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Abstract

Background

Outcomes of coronavirus disease 2019 (COVID-19) in patients with neuromyelitis optica spectrum disorders (NMOSD) or myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), often treated with immunosuppressive therapies, are still unknown.

Methods

We conducted a multi-center, retrospective, observational cohort study among all French expert centers for neuromyelitis optica and related disorders. Patients with NMOSD or MOGAD included in the study received a confirmed or highly suspected diagnosis of COVID-19 between March 1, 2020 and June 30th, 2020. Main outcome was COVID-19 severity score assessed on a 7-point ordinal scale ranging from 1 (not hospitalized with no limitations on activities) to 7 (death).

Results

Fifteen cases (mean [SD] age: 39.3 [14.3] years, 11 female) were included. Five patients (33.3%) were hospitalized, all receiving rituximab. A 24-year-old patient with positive aquaporine-4 antibody, with obesity as comorbidity, needed mechanical ventilation. Outpatients were receiving anti-CD20 (5), mycophenolate mofetil (3) or azathioprine (3). They were younger (mean [SD] age: 37.0 [13.4] years), with a longer disease duration (mean [SD]: 8.3 [6.3] years) and had a lower EDSS score (median [range] EDSS: 2.5 [0-4]) relative to patients requiring hospitalization (mean [SD] age: 44.0 [16.4] years, mean [SD] disease duration: 5.8 [5.5] years, median [range] EDSS: 4 [0-6.5]).

Conclusions

COVID-19 outcome was overall favorable in this cohort. Larger international studies are needed to identify risk factors of severe COVID-19, however we recommend personal

protective measures to reduce risk of SARS-CoV-2 infection in this immunocompromised population.

Introduction

The severity of coronavirus disease 2019 (COVID-19) in patients with pre-existing neurological condition has been little described. While the first cohorts of patients with multiple sclerosis (MS) and COVID-19 do not seem to indicate a marked increased risk of severe form[1, 2], the impact of COVID-19 in patients with neuromyelitis optica spectrum disorders (NMOSD) or myelin oligodendrocyte glycoprotein (MOG) antibody-associated disease (MOGAD) is unknown.

NMOSD are associated with a more severe onset attacks, a higher relapse frequency and greater disability at follow-up compared to MS, which could predispose to severe infections. In addition, almost all patients receive immunosuppressive therapy, the worsening or possibly protective role of which during coronavirus infection remains to be determined[3]. Interestingly, monoclonal antibodies such as anti IL6 receptors (satralizumab, tocilizumab)[4, 5] and C5 inhibitors (eculizumab)[6], known to reduce relapse rate in NMOSD are currently being tested in clinical trials in COVID-19 related acute respiratory distress syndrome due to their possible effect on the “cytokine storm”.

In this study, we collected the cases of patients with NMOSD or MOGAD and COVID-19 in order to describe outcomes of COVID-19 and to identify risk factors associated with COVID-19 severity in this population.

Methods

Data collection

Patients were included in the Covisep registry, a multi-center, retrospective, observational cohort study of patients with MS, NMOSD or MOGAD with confirmed or highly suspected COVID-19 diagnosis (ClinicalTrials.gov, NCT04355611). All French MS expert centers and members of the French MS Society (Société Francophone de la Sclérose en plaques) participated in the collection of data. The study received approval from the ethic committee of Sorbonne University and is registered at the Institut National des Données de Santé for the use of confidential electronically processed patient data.

Inclusion criteria were: patient with NMOSD or MOGAD and at least one of the following four criteria: i) biologically confirmed COVID-19 diagnosis based on SARS-CoV-2 polymerase chain reaction (PCR) positivity in naso-pharyngeal swab; ii) typical thoracic computerized tomography (CT) abnormalities (ground glass opacities) in epidemic areas; iii) anosmia or ageusia of sudden onset in the absence of rhinitis or nasal obstruction; iv) typical symptoms (triad associating cough, fever, asthenia) in epidemic zone of COVID-19[7]. Non-inclusion criterion was the patient's opposition to the use of his medical data.

Study endpoints

Demographics, current disease modifying therapy, expanded disability severity score (EDSS) before COVID-19 and co-morbidities were collected. Regarding COVID-19, we collected symptoms, diagnostic criteria, and disease severity at the most severe point of the disease course, according to a 7-point ordinal scale[2]: 1. Not hospitalized, no limitations on activities; 2. Not hospitalized, limitation on activities; 3. Hospitalized, not requiring supplemental oxygen; 4. Hospitalized, requiring supplemental oxygen; 5. Hospitalized, on non-invasive ventilation or high flow oxygen devices; 6. Hospitalized, on invasive mechanical ventilation or ECMO; 7. Death.

