

COVID-19 pneumonia: a tailor-made dress for a Down syndrome patient

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ABSTRACT

We report here a case of coronavirus disease 2019 pneumonia in a 40-year-old Caucasian woman with Down syndrome admitted to the Internal Medicine Unit. She was initially treated with hydroxychloroquine and azithromycin. When respiratory conditions dramatically worsened, she was not admitted to the intensive care unit because of impaired cognitive function. Thus helmet-based continuous positive airway pressure was started. The respiratory conditions progressively improved, reaching spontaneous breathing.

Case Report

A 40-year-old Caucasian woman with Down syndrome (DS) was admitted to the Internal Medicine Unit, Hospital of Mirandola, last 26th March. She was intellectually disabled, and she had a congenital solitary kidney with normal renal function. She had a body mass index of 35.8 kg/m². Other than these, previous medical history was unremarkable. She had a 4-day history of fever. She presented with fever (38°C), dry cough, and pharyngodynia. Severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2) positivity was confirmed with one nasal/throat

swab test of SARS-CoV-2 by qualitative real-time reverse-transcriptase-polymerase-chain-reaction (RT-PCR) assay. The initial physical examination revealed oxygen saturation (SpO₂) 95% under ambient air, respiratory rate of 22 breaths/minute, blood pressure of 100/80 mm Hg, and pulse of 104 bpm. The laboratory findings showed elevated C-reactive protein (3.7 mg/dL, reference <0.5) and low white blood cell count (1800 mL⁻¹). On admission, a chest X-ray revealed multiple bilateral pulmonary infiltrates, in the upper and lower lobes, involved by consolidations (Figure 1). The comparison of laboratories findings during the hospitalization was presented in Table 1.

On day 1, she had dyspnea, hypoxemic acute respiratory failure (paO₂/FiO₂ 195), and oxygen supply through the Venturi mask, labeled at 28% fraction of inspired oxygen (FiO₂). Thus, hydroxychloroquine and azithromycin were started. She received hydroxychloroquine 400 mg twice on day 1, followed by 200 mg twice per day on days 2-5, and azithromycin 500 mg once for 5 days. We have also administered low molecular weight heparin (40 mg once a day) for prophylaxis of deep vein thrombosis.

On day 3, her body temperature returned to normal, but she still had dyspnea, and needed high-flow oxygen (8 L/min) through a Venturi mask. Thus, tocilizumab was given subcutaneously at 162 mg administered in two simultaneous doses, one in each thigh (324 mg in total) because the endovenous formulation was unavailable.

On day 5 she presented uncontrollable respiratory distress (paO₂/FiO₂ 70) despite maximal oxygen supply. She was not admitted to the intensive care unit because of impaired cognitive function.

Thus, it was started a helmet-based continuous positive airway pressure (helmet CPAP) with positive

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Key words: Severe acute respiratory syndrome-related coronavirus 2; continuous positive airway pressure; morphine; Down syndrome.

Conflict of interests: the authors declare no potential conflict of interests.

Ethics approval: not required.

Informed consent: the patient gave informed consent.

Received for publication: 27 September 2020.

Accepted for publication: 20 October 2020.

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Italian Journal of Medicine 2021; 15:59-63

doi:10.4081/ijm.2021.1377

end-expiratory pressure 10 cm H₂O. Simultaneously we administered methylprednisolone 40 mg/day for 7 days. She was given subcutaneously morphine 10 mg per day for dyspnea and strong negative emotions, for five days, without any side effects. Carbon dioxide level increased on day 8, with resolution in the following days after stopping using the helmet because helmet CPAP might facilitate CO₂ rebreathing. On day 15, the second chest-X-rays

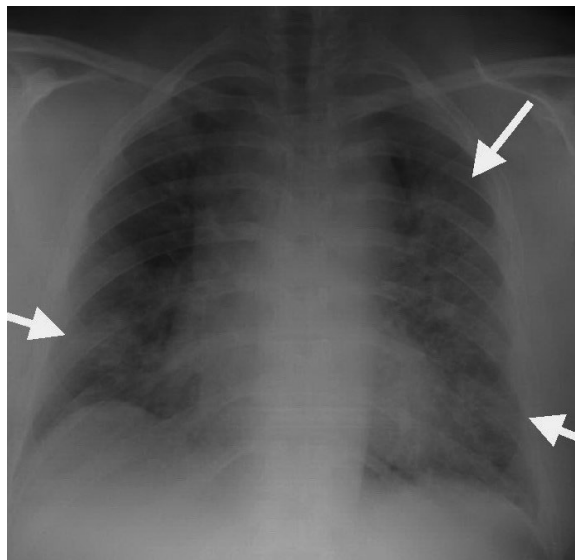


Figure 1. On admission to the hospital, the chest film shows ill-defined bilateral alveolar consolidation with peripheral distribution, in the right lower lobe and in the upper and lower left lobe (arrows).

