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Case report

Clinical outcome of SARS-CoV-2 infection in 7 adults with Duchenne muscular dystrophy attending a specialist neuromuscular centre

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Abstract

Due to their frailty and cardiorespiratory compromise adults with DMD are considered extremely vulnerable and at high risk of severe infection should they contract COVID-19. We report 7 adults with DMD aged 17–26 years who tested positive on a nasopharyngeal PCR swab for SARS-CoV-2. Despite long term corticosteroid treatment, severe respiratory compromise requiring night-time ventilation and receiving treatment for moderate to severe cardiomyopathy, none of the patients developed moderate to severe symptoms; in fact two remained asymptomatic and two developed only anosmia and reduced sensation. The remaining three developed transient fever with or without sore throat, cough and runny nose. All recovered fully without complication and no patient required hospitalization.

Keywords: COVID-19; SARS-Cov-2; Duchenne muscular dystrophy; DMD.

1. Background

A global pandemic caused by coronavirus disease (COVID-19) began in Wuhan, China, in December 2019 resulting in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The United Kingdom experienced a severe second wave in the winter of 2020/2021 due to a mutation in the virus leading to a new strain estimated to be at least 50% more transmissible. As a consequence, there has been a very sharp rise in infections and hospital admissions. The risk of critical illness and death is greatest in the elderly and those with pre-existing underlying health conditions [1,2]. At the time of writing this article, John Hopkins University have reported more than 1.9 million deaths and 90 million people infected worldwide (BBC news website 10th January 2021).

People with neuromuscular disease are considered particularly vulnerable to severe complications of COVID-19 due to their frailty and cardiorespiratory compromise [3,4]. Amongst this group, adults with DMD are considered to be at very high risk due to their reduced respiratory function, cardiomyopathy and immunosuppression from long-term corticosteroid treatment. As a consequence, all DMD adults have been advised to shield along with other vulnerable neuromuscular patients. Shielding means self-isolating, not going out of the home and avoiding mixing with others. Hospital out-patient appointments were converted from 'face to face' to 'remote' by video or telephone and all but essential routine cardiac and respiratory assessments were placed 'on hold'. Many patients have not left their home for months and not attended school, college, university or work. These measures have protected patients from contracting COVID-19 infection. Despite the recommendation to shield, there has been little, if any, published evidence on the outcome of COVID-19 infection in this population.

One very recent publication reported the effects of COVID-19 infection in children with neuromuscular disease who

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Table 1
Assessment of severity of COVID-19 infection taken from Netera-de-Benito et al. [5].

Asymptomatic	Positive SARS-CoV2 test without symptoms
Mild	Symptoms: anosmia, Upper respiratory tract symptoms including fever, fatigue, myalgia, cough, sore throat, runny nose and sneezing without pneumonia
Moderate	Pneumonia, frequent fever and cough, respiratory distress but no respiratory deterioration
Severe	Patients with severe respiratory deterioration
Critical	Patients with acute respiratory distress syndrome or respiratory failure, shock or multiple organ failure

were younger than 18 years of age [5]. Within this cohort of 29 patients, four had DMD, although details of their clinical status were not revealed, however, the majority of children in the cohort described had only mild disease. The only patients to develop severe COVID-19 infection requiring hospitalization had type 1 SMA and were between 1 and 3 years of age, only one of these patients required intensive care [5]. To date there have been no reports of the effect of COVID-19 infection in adults with DMD. Here we describe the clinical course and characteristics of 7 adults with DMD aged 17–26 years who tested positive for SARS-CoV-2 on a PCR nasopharyngeal swab.

2. Patients

All patients were regular attenders at the Neuromuscular Complex Care Centre (NMCCC) at the National Hospital for Neurology and Neurosurgery, London. The NMCCC offers 'one-stop' elective overnight admissions for all aspects of care defined in the international standards of care for DMD [6,7,8]. The unit was able to continue to offer assessments for some patients during the pandemic by putting in place a risk assessed protocol aimed to protect patients from contracting infection. This included pre-admission screening of all patients and carers with SARS-CoV-2 PCR nasopharyngeal swabs, isolation, barrier nursing and weekly testing for SARS-CoV-2 infection amongst staff. In addition, all patients known to the NMCCC (including 164 DMD patients) were telephoned on a regular basis to monitor their health and well-being.

We retrospectively reviewed case notes of NMCCC patients who contracted COVID-19. Between October 2020 and January 2021, we were made aware of 7 adults with DMD who tested positive on a PCR nasopharyngeal swab for SARS-CoV-2. Each of these patients was monitored remotely by telephone every few days for three weeks from the date of the positive swab and the outcome documented.

Severity of COVID-19 infection was assessed using the same criteria as the paediatric neuromuscular cohort published by Natero-de Benito et al. [5] and is shown in Table 1. The clinical course of Covid-19 infection in each patient is described below and summarised in Table 2.