Statistics

Descriptive statistics (mean, standard deviation (SD), median, range) were performed on the demographic and clinical variables. No inference statistics were performed due to the low number of patients.

Results

As of June 30th, 2020, 15 patients with NMOSD or MOGAD from 11 centers were included. Individual demographics and COVID-19 outcomes are presented in **Table** and a plot associating age, EDSS, AQP4 and MOG serological status and COVID-19 severity is presented in **Figure**. Mean (SD) age was 39.3 (14.3) years, and 11 patients were female. Mean (SD) disease duration was 7.5 (6.0) years and median EDSS was 3 (range: 0-6.5). Serological status for NMOSD diagnosis included 5 patients with aquaporin-4 (AQP4) antibodies, 5 patients with MOG antibodies, and 5 patients without AQP4 and MOG antibodies. Disease modifying therapies were distributed as follows: 10 patients were on anti-CD20 therapies (9 rituximab and 1 ofatumumab), 2 patients were on azathioprine and 3 patients were on mycophenolate mofetil.

Common COVID-19 symptoms were asthenia (12/15, 80.0%), fever (10/15, 66.7%), cough (7/15, 46.7%), anosmia or ageusia (7/15, 46.7%), headache (6/15, 40.0%), dyspnea (6/15, 40.0%), and digestive disorders (6/15, 40.0%). COVID-19 course required hospitalization for 5 (33.3%) NMOSD patients. Two patients needed oxygen, and one 24-year-old female patient receiving rituximab was hospitalized in intensive care unit during 44 days and was under mechanical ventilation 3 days after COVID-19 onset starting with anosmia. The only

comorbid condition was obesity (BMI=40). Outpatients were younger (mean [SD] age: 37.0 [13.4] years), with a longer disease duration (mean [SD]: 8.3 [6.3] years) and had a lower EDSS score (median [range] EDSS: 2.5 [0-4]) relative to patients requiring hospitalization (mean [SD] age: 44.0 [16.4] years, mean [SD] disease duration: 5.8 [5.5] years, median [range] EDSS: 4 [0-6.5]). All patients requiring hospitalization were receiving rituximab. Median time from last rituximab infusion was 5.25 months (range: 4-5.5) in the outpatient group versus 3 months (range: 0-4) in the group of patients who required hospitalization. Two out of 5 patients who required hospitalization had lymphopenia (grade 2 and grade 3), whereas one patient from 10 outpatients had grade 1 lymphopenia.

Discussion

Although none of the patients with NMOSD or MOGAD from this cohort died of COVID-19, the hospitalization rate (33.3%) appears to be high for this relatively young population. Unlike the patients with MS from the Covisep registry[2], all the patients were ambulatory (EDSS <7), precluding the evaluation of the correlation between COVID19 severity and neurological disability.

A potential aggravating factor could be the use of immunosuppressive treatments, which concerns all patients in this cohort. A study from the Global Rheumatology Alliance registry on 600 cases, 46% of which were hospitalized due to COVID-19, found no increased risk of hospitalization related to immunosuppressive treatments[8]. In our cohort, all patients requiring hospitalization were on Rituximab, and time to last infusion was shorter compared to patients with milder COVID-19. Therapies targeting IL6 receptor or C5 complement are not currently used in France in NMOSD outside clinical trials, but given their potential effect on the cytokine storm during COVID-19, it could be interesting to investigate if these

treatments are associated with a lower risk of severe COVID-19 in patients with NMOSD. However, as NMOSD and MOGAD are rare conditions, it will be difficult to obtain large-scale data to identify the risk factors for the severity of COVID-19 infection. The collection of comorbidities remains crucial, in particular obesity which was noted in the patient having experienced the most severe course of COVID-19 in our cohort. Obesity has also been identified as a risk factor for COVID-19 severity in MS[2] and in the general population[9]. To date, only twelve patients with NMOSD and COVID-19 have been reported[10-13], including 5 patients requiring hospitalization, with a favorable outcome and no worsening of neurological disability at follow-up, and one 61-year-old patient with AQP4+ NMOSD treated with prednisone having a fatal outcome[12].

Although it is possible that only the most severe cases of COVID-19 have been reported, we recommend personal protective measures to reduce risk of SARS-CoV-2 infection, especially as immunosuppressants should not be suspended in these patients to prevent the occurrence of severe relapse.

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Legend to Figure

Figure: Plot associating age, EDSS, disease modifying therapy, aquaporin 4 and myelin oligodendrocyte glycoprotein antibody status, and COVID-19 severity

The numbers under the symbols correspond to the patient number of the Table.

AQP4: aquaporin 4; MOG: myelin oligodendrocyte glycoprotein antibody; Rx: rituximab; OF: ofatumumab; Az: azathioprine; MMF: mycophenolate mofetil; P: prednisone