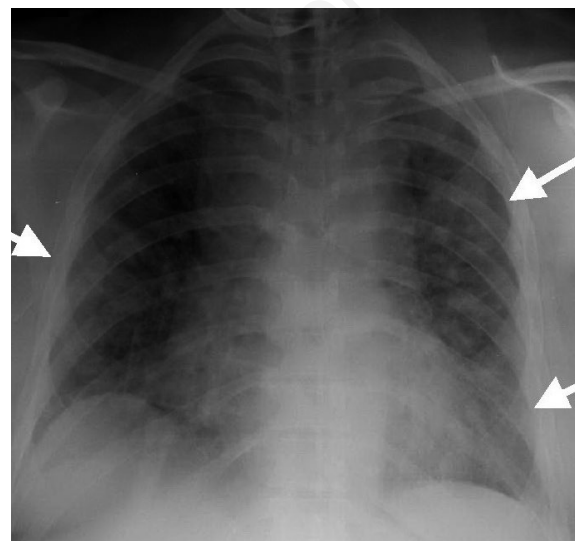


Figure 2. Chest X-ray with evidence of partial clearance (arrows) of bilateral pulmonary infiltrates was seen.

Table 1. Laboratory findings during hospitalization (2020).

Date	26/07	27/03	28/03	29/03	30/03	31/03	01/04	02/04	03/04	04/04	05/04	06/04	07/04	08/04	09/04	10/04	11/04	12/04	13/04	14/04	15/04	
Day of admission	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	
pH	7.41	7.39	7.41	7.39	7.43	7.38	7.35	7.35	7.35	7.35	7.35	7.39	7.39	7.41	7.43	7.43	7.42	7.42	7.42	7.43	7.43	7.44
PaCO ₂ (mmHg)	42	46.7	46.7	46.7	46	57	64	62.4	62.4	62.4	62.4	54.6	54.6	53.3	49.8	49.8	47.6	47.6	47.6	42	42	41.5
PaO ₂ (mmHg)	54.5	66.6	66.6	66.6	58.6	61	74	59.6	59.6	59.6	59.6	82	82	59.6	118	118	101	101	101	86	86	75
PaO ₂ /FiO ₂ ratio	195	167	167	167	97.6	101	74	62.7	62.7	62.7	62.7	136	136	149	336	336	362	362	362	360	360	357
Arterial blood pressure (mmHg)	120/70	120/70	140/75	100/60	120/60	110/70	150/90	115/58	100/60	120/70	145/80	105/65	100/60	100/50	100/50	100/50	100/60	100/60	110/55	110/60	105/65	120/70
Oxygen supply (L/min)	4	4	8	8	8	15	6	15	15	15	15	15	15	12	12	6	4	2	2	2	2	0
White blood cell count (mL ⁻¹)	1.8	2.1	2.1	2.1	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	6.1
C-reactive protein (mg/dL)	3.7	6.6	6.6	6.6	6.6	6.6	6.6	6.6	6.6	6.6	6.6	6.6	6.6	6.6	6.6	6.6	6.6	6.6	6.6	6.6	6.6	0.5
Platelet count (mL ⁻¹)	108	131	131	131	180	180	180	180	180	180	180	180	180	180	180	180	180	180	180	180	180	154

(Figure 2) revealed partial clearance of pulmonary infiltrates, while $p\text{CO}_2$ decreased from 53 mmHg to 49 mmHg, and O_2 increased from 59 mmHg to 118 mmHg. The respiratory condition progressively improved, reaching spontaneous breathing on day 16. Two consecutive nasal/throat RT-PCR swab samples were confirmed negative for RNA virus, so the patient was discharged on 29th April. The comparison between respiratory parameters during CPAP and pharmacological therapy was presented in Table 2.

Just 2 months after discharge, the patient underwent a follow-up examination in our operative unit: she was fine, afebrile, alert, and eupneic. The physical examination revealed SpO_2 98% under ambient air and arterial blood pressure of 125/70 mmHg.

Discussion

Currently, there is no specific antiviral treatment for COVID-19. In the meantime, scientists are working hard to develop effective treatments. An antiviral drug must be able to target the specific part of a virus' life cycle that is necessary for it to reproduce. Viruses are highly adaptive. Because they reproduce so rapidly, they have the opportunity to mutate with each new generation, developing resistance to whatever drugs we develop.

