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ORIGINAL COMMUNICATION

COVID-19 in children with neuromuscular disorders

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Abstract

Objective Children with neuromuscular disorders have been assumed to be a particularly vulnerable population since the beginning of COVID-19. Although this is a plausible hypothesis, there is no evidence that complications or mortality rates in neuromuscular patients are higher than in the general population. The aim of this study is to describe the clinical characteristics and outcome of COVID-19 in children with neuromuscular disorders.

Methods A registry of children with neuromuscular conditions and laboratory-confirmed-SARS-CoV-2 infection was set up by the Neuromuscular Working Group of the Spanish Pediatric Neurology Society (SENEP). Data to be collected were focused on the characteristics and baseline status of the neuromuscular condition and the course of COVID-19.

Results Severe complications were not observed in our series of 29 children with neuromuscular disorders infected by SARS-CoV-2. Eighty-nine percent of patients were clinically categorized as asymptomatic or mild cases and 10% as moderate cases. Patients with a relatively more severe course of COVID-19 had SMA type 1 and were between 1 and 3 years.

Conclusions The course of COVID-19 in children with neuromuscular disorders may not be as severe as expected. The protective role of young age seems to outweigh the risk factors that are common in neuromuscular patients, such as a decreased respiratory capacity or a weak cough. Further studies are needed to know if this finding can be generalized to children with other chronic diseases.

Keyword Duchenne muscular dystrophy · Myasthenia · Neuropathy · Myopathy · SARS-CoV-2 · Spinal muscular atrophy

Introduction

Since the end of December 2019, the coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome virus (SARS-CoV-2) has rapidly spread all over the world, emerging as a global pandemic. Spain, which like many other countries is currently facing the second wave of the pandemic, has been one of the hardest hit countries so far, recording more than 1,500,000 cases and 41,688 deaths at the time of writing (November 17, 2020) [1]. All the existing studies coincide in pointing out that older people and also individuals with comorbidities are more likely to experience serious and life-threatening complications from COVID-19 [2, 3].

Patients with neuromuscular disorders have been assumed to be a particularly vulnerable population since the beginning of the pandemic [4–6], especially those with low respiratory capacity [7]. Although this is a more than plausible hypothesis, there is no evidence that complications or mortality rates in neuromuscular patients are higher than in the general population. If we specifically focus on the pediatric population with neuromuscular disorders, the available data are even more scarce. Age would be expected to act as a protective factor for this population, since children with

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COVID-19 infrequently have notable disease symptoms [8, 9] but, on the other hand, children with underlying medical conditions seem more susceptible to COVID-19 complications [10–13].

Risk assessment is crucial for identifying patients who are at increased risk of suffering from severe COVID-19 complications. The aim of our retrospective, multicenter study is to describe the clinical characteristics and outcome of COVID-19 in children with neuromuscular disorders.

Methods

A registry of children with neuromuscular conditions and laboratory-confirmed-SARS-CoV-2 infection was set up by the Neuromuscular Working Group of the Spanish Pediatric Neurology Society (SENEP). Irrespectively of clinical signs and symptoms, only patients with a laboratory confirmation of SARS-CoV-2 infection, via real-time reverse-transcription polymerase chain reaction (rRT-PCR) test, serological test and/or antigen test, were included. Data to be collected were defined by the Neuromuscular Working Group of SENEP and were focused on (i) the characteristics and baseline status of the neuromuscular condition and (ii) the course of COVID-19. A request for collaboration was sent to the 486 active members of SENEP (virtually all Spanish pediatric neurologists are members of SENEP). The initial email announcing data collection was sent on October 2, 2020, with a reminder email sent 3 weeks later. Moreover, the records of children hospitalized for COVID-19 in the main Spanish hospitals between March 1, 2020 and November 15, 2020 were reviewed, looking for those who had previously suffered from neuromuscular diseases. Finally, the main Spanish neuromuscular disorders associations (ASEM, Duchenne Parent Project España, FundAME) were informed about this study, and patients with a laboratory-confirmed-SARS-CoV-2 infection were invited to contact us to be included in the registry.

Clinical severity of COVID-19 was categorized in five groups: asymptomatic, mild, moderate, severe, and critical, based on previous classifications (Table 1) [14, 15].

