Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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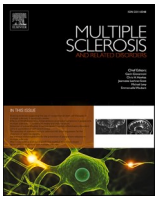

COVID-19 in neuromyelitis optica spectrum disorder patients in Poland

1. Introduction

The course of COVID-19 in patients with autoimmune diseases aroused great interest among doctors from the beginning of the pandemic. Central nervous system autoimmune diseases occupy a special place here. The most common is multiple sclerosis which is well evidenced. Neuromyelitis optica spectrum disorders (NMOSD) on the other hand is a rare disease, therefore data on the course of COVID-19 in these patients are so far limited. Experience in taking care of MS patients cannot be transferred to NMOSD patients because these two groups are clearly different. NMOSD patients are older and therefore may have more comorbidities. In addition, they often have a higher degree of disability compared to MS patients, which was associated with a higher risk of severe COVID-19 course. Due to aggressive course of NMOSD immunosuppressive treatment is necessary. According to our current knowledge NMOSD therapies are associated with an increased risk of infections (viral and bacterial) (Holmoy et al., 2020). At the time of the COVID-19 pandemic, the question arose about the impact of SARS-CoV-2 infection on NMOSD patients and whether immunosuppressive treatment, e.g. with anti-CD20 or anti-CD19, is safe. The aim of this study was to describe the clinical characteristics and outcomes of NMOSD patients infected with COVID-19.

2. Material and methods

Department of Neurology Medical University of Warsaw is a reference center for treatment of NMOSD patients in Poland. We take care of eighty-one patients meeting the 2015 International Panel for NMOSD criteria (about 40% of estimated Polish NMOSD patients). Patients' data are collected in the Polish registry of NMOSD patients. Registry has been approved by the Ethics Committee of the Medical University of Warsaw. Data collection was related to specific variables such as sex, comorbidities, age at disease onset, disease duration, aquaporin-4 antibody and anti-MOG status, disability at the last follow-up evaluated by Expanded Disability Status Scale (EDSS), treatment, infections.

SARS-CoV2 infection was confirmed by reverse transcription polymerase chain reaction [RT-PCR] and/or IgM or IgG seropositivity. The severity of SARS-CoV-2 infection was assessed using WHO Clinical Progression Scale (0 - non-viral RNA detected; 1 - ambulatory asymptomatic, viral RNA detected; 2 - ambulatory symptomatic, independent; 3 - ambulatory symptomatic, assistance needed; 4 –mild disease hospitalized, no oxygen therapy; 5 - mild disease hospitalized, oxygen by mask or nasal prongs; 6 - severe disease hospitalized, oxygen by NIV or High flow; 7 - severe disease intubation and mechanical ventilation, O2/FIO2>=150 or SpO2/FIO2>=200; 8 - severe disease mechanical ventilation, (pO2/FIO2<150 or SpO2/FIO2<200) or vasopressors (norepinephrine >0.3 μg/kg/min); 9 - severe disease, mechanical ventilation, pO2/FIO2<150 AND vasopressors (norepinephrine >0.3 μg/kg/min), or dialysis or ECMO; 10 – death). Chest CT data were recorded when available.

3. Results

As of April 30, 2021, we registered 22 SARS-CoV-2 infections in our NMOSD patients (19 females, 3 males). Mean age of patients was 48.7 years (range 30 – 67), mean duration of the disease 75.5 months (range 4 – 150), mean EDSS 4.5 (range 2.0–8.0). Anti-Aquaporin 4 antibodies were positive in 12 patients (54.5%), anti-MOG antibody was found in one patient. Twelve patients (54.5%) had no comorbidity. Hypertension (27.2%), obesity (36.3%), dyslipidemia (18.2%) and diabetes (9%) were the most common comorbidities.

Twenty (90.9%) patients were on immunosuppressive therapy. Thirteen patients were treated with anti-CD20 or anti-CD19 therapies (rituximab – 10 persons, inebilizumab – 3). Four patients were taking oral corticosteroids, and the remaining drugs were given to individual patients (azathioprine - 1, satralizumab - 1, mycophenolate mofetil - 1).

Main symptoms of COVID-19 included fever or chill (50%), dry cough (36.4%), myalgia (40.9%), fatigue (68.2%), rhinitis (13.6%) and dyspnea (40.9%). Gastrointestinal symptoms that occurred in 3 of 22 patients were diarrhea (2; 9%) and abdominal pain (1; 4.5%). Neurologic symptoms included headache (31.8%), anosmia (22.7%) and ageusia (31.8%). None of the patients died. 64% (14) of patients were asymptomatic or had mild symptoms of SARS-CoV-2 infection (score 1 in 11 patients, score 2 in 3 patients).