Therapies under investigation include drugs used to treat malaria and autoimmune diseases, corticosteroids, and antibodies from people who have

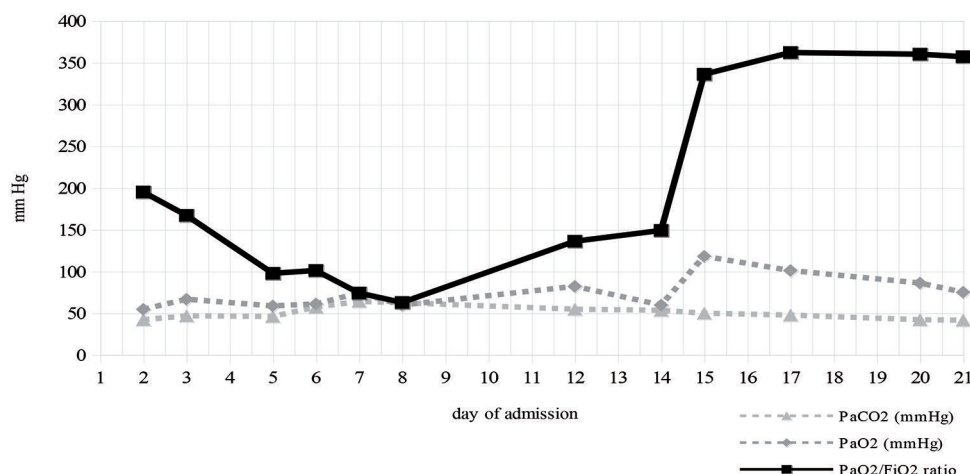
recovered from COVID-19. The association of azithromycin and hydroxychloroquine was the standard treatment, according to our local protocol. Azithromycin is an antibiotic used to prevent or treat co-infection by bacteria. Hydroxychloroquine proved to kill the COVID-19 virus in the laboratory dish.¹ Hydroxychloroquine can predispose patients to life-threatening arrhythmias. Hydroxychloroquine interferes with ventricular repolarization, leading to prolonged QTc interval and an increased risk of *torsades de pointes*. In our experience, it was challenging to correct hypokalemia because of the continuous renal potassium loss. The high prevalence of hypokalemia among patients with COVID-19 suggests the presence of disordered renin-angiotensin system activity, which increases due to reduced counteractivity of angiotensin-converting enzyme 2, which is bound by COVID-19 pneumonia.²

Tocilizumab (TCZ), a humanized monoclonal antibody targeting the interleukin-6 receptor, seems a very promising drug. An important Italian study treated with TCZ 100 patients, the largest cohort until now, and found that the treatment was associated with a clinical improvement in more than three-quarters of patients. These preliminary results are encouraging, considering that the response to TCZ was rapid, within 12 to 72 h, and sustained, as all patients with initial response continued to improve over the next ten days.³ TCZ efficacy needs to be validated in large clinical randomized trials.

In the context of great healthcare stress, Intensive

Table 2. Shows arterial blood gas during helmet-based continuous positive airway pressure (CPAP) and pharmacological therapy.

Day of admission	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	
Hydroxychloroquine						0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Azithromycin						0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Tocilizumab	0	0		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Methylprednisolone	0	0	0	0									0	0	0	0	0	0	0	0	0	0
Morphine	0	0	0	0						0	0	0	0	0	0	0	0	0	0	0	0	0
Helmet CPAP	0	0	0	0						0	0	0	0	0	0	0	0	0	0	0	0	0



PaCO₂, partial pressure of carbon dioxide; PaO₂, partial pressure of oxygen; FiO₂, fraction of inspired oxygen.

Care Units may reach saturation. Thus, authorities converted internal medicine units into new respiratory intermediate care units, staffed by quickly trained personnel and equipped with noninvasive ventilation (NIV) devices. In our experience, we used helmet CPAP. Helmet CPAP was developed in 1991 in Italy, and is commonly used in emergency departments, in hospital and pre-hospital settings. In the COVID-19 pandemic, we have used helmet CPAP also in the internal medicine units to approach hypoxemic acute respiratory failure. Helmet CPAP confines aerosolized viral particle spread within the helmet.⁴ An independent metanalysis, including 4 randomized clinical trials that enrolled 377 patients, found that helmet CPAP significantly increased the $\text{PaO}_2/\text{FiO}_2$, decreased arterial CO_2 levels, and reduced intubation rate and hospital mortality.⁵ In this case that we report, we stopped helmet CPAP for CO_2 rebreathing. A possible problem related to helmet CPAP is the rebreathing of CO_2 . A traditional face mask is essentially an additional anatomical dead space, and its effect on CO_2 rebreathing is proportional to its volume. Compared with the face mask, the helmet, due to its larger internal volume, which is always bigger than the tidal volume, might facilitate CO_2 rebreathing.⁶

