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Letter

Natalizumab safety in paediatric-onset multiple sclerosis at the time of SARS-Cov-2 pandemic

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In their recent review, Hacohen et al.[1] have highlighted two major questions in treating paediatric onset multiple sclerosis (POMS): (1) are first-line disease-modifying therapies still an optimal option for children/teens? (2) are highly effective second-line immunosuppressive therapies safe in POMS, especially during a viral pandemic?

The authors, considering the impact of MS on brain atrophy and the high risk POMS have to develop cognitive impairment and evolve in the secondary progressive disease phase, recommend to keep in mind that MS in children/teens is a severe, highly active form of disease, and suggest the early use of highly effective second-line disease modifying drugs rather than the first-line injectable ones. We fully agree with these recommendations and, actually, several years ago we started to treat POMS with natalizumab (NTZ), with excellent clinical results, no severe adverse event and favoring a better quality of life of children/teens.[2,3]

Undoubtedly, the SARS-Cov-2 pandemic constitutes a major concern for MS patients treated with drugs that reduce lymphocyte number and function (including blood-brain barrier trafficking). May these drugs expose POMS to a greater risk of SARS-Cov-2 infection as well as to a symptomatic and potentially more severe COVID-19 or to long-term autoimmune severe adverse events? No pre-established answer is available. Some reports seem to indicate that second-line therapies do not significantly increase the risk of COVID-19, with some concerns about therapy with anti-CD20 monoclonal antibodies.[4,5] However, no data have been published in POMS.

We would like to briefly share our experience. The Veneto Region of Italy, where the City and Province of Padua are located, was early ran over by the SARS-Cov-2 pandemic and marked as a red zone as early as March 8, 2020. Despite the lockdown and uncertainty about immunosuppressive/immunomodulating drugs, we decided to continue POMS treatment with NTZ. From the beginning of March to the end of July 2020, 26 POMS (5 males and 21 females), having a mean age of 15.5 ± 1.2 (range 13–17) years and a mean disease duration of 1.8 ± 1.7 (range 0–7) years have been treated with NTZ either with standard interval dosing (every four weeks, $n = 24$) or with the extended interval dosing (every six weeks, $n = 2$), without interruption. All patients and parents were advised in detail on the Covid-19 risk and were instructed on the use of the individual protection devices as well as to apply scrupulously the recommendations of the Italian Ministry of Health. NTZ was administered only after having obtained, before each infusion, a detailed history about recent infective symptoms and body temperature recording.

During the observational period, only one patient complained a mild upper respiratory tract syndrome (low-grade transient fever and mild coughing), but three consecutive nasopharyngeal swabs and RT-PCR testing for SARS-Cov-2 gave negative results. All the other patients remained completely asymptomatic. Antibody testing for SARS-Cov-2 were not available before June 2020, and, actually, the internal guidelines of our University Hospital do not consider antibody testing in asymptomatic patients.

NTZ treatment does not seem not to expose POMS to a higher risk of SARS-Cov-2 infection. Although a mild association of NTZ with the risk of Covid-19 ($p = 0.02$) was observed in adult MS patients in the Italian Musc-19 Study,[4] after adjusting for age, sex, progressive MS course and recent methylprednisolone use, only the anti-CD20 therapy (ocrelizumab or rituximab) was significantly associated

($p < 0.001$) with an increased risk of severe Covid-19 course.

Of course, the possibility exists that some patients, given their young age, could have contract the virus remaining asymptomatic. If that's the case, however, we may suppose that NTZ did not increase the risk of having clinically overt or severe disease. Moreover, the scrupulous observance of the rules aimed at preventing outside exposure to infection, that patients and relatives were strongly invited to respect, have certainly contributed to the safety of the treatment.

Our findings are particularly comforting in view of the possible second pandemic wave expected in Autumn.

Conflict of interests

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