



Commentary

Monkeypox in Multiple Sclerosis patients: Should we be alert?

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Dear Editor,

Previously reported as sporadic outbreaks in West and Central Africa, monkeypox virus infection is now occurring worldwide and has been classified by World Health Organization (WHO) as a Public Health Emergency of International Concern (PHEIC). Until 25 June, 3,000 cases of monkeypox had been reported in 47 countries. Strikingly, by 23 July, more than 16,000 cases from 75 countries and territories were already reported causing five deaths (Taylor, 2022). According to WHO, by 06 October, there are a total of 71,237 laboratory-confirmed cases of the disease and 1,097 probable cases, including 26 deaths. To date, the 10 most affected countries globally are: United States of America ($n = 26,723$), Brazil ($n = 8,147$), Spain ($n = 7,209$), France ($n = 4,043$), The United Kingdom ($n = 3,654$), Germany ($n = 3,640$), Peru ($n = 2,587$), Colombia ($n = 2,453$), Mexico ($n = 1,968$) and Canada ($n = 1,400$). Together, these countries account for 86.8% of the total cases reported for monkeypox worldwide (WHO, 2022).

From April to June 2022, Thornhill and coworkers (Thornhill et al., 2022) reported a cohort of 528 infected individuals, in which transmission was almost totally (95%) suspected to occurring through sexual activity among white (75%), gay or bisexual men (98%) with the diagnosis (41%) of human immunodeficiency virus (HIV) infection. In this cohort, the most common clinical findings included: rash or skin lesions (95%), fever (62%), lymphadenopathy (56%), lethargy or exhaustion (41%), myalgia (31%), headache (27%), among others. Hospitalization was more likely associated with pain management and soft-tissue superinfection, less commonly with acute kidney injury and myocarditis.

To date, as reported, amplification of transmission through sexual networks disproportionately affected men who have sex with men; however, besides sexual and close contact with skin lesions, nosocomial transmission and contaminated fomites (Adler et al., 2022; Thornhill et al., 2022) could rapidly spread monkeypox virus.

Worldwide dissemination would particularly impact young children,

pregnant women, and immunocompromised individuals who would be more prone to experience serious events such as encephalitis and secondary bacterial infections (Thornhill et al., 2022). Moreover, considering the impaired immune responses during autoimmunity, it is possible to speculate that Multiple Sclerosis (MS) patients (particularly under certain types of treatments) would also experience the worst outcomes during monkeypox infection.

For instance, the recent experience with COVID-19 showed that MS patients with increased disability (as measured by EDSS) and using anti-CD20 therapies (rituximab and ocrelizumab) presented the worst outcomes including severe infection, hospitalization and mortality (Barzegar et al., 2020; Ponzano et al., 2022; Salter et al., 2021; Schiavetti et al., 2022).

Regarding vaccination, MS patients presented different neutralizing antibody responses against SARS-CoV-2 (77%) vs. healthy controls (93%). MS patients during disease-modifying therapies (DMTs) exhibited: >93% positive antibody responses during glatiramer acetate, beta-interferons, dimethyl-fumarate, teriflunomide, alemtuzumab, and natalizumab; while those treated with fingolimod (27%) and anti-CD20 therapies (44%) showed lower positive antibody responses (Etemadifar et al., 2022; Gombolay et al., 2022).

Lower effective cellular immune responses through CD4⁺ and CD8⁺ T lymphocytes after SARS-CoV-2 vaccination were also suggested for MS patients during interferon, fingolimod and cladribine treatments (Etemadifar et al., 2022; Gombolay et al., 2022; Iannetta et al., 2022; Tortorella et al., 2022).

We can hypothesize that similar features of defective antiviral immune responses observed with COVID-19 may occur in the event of monkeypox infection in MS patients treated with DMTs (summarized in Fig. 1).

The risk of suboptimal immune responses in MS patients raises our concerns regarding the need for careful management of the DMTs schedule, the introduction of antiviral therapies, vaccination, and the

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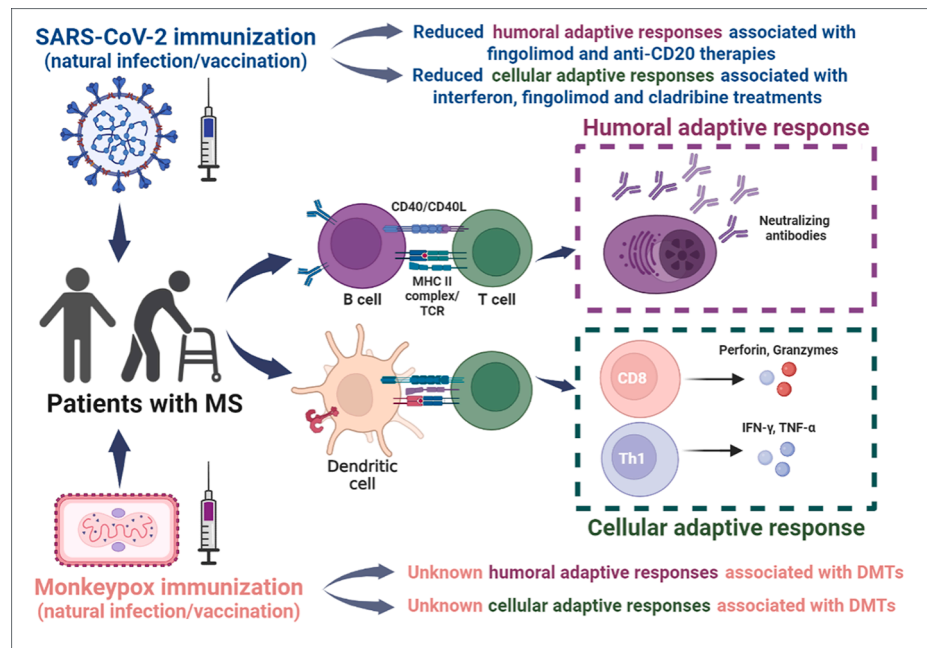


Fig. 1. Proposed impaired immunological responses during Monkeypox infection/vaccination in MS patients using DMTs. Defective humoral/cellular immune adaptive responses were described for SARS-CoV-2 natural infection/vaccination in MS patients during disease modifying therapies (DMTs). Similarly, these mechanisms may also be impacted during monkeypox natural infection/vaccination in MS patients using DMTs. Created with BioRender.com.

eventual risk for disease exacerbation on the occasion of widespread monkeypox infection.

Author's contributions

V.O.B., A.D. and C.L.Y. wrote the manuscript.

Declaration of Competing Interest

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