Eight patients (36%) were hospitalized: mean age of these patients was 43.6 years (range 30 – 59), mean EDSS 5.4 (range 3.0–8.0), mean duration of the disease 62.7 months (range 2 – 150). Four of these patients were treated with corticosteroids, two with rituximab and corticosteroids, and two with rituximab. In 3 cases these were patients with newly diagnosed NMOSD. Four patients developed infection during relapse treatment (corticosteroids and plasmapheresis). Only 4 out of eight hospitalized patients required oxygen therapy.

A severe course of COVID-19, requiring intubation and mechanical ventilation, occurred in one patient (score 7). Prior to COVID-19 this patient was successfully treated with rituximab due to very active NMOSD. SARS-CoV-2 infection occurred shortly after the second dose of rituximab was administered. The patient came to the hospital very late, as 95% of his lungs were already infected. He required mechanical ventilation for 35 days. The SARS-CoV-2 infection resulted in a severe relapse (EDSS 8.0) but all relapse symptoms resolved after treatment with corticosteroids. Patient is fully ambulatory, works in the previous position, this patient's current EDSS is 3.5. In total, 4 patients treated with rituximab were hospitalized. In 3 patients, SARS-CoV-2 infection developed during relapse treatment in the hospital. Two patient had

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mild symptoms of COVID-19 and SARS-CoV-2 infection only extended hospitalization resulting from relapse therapy. Only one patient required oxygen therapy for 3 days. Currently, this patient is in a similar neurological condition to that before COVID-19. In summary, out of 13 patients treated with anti-CD20 or anti-CD-19 therapy, 2 experienced severe or moderate symptoms of COVID-19. The remaining 11 patients had COVID-19 with mild ($n = 7$) or no symptoms ($n = 4$). COVID-19 triggered an NMOSD relapse in 2 more patients. In one case, it was a patient treated with satralizumab. She had no symptoms of COVID-19, and the disease was confirmed because other members of her family were ill. The relapse was mild, all symptoms resolved after treatment with intravenous corticosteroids. The second relapse occurred in a patient who was not currently receiving immunosuppressive treatment. At the time of data collection, none of our patients had been vaccinated against SARS-CoV-2. During SARS-CoV-2 infection, treatment with corticosteroids, azathioprine, satralizumab and mycophenolate mofetil was continued. The administration of rituximab was delayed in most patients by 2–3 months. Before each treatment of rituximab, we evaluate the phenotyping of CD19/CD20 cells, and the subsequent administration of the drug depends on the degree of B lymphocyte repopulation.

4. Discussion

There have been many reports of COVID-19 in patients with multiple sclerosis, while data on NMOSD patients is sparse. The data from the literature are contradictory. North American authors reported high mortality (Newsome et al., 2021), while Brazilian authors (Apostolos-Pereira et al., 2021) indicated rather mild course of COVID-19 in NMOSD patients. Another reports (Esmaeili et al., 2021; Alonso et al., 2021) concluded that rituximab treatment was not safe during the pandemic. In our patient group there were no deaths and only 1 patient (4.5%) experienced severe COVID-19. Also, most of the patients treated with anti-CD20 or anti-CD19 therapies had a mild course of COVID-19. Taking into consideration the high risk of relapse, switching or discontinuing treatment seems to be much more dangerous than the potential effects of COVID-19. In our group, the high frequency of SARS-CoV-2 infection is noticeable (27%). It seems that this is due to the fact that PCR tests were performed even with minor symptoms of infection, and also at each addmission to the hospital (in asymptomatic patients).

5. Conclusion

In conclusion, the immunosuppressive treatment of NMOSD patients seems safe and the pandemic should certainly not be a reason for discontinuing this therapy. Nevertheless people with NMOSD should avoid exposure and adopt measures to minimize the risk of infection by SARS-CoV-2. Further data is also needed, including the effectiveness of vaccination against SARS-CoV-2 in these patients.

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Declaration of Competing Interest

Aleksandra Podlecka-Piętowska declares no conflict of interest with the study project.

Krzysztof Barć declares no conflict of interest with the study project.

Agata Denisiuk declares no conflict of interest with the study project.

Monika Nojszewska declares no conflict of interest with the study project.

Beata Zakrzewska-Pniewska declares no conflict of interest with the study project.

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Aleksandra Podlecka-Piętowska*, Krzysztof Barć, Agata Denisiuk, Monika Nojszewska, Beata Zakrzewska-Pniewska
Departament of Neurology, Medical University of Warsaw, Banacha 1a, 02-097 Warsaw, Poland

* Corresponding author.
E-mail addresses: apodlecka@wum.edu.pl (A. Podlecka-Piętowska), k.barc@wp.pl (K. Barć), monika.nojszewska@wum.edu.pl (M. Nojszewska), beata.zakrzewska@wum.edu.pl (B. Zakrzewska-Pniewska).