Results

Responses to the call were provided by a large number of hospitals spread throughout Spain, including the 21 centers that have pediatric neurology units accredited by SENEP. A total of 29 individuals under 18 years with a laboratory-confirmed-SARS-CoV-2 infection were included, of which 20 were males and 9 females. The mean age was 8.4 years, ranging from 4 months to 17 years. The most prevalent neuromuscular condition was spinal muscular atrophy (11/29, 38%), including 6 patients with SMA type 1 and 5 patients with SMA type 2. It was followed by Duchenne muscular dystrophy (4/29, 14%), congenital myopathy (2/29, 7%), congenital muscular dystrophy (2/29, 7%), myasthenia gravis (2/29, 7%), neurogenic arthrogryposis (2/29, 7%), hereditary polyneuropathy (1/29, 3%), PIEZO2-related distal arthrogryposis with impaired proprioception (1/29, 3%), congenital myasthenic syndrome (1/29, 3%), myotonic dystrophy type 1 (1/29, 3%), Becker muscular dystrophy (1/29, 3%) and limb-girdle muscular dystrophy (1/29, 3%). Eight of the patients with SMA were being treated with nusinersen, two with risdiplam and one with salbutamol. The four patients with DMD were undergoing treatment with deflazacort at 0.9 mg/kg/day. One of the two patients with myasthenia gravis was being treated with pyridostigmine, prednisone and azathioprine, and the other one with pyridostigmine and tacrolimus. The patient with neurogenic arthrogryposis was taking aripiprazole for behavioral difficulties. The clinical characteristics of patients before SARS-CoV-2 infection are summarized in Table 2. The proportion of patients included in our series with severe phenotypes was remarkable: 15/29 patients (52%) were wheelchair bound, 12/29 (41%) required respiratory support, and 5/29 (17%) had a gastrostomy tube. By disease group, the proportion of SMA patients who required ventilatory support was particularly high (9/11, 82%). It is worth noting that 9 out of 29 patients (31%) had been hospitalized due to respiratory decompensation in the last 5 years, with a range between 1 and 10 admissions (mean 1.2, SD 2.5).

Twenty-six patients (90%) were diagnosed by PCR and 3 patients (10%) by antibody serology testing. Fourteen

Table 1 Categorization of clinical severity in COVID-19

Asymptomatic infection	Patients with positive SARS-CoV-2 test without any clinical sign or symptom
Mild	Patients with symptoms of acute upper respiratory tract infection, including fever, fatigue, myalgia, cough, sore throat, runny nose, and sneezing without pneumonia
Moderate	Patients with pneumonia, frequent fever and cough. Patients with mild respiratory distress, but no respiratory deterioration, were included within this group
Severe	Patients with respiratory deterioration
Critical	Patients with acute respiratory distress syndrome or respiratory failure, shock, or multiple organ dysfunction

Table 2 Characteristics of the cohort of children with neuromuscular conditions ($n=29$) and baseline status before COVID-19

Male, *n* (%)	20 (69%)
Age. mean (range)	8.4y (4m-17y)
Neuromuscular condition	
Spinal muscular atrophy 1	6 (21%)
Spinal muscular atrophy 2	5 (17%)
Duchenne muscular dystrophy	4 (14%)
Other	14 (48%)
Non-ambulant, *n* (%)	15 (52%)
Ventilatory support required, *n* (%)	
NIV, *n* (%)	10 (34%)
Tracheostomy, *n* (%)	2 (7%)
Gastrostomy tube, *n* (%)	5 (17%)
Cardiac involvement, *n* (%)	0 (0%)
Cognitive involvement, *n* (%)	4 (14%)
Hospitalizations due to respiratory decompensation in the last 5 years, *mean* (SD, range)	1.2 (2.5; 0–10)

Table 3 COVID-19 characteristics in children with neuromuscular conditions

Clinical features, *n* (%)	
Fever/Low-grade fever	9 (31%)
Nasal congestion/rhinorrhea	9 (31%)
Cough	3 (10%)
Headache	3 (10%)
Myalgia	2 (7%)
Sore throat	2 (7%)
Diarrhea	1 (3%)
Vomiting	1 (3%)
Anosmia	1 (3%)
Pneumonia, *n* (%)	2 (7%)
COVID treatment, *n* (%)	
Oxygen/Increased need for respiratory support	2 (7%)
Drugs for COVID-19	2 (7%) Hydroxychloroquine Corticosteroids
Outcomes, *n* (%)	
No hospitalization	26 (90%)
Hospitalization	3 (10%)
Intensive care unit	1 (3%)