3. Patient 1

An 18 year-old male with a DMD deletion in exon 44, had been taking daily deflazacort for more than 10 years. In October 2020, his BMI was 31.3, FVC 1.99 l (72% predicted), FEV1 1.45 l (68% predicted) Peak Cough Flow (PCF) 270 l/min. Cardiac function was normal in February 2020: cardiac echo showed Left ventricular ejection fraction (LVEF) 60%, Left ventricular fractional shortening (LVFS) 35% and cardiac MRI in September 2020 showed LVEF 76% and right ventricular ejection fraction (RVEF) 75%. Medication included: perindopril, bisoprolol, metformin, cholecalciferol, testosterone, lanzoprazole and tamoxifen (self-administered). He shielded for six months during the first wave of COVID-19 infections in the UK, but in September 2020, he decided to return to College to complete his A-level studies.

In December 2020, his father developed COVID-19 symptoms and tested positive on a PCR nasopharyngeal swab for SARS-Cov-2, the patient, who was asymptomatic at the time, was also tested and found to have a positive PCR swab. Two days after the positive result, he awoke in the morning with symptoms including headache, cough and temperature 38.6°C, however, by the evening of the same day his temperature returned to normal and he felt much better. Over the next 10 days he had brief episodes of fever to 38 °C and mild intermittent cough. He was sent an oxygen saturation monitor by courier and his parents reported oxygen saturations >95%. He remained systemically well and was cared for at home by his parents.

4. Patient 2

A 27-year-old DMD man with a DMD duplication in exon 51 who was steroid Naïve lost ambulation at the age of 11 years and had scoliosis surgery at the age of 16 years. He was known to have severe respiratory insufficiency and had been using night-time BiPAP since he was 20 years of age. In September 2020, respiratory function was assessed as follows: FVC 0.45 l (11% predicted), FEV1 0.45 l (13% predicted). Peak cough flow was so poor that it was undetectable, and he relied on a cough assist machine for chest clearance. He was known to have mild cardiomyopathy, in October 2020, routine cardiac echo showed LVEF 50–55%. Medication included: perindopril, bisoprolol and ivabradine.

In November 2020, he noticed sudden onset of anosmia and reduced taste sensation. He was tested for COVID-19 with a PCR nasopharyngeal swab which came back positive for SARS-CoV-2 infection. He developed no other symptoms during the course of his COVID-19 infection.

5. Patient 3

An 18-year-old man with a DMD nonsense mutation in exon 35, had been taking prednisolone 15 mg 10 days on 10 days off since he was 5 years of age. He lost ambulation at the age of 9 years. He had reduced respiratory function which was last assessed in August 2020 and showed:

Table 2
Summary of DMD patients' clinical status and COVID-19 symptoms.

Patient	Age (Years)	DMD mutation	Current Steroid therapy	Ethnicity	BMI	FVC litres (% predicted)	Cardiac function (LVEF%)	BiPAP	COVID-19 symptoms
1	18	Exon 44	Deflazacort 36 mg/day	Asian	31.2	1.99(98%)	66%	NO	Mild Fever 38.6 °C, cough and headache Lasting 10 days
2	27	Duplication Exon 51	None	Caucasian	17.2	0.45(11%)	50–55%	YES Night-time	Mild Anosmia, loss of taste
3	18	Deletion Exon 35	Prednisolone 15 mg 10 day on 10 day off	Caucasian	32.3	1.64(37%)	45–50%	YES Night-time	Mild Anosmia, loss of taste
4	19	Deletion exon 45–54	Prednisolone 20 mg 10 days on 10 days off	Asian	32.8	1.86(42.8%)	25–30%	NO	Mild Fever 38.4°CLasting 24 h
5	20	Deletion exon 45–52	None	Caucasian	17.6	Unable to perform	30–35%	YES night-time	Asymptomatic
6	26	Deletion 45–52	None	Caucasian	36.1	0.68(9%)	40–45%	YES night-time	Mild Runny nose and mild sore throat lasting 11 days. No fever
7	23	Duplication exon 18	None	Afro-Caribbean	20.6	1.5 (37%)	35–40%	YES night-time	Asymptomatic

FVC 1.64 l (37%), PCF 365 l/min. At that time, he was commenced on night-time BiPAP for respiratory insufficiency. He was known to have cardiomyopathy, in August 2020 echocardiography showed LVEF 45–50%. Regular medication included perindopril and bisoprolol.

In November 2020, he complained of anosmia and reduced taste sensation, a nasopharyngeal swab for SARS-Cov-2 PCR was arranged and came back positive. He developed no other symptoms during the course of his COVID-19 infection.

6. Patient 4

A 19-year-old man with DMD deletion exon 45–54, had been treated with Prednisolone 20 mg 10 days on 10 days off since early childhood. He lost ambulation at the age of 13 years. Severe dilated cardiomyopathy was diagnosed in August 2019, his most recent cardiac ECHO in August 2020 showed severely reduced LV function, LVEF 25–30%. In addition, he was known to have respiratory insufficiency, respiratory function last assessed in August 2020, showed: FVC 1.86 l (42.8%), FEV1 1.67 l (44.06%), PCF 310 l/min, a sleep study performed at the same time showed evidence of mild nocturnal hypoventilation that was not severe enough to require initiation of BiPAP. Medication included: perindopril, carvedilol and epleronone

In November 2020, his mother developed symptoms of COVID-19 and had a positive nasopharyngeal SARS-CoV-2 PCR swab. The patient was also tested, despite being asymptomatic, and was found to also be positive. He subsequently developed a fever of 38.4 °C which resolved spontaneously after 24 h. He developed no other symptoms during the course of his COVID-19 infection.