In this case, we used helmet CPAP to avoid severe complications and comorbidity after invasive mechanical ventilation through an endotracheal tube. Compared to invasive mechanical ventilation through an endotracheal tube, helmet CPAP is much safer and has fewer complications, such as upper airway trauma, laryngeal swelling, post-extubation vocal cord dysfunction, and nosocomial infection. Furthermore, in Down syndrome patients, many factors frequently subclinical or underdiagnosed may contribute to respiratory difficulties: hypotonia, tracheobronchomalacia, and adenoid hypertrophy, abnormal lung vasculature growth, alveolar hypoventilation, recurrent pulmonary infections, abnormal media of pulmonary arterioles, diminished alveoli density, gastroesophageal reflux. In DS patients, prolonged ventilation and hospitalization are required after invasive mechanical ventilation for cardiac surgery.⁷ A French single-center retrospective study evidenced the high mortality rate observed in children with DS admitted to the intensive care unit. The most frequent reason for admission was a respiratory disease. A history of mechanical ventilation was independently associated with death. This study has suggested that the advent of NIV could provide significant clinical improvement in children with DS who have upper airway obstruction, congestive cardiac failure, and pulmonary arterial hypertension.⁸

In the presence of dyspnea, we are used to giving

low doses of morphine to avoid respiratory depression. Which role can play morphine in COVID-19 pneumonia? Accompanying patients at the end of life remains a priority for healthcare teams everywhere. Every patient's right to receive analgesia and sedation until death to prevent all suffering must be guaranteed. Morphine may alleviate the symptoms of COVID-19: it lowers the respiratory rate and reduces shortness of breath.⁹ Thus, morphine causes a reduction of both the filling pressure and the arterial pressure, having a relaxing effect on the smooth muscles in both veins and arteries. Morphine reduces preload and afterload and has been frequently used in acute pulmonary edema. Moreover, in the hypothesis that COVID-19 is not a typical acute respiratory distress syndrome, because COVID-19 patients show significant vasoconstriction of small blood vessels,¹⁰ the vasodilator effect of morphine, should help the patient overcome the disease. Naturally, it is only a suggestion, and further validation with more substantial evidence is required.

Conclusions

COVID-19 became a public health emergency, causing tremendous stress on healthcare systems. In Northern Italy, internal medicine departments were reorganized entirely to face the emergency. This emergency well emphasizes the strategic role of Internal Medicine in the Italian Healthcare System. The admission of a patient with cognitive disability and chromosomal pathology may represent a huge challenge and request a person-centered and empathic approach. We used a CPAP helmet to avoid severe complications and comorbidity after invasive mechanical ventilation through an endotracheal tube.

References

1. Meo SA, Klonoff DC, Akram J. Efficacy of chloroquine and hydroxychloroquine in the treatment of COVID-19. *Eur Rev Med Pharmacol Sci* 2020;24:4539-47.
2. Chen D, Li X, Song Q, et al. Assessment of hypokalemia and clinical characteristics in patients with coronavirus disease 2019 in Wenzhou, China. *JAMA Netw Open* 2020;3(6) [Epub ahead of print].
3. Toniati P, Piva S, Cattalini M, et al. Tocilizumab for the treatment of severe COVID-19 pneumonia with hyperinflammatory syndrome and acute respiratory failure: A single center study of 100 patients in Brescia, Italy. *Autoimmun Rev* 2020;19(7) [Epub ahead of print].
4. Ing RJ, Corey B, Glenn M, et al. Role of helmet-delivered noninvasive pressure support ventilation in COVID-19 patients. *J Cardiothorac Vasc Anesth* 2020 May 8 [Epub ahead of print].
5. Liu Q, Gao Y, Chen R. Noninvasive ventilation with helmet versus control strategy in patients with acute

- respiratory failure: A systematic review and meta-analysis of controlled studies. *Crit Care* 2016;20:265.
6. Taccone P, Hess D, Caironi P, Bigatello LM. Continuous positive airway pressure delivered with a "helmet": effects on carbon dioxide rebreathing. *Crit Care Med* 2004;32:2090-6.
 7. Joffe, Lesage F, Bustarret O, et al. Children with Down syndrome: clinical course and mortality-associated factors in a French medical pediatric intensive care unit. *J Pediatr Child Health* 2016;52:595-9.
 8. Robert R, Le Gouge A, Kentish-Barnes N, et al. Sedation practice and discomfort during withdrawal of mechanical ventilation in critically ill patients at end-of-life: a post-hoc analysis of a multicenter study. *Intensive Care Med* 2020;46:1194-203.
 9. Pattinson KT. Opioids and the control of respiration. Clinical phenotypes of SARS-CoV-2: implications for clinicians and researchers. *Br J Anaesth* 2008;100:747-58.
 10. Rello J, Storti E, Belliato M, Serrano R. Clinical phenotypes of SARS-CoV-2: implications for clinicians and researchers. *Eur Respir J* 2020;55(5) [Epub ahead of print].

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