count.

<table>
<thead>
<tr>
<th>Group</th>
<th>Subjects (n=79)</th>
<th>Anti-CD20</th>
<th>S1P modulators</th>
<th>Other or off DMT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-CD20</td>
<td>37</td>
<td>16</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Gender (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>25 (67.6)</td>
<td>14 (87.5)</td>
<td>11 (69.2)</td>
<td></td>
</tr>
<tr>
<td>Age (years) (SD)</td>
<td>48.0 (14.7)</td>
<td>48.30 (13.0)</td>
<td>51.6 (11.6)</td>
<td></td>
</tr>
<tr>
<td>Diagnosis (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD10</td>
<td>-</td>
<td>-</td>
<td>3 (11.5)</td>
<td></td>
</tr>
<tr>
<td>PPMS</td>
<td>6 (16.2)</td>
<td>-</td>
<td>1 (3.8)</td>
<td></td>
</tr>
<tr>
<td>RRMS</td>
<td>26 (70.3)</td>
<td>14 (87.5)</td>
<td>18 (69.2)</td>
<td></td>
</tr>
<tr>
<td>SPMS</td>
<td>5 (13.5)</td>
<td>2 (12.5)</td>
<td>3 (11.5)</td>
<td></td>
</tr>
<tr>
<td>TM</td>
<td>1 (2.7)</td>
<td>-</td>
<td>1 (3.8)</td>
<td></td>
</tr>
<tr>
<td>Disease duration (SD)</td>
<td>10.36 (6.11)</td>
<td>11.09 (8.63)</td>
<td>14.6 (10.4)</td>
<td></td>
</tr>
</tbody>
</table>

Race (%)

- Asian               | 8 (21.6)       | 1 (6.2)  | 1 (3.8)        |
- Black                | 1 (2.7)        | 1 (6.2)  | -              |
- White                | 22 (59.2)      | 12 (75.6) | 22 (84.6)     |
- Other                | 5 (13.5)       | 1 (6.2)  | 3 (11.5)       |
- Unknown              | 1 (2.7)        | 1 (6.2)  | -              |

Ethnicity (%)

- Hispanic/Latino      | 2 (5.4)        | 1 (6.2)  | 3 (11.5)       |
- Non-Hispanic         | 35 (94.6)      | 13 (81.2) | 23 (88.5)     |
- Unknown              | -              | 2 (12.5) | -              |

Type of Vaccine (%)

| mRNA                  | 26 (97.6)      | 16 (100) | 24 (92.3)      |
| Viral Vector          | 1 (2.7)        | -        | 2 (7.7)        |
| Fully Vaccinated (%)  | 33.55 (58.3)   | -        | 290 (182.5)    |

CD19 count (SD)6

- 1268 (509.0)        | 545.5 (597.5)  | 2299.3 (1928.7) |

ALC (SD)^7

- 8 (21.6)            | 1 (6.2)        | 25 (96.2)    |
- Igg and IGRA response (%)^6

| Igg and IGRA response | 8 (21.6) | 1 (6.2) | 25 (96.2) |

| Igg response only     | -        | 2 (12.5) | -          |
| IGRA response only    | 26 (70.3) | 2 (12.5) | 1 (3.8)    |
| No response           | 3 (8.1)  | 11 (68.8) | -          |

Results

- Table 1: Baseline demographics and clinical characteristics according to DMT.

Figure 1: Types of disease modifying treatment (DMT) used by MS patients at the time of vaccination.

Figure 2: Vaccine response according to DMT.

Figure 3: Mean CD19 count according to DMT.

Figure 4: Mean ALC according to DMT.

Figure 5: A) Change in ALC per patient with anti-CD20 therapy, B) Change in ALC per patient with delayed interferon (4 months), C) ALC per patient on anti-CD20 with no Interferon Response.

Conclusions

- Treatment with anti-CD20 therapy and S1P modulator therapy was associated with attenuated immune response to COVID-19 vaccination.
- Treatment with anti-CD20 therapy was associated with attenuated humoral response (IgG) but preserved cellular T cell response to vaccination.
- Treatment with S1P modulators yielded absence of both humoral and cellular response to vaccination.
- MS patients treated with other DMT classes including interferon beta, glatiramer, fumarates and natalizumab showed measurable humoral and cellular response to COVID vaccination.
- MS patients off DMT showed measurable B cell and T cell response to COVID vaccination.
- Clinical correlation with the results of SARS-CoV-IgG and SARS-CoV-2 IRGA is not established.
- Possible confounding effects of natural asymptomatic or unconfirmed COVID infection are not assessed in this study.

References


Disclosures

Support for this research and attendant analysis was provided by Project BIG, the CRUSH MS Foundation, and The Garrett Fund, free of commercial or institutional sponsorship. Individual author COI are as listed in AAN registry.

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