7. Patient 5

A 20-year-old patient with DMD deletion in exons 45–52 was treated with corticosteroids between 2004 and 2010. Steroids were stopped due to behavioural side-effects. He lost ambulation before teenage years and had scoliosis surgery at the age of 15 years. He was unable to perform spirometry and his Peak Cough Flow was severely reduced to 90 l/min. He used a cough assist device for secretion clearance. He has used night-time BiPAP since he was 14 years of age.

He was known to have moderate-severe dilated cardiomyopathy, his most recent echocardiogram performed in August 2020 showed LVEF 30–35%. Medication included: perindopril, bisoprolol, epleronone.

In October 2020, both of his parents developed COVID-19 symptoms. Although he had no symptoms, he was tested for SARS-CoV-2 PCR via nasopharyngeal swab along with his parents. All three tested positive, however, despite his parents having symptoms, he remained asymptomatic.

8. Patient 6

A 26-year-old man with a DMD deletion in exons 45–52. He had a trial of steroids, 10 days on, 10 days off between 2004 and 2005 but discontinued due to excessive weight gain. He lost ambulation at the age of 11 years and underwent spinal fusion when he was 15 years old. He has used night-time BiPAP since he was 13 years of age. His-respiratory function was severely reduced, he was last assessed in February 2020: FVC 0.68 l (10%) and PCF 140 l. Assessment in October 2020 showed him to be obese: BMI 36.1. He had moderately reduced cardiac function assessed by echocardiography: LVEF 40–45%. Medication included: losartan, nebivolol and spironolactone.

In November 2020, his parents and siblings developed symptoms of COVID-19 and his mother was hospitalised for 2 weeks with COVID-19 pneumonia requiring oxygen therapy. The DMD patient, who also tested positive on a SARS-Cov-2 PCR swab, developed symptoms including a runny nose and mild sore throat that lasted for 11 days. He had no fever and at no time did he feel systemically unwell, in fact the family reported that he had the 'mildest symptoms of all of them'. He remained at home during the course of his illness.

9. Patient 7

A 23-year-old man with DMD duplication in exon 18, with severe autism and mild learning difficulties received corticosteroid treatment for 3 months as a child but stopped due to severe behavioural side-effects. He lost ambulation at the age of 13 years and developed mild scoliosis in adolescence which did not require surgery. He was known to have moderately severe cardiomyopathy, a cardiac echo undertaken in September 2020 showed moderately impaired systolic function: LVEF 35–40%. He has used BiPAP at night-time since he was 19 years of age, but his compliance was poor. Respiratory assessment in September 2020 showed: PCF 250 l/min, FVC 1.5 l (37%), FEV1 1.43 l (41%). He reported mild symptoms of dysphagia but his weight was stable.

He lived in a care home where two other residents became symptomatic and tested positive for COVID-19. Along with the remaining care home residents, he was tested and had a positive nasopharyngeal PCR swab for SARS-Cov-2. However, he remained asymptomatic.

10. Discussion

Since the onset of the COVID-19 pandemic, adults with DMD have been considered at high risk of severe complications should they become infected. Shielding has successfully prevented infection in many vulnerable people, although patients and their families report being highly anxious about the potential consequences of them contracting the disease. This anxiety, in some families has been so severe that they have declined sleep studies and cardiac evaluation for 12 months or more despite a strict risk assessed protocol being in place to ensure their safety.

In the small cohort described here, none of the DMD patients who tested positive for SARS-CoV-2 on a nasopharyngeal PCR swab developed moderate or severe disease. In fact, two out of seven patients remained asymptomatic and another two experienced only anosmia and change in taste sensation. The remaining three patients experienced mild symptoms and none required hospitalization. This is despite three of the patients having been treated with corticosteroids for many years, five had severe respiratory insufficiency requiring night-time BiPAP and five had evidence of moderate to severe cardiomyopathy.

Although this is a small cohort and the oldest adult was still relatively young at 26 years of age, it does provide some reassurance that being a young man with DMD may not necessarily be a risk factor for severe COVID-19 infection and that other risk factors previously reported [1,2] including older age, acquired co-morbidities such as diabetes and BMI> 40 may be more important for developing severe complications of infection. While we would still consider adults with DMD to be at risk and thus continue to recommend shielding until vaccination is offered, we believe the effect of COVID-19 infection in adults with DMD in our cohort may offer some reassurance to other families and clinicians that COVID-19 infection does not necessarily result in a severe illness. While, on the other hand, failure to attend regular cardiac and respiratory follow up appointments may increase the risk of severe complications related to DMD. We hope that our experience may encourage patients and carers to balance the benefit against the risk of having their routine cardiorespiratory assessments according to the standards of care [6,7,8].

In the future, national and international COVID-19 databases may provide further valuable information on the effect of SARS-CoV-2 infection in adults with DMD.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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