patients (48%) were tested after being in close contact with a positive case, 8 patients (28%) were tested, because they needed a negative SARS-CoV-2 PCR test prior to medical procedures (spirometry, nusinersen administration, scoliosis surgery) and only 7 patients (24%) were tested, because they had symptoms. Only 11 of the 29 patients (38%) had attended school in the 7 days prior to the test. Eleven patients (38%) remained asymptomatic throughout the course of infection, 16 patients (55%) presented some mild symptoms, and 3 patients (10%) with SMA 1 were categorized as moderate, one of them being admitted in the pediatric intensive care unit for 3 days. Fever/low-grade fever (9/29, 31%) and nasal congestion/rhinorrhea (9/29, 31%) were the most common symptoms. Other less commonly observed symptoms are summarized in Table 3. Apart from one asymptomatic SMA 1 patient who was kept under observation for 3 days and did not require inpatient care, 3 of the 29 patients (10%) were hospitalized for an average of 7 days (range 3–10 days). These three patients had SMA type 1, were between 1 and 3 years and, based on the clinical severity of COVID-19, were categorized as moderate. Two of the three hospitalized patients had mild respiratory distress without a clear respiratory deterioration (daily hours of non-invasive ventilation were increased from being exclusively nocturnal to being continuous for 3 days, but pressure settings were not modified) and the third developed a pneumonia without respiratory distress. The background treatment regimen was not modified in any of the 29 patients during the infection period.

Discussion

The clinical spectrum of COVID-19 ranges from asymptomatic to severe pneumonia, acute respiratory distress syndrome and even death. Our study is the first to assess the impact of COVID-19 in children with neuromuscular conditions, a group of patients that has understandably been considered to be highly vulnerable to SARS-CoV-2, despite the absence of reliable data [5–7].

Our results suggest that the course of COVID-19 in children with neuromuscular disorders may not be as severe as expected, although children with SMA 1 appear to be a more vulnerable group. Respiratory complications or need of extra ventilatory support were uncommon in our series, despite the fact that more than 40% of our patients had severe respiratory involvement prior to SARS-CoV-2 infection (defined as use of non-invasive ventilation for at least 8 h a day). Except for three cases, all patients presented here were categorized as asymptomatic or mild, similar to what has been previously observed in healthy children [8, 10, 13]. All three patients who were hospitalized and some other patients who successfully overcame the SARS-CoV-2 infection with hardly any symptoms had a previous history of frequent hospital admissions in the past years due to respiratory decompensations triggered by other infectious agents. According to our data, it does not appear that SARS-CoV-2 infection is more life threatening for these children than other viruses such as rhinovirus or influenza.

Our study has several limitations worth noting. Our method of case capture has proven to be successful, but it is not exhaustive and may not identify all cases. Spanish reports provide a description of COVID-19 cases by age but do not include information about whether an individual who has been infected by SARS-CoV-2 had a neuromuscular condition. In addition, we cannot accurately calculate the incidence of SARS-CoV-2 among Spanish children with neuromuscular disorders, since mild COVID-19 cases have not been systematically tested throughout the pandemic in our country and asymptomatic cases remain unrecognized. Therefore, due to the Spanish testing policy, we assume that many mild cases may have gone unnoticed, unlike moderate, severe or critical cases. This reinforces our idea that COVID-19 in children with neuromuscular conditions may be not as severe as expected.

According to our early results, the protective role of young age seems to outweigh the risk factors that are common in neuromuscular patients, such as a decreased respiratory capacity or a weak cough. We wonder if this finding can be generalized to children with other chronic diseases. The fact that the vast majority of children with neuromuscular diseases overcome SARS-CoV-2 infection without short-term complications is reassuring news for families and professionals in these times of uncertainty. Despite this, caution must be exercised until our suggestive data can be confirmed and extended in larger cohorts of patients. The results of this study cannot be extrapolated to the adult population. Social distancing should still be the primary advice for all children with neuromuscular disorders and their caregivers to reduce the risk of contracting the virus.

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Data availability Any data not published within the article will be shared, upon reasonable request.

Compliance with ethical standards

Conflicts of interest None of the authors has any conflict of interest to disclose.

Ethical approval This study was carried out following the ethical guidelines of each of the institutions involved. Written informed consent and age-appropriate assent for study participation were obtained by a qualified investigator [Protocol approved by the Clinical Ethics Committee of Hospital Sant Joan de Déu, Barcelona (PIC 258–20)].

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