Patients with Down's Syndrome and COVID-19 Pneumonia Requiring Ventilatory Support - A case series

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Received: 17 August 2021

Accepted: 4 July 2022

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DOI 10.5001/omj.2023.29

Abstract

Downs syndrome (DS), which is due to Trisomy21 is the most common chromosomal abnormality found in humans. These patients manifest anatomical abnormalities in the respiratory tract like smaller trachea, enlarged adenoids, and tonsils, macroglossia, narrowing of the upper airway, tracheobronchial malacia, hypotonia of upper airway predisposing them to aspiration, and glossoptosis. Patients with DS have unfavourable characteristics like mental retardation, attention problems, cognitive dysfunction, tantrums all of which make them unsuitable for non-invasive ventilation (NIV). In the Sultanate of Oman, the birth prevalence of DS is 2.4 in 1000 which leads to about 120 affected births/ year. Underlying compromised cardiopulmonary status predisposes these patients to a serious course of viral illness. They also have an exaggerated cytokine storm due to underlying immune dysregulation. We wish to report our experience with 3 DS patients who were admitted to our intensive care unit (ICU) with COVID19 pneumonia which was confirmed on a positive reverse transcriptase-polymerase chain reaction (RT-PCR) from a nasopharyngeal swab. Although one patient was successfully managed with NIV, two patients required invasive ventilation but were eventually extubated and discharged from the hospital. We want to emphasize that patients with DS should be considered susceptible for serious outcomes due to COVID19 disease and should be offered immunization in the Sultanate of Oman as a top priority.

Keywords: Adult Respiratory Distress Syndrome; COVID19; Down's Syndrome; Mechanical Ventilation; Non-Invasive Ventilation; Pneumonia; Ventilation.

Introduction

Downs syndrome (DS), which is due to Trisomy 21 is the most common chromosomal abnormality found in humans. These patients manifest anatomical abnormalities in the respiratory tract like smaller trachea, enlarged adenoids and tonsils, macroglossia, narrowing of upper airway, tracheobronchial malacia, hypotonia of upper airway predisposing them to aspiration, and glossoptosis. A review by Watts et al revealed that lower respiratory tract infections (LRTI) are responsible for 43-78% of hospitalizations. At least 50% of these patients required ventilatory support. [1] Patients with DS have several issues like anatomical aberrations in the upper respiratory tract, underlying immune dysregulation, and are uncooperative for non-invasive ventilation as many are mentally challenged. Therefore, when they develop serious respiratory illness like COVID19, they have a stormy course and at times have unfavorable outcome. These patients should be monitored closely and also offered invasive ventilation based on their clinical presentation.

We report our experience of 3 DS patients who were admitted to our intensive care unit (ICU) with COVID19 infection which was confirmed on a positive reverse transcriptase polymerase chain reaction (RT-PCR) from nasopharyngeal swab.

Case series

Patient 1

A 37-year female, a known case of Down's syndrome, was admitted to COVID ICU with tachypnoea (respiratory rate of 35/minute) and oxygen saturation (SpO_2) of 88% and with bilateral infiltrates on chest radiograph [Figure 1a]. Non-invasive ventilation (NIV) was initiated on arrival with following settings- pressure support (PS) of 15 cm of water, positive end expiratory pressure (PEEP) of 10 cm of water, and fraction of inspired oxygen (FiO_2) of 0.6. After 6 days of NIV, she improved clinically and radiologically with acceptable PaO_2/FiO_2 (P/F) ratio. She was discharged on day 14 of admission from the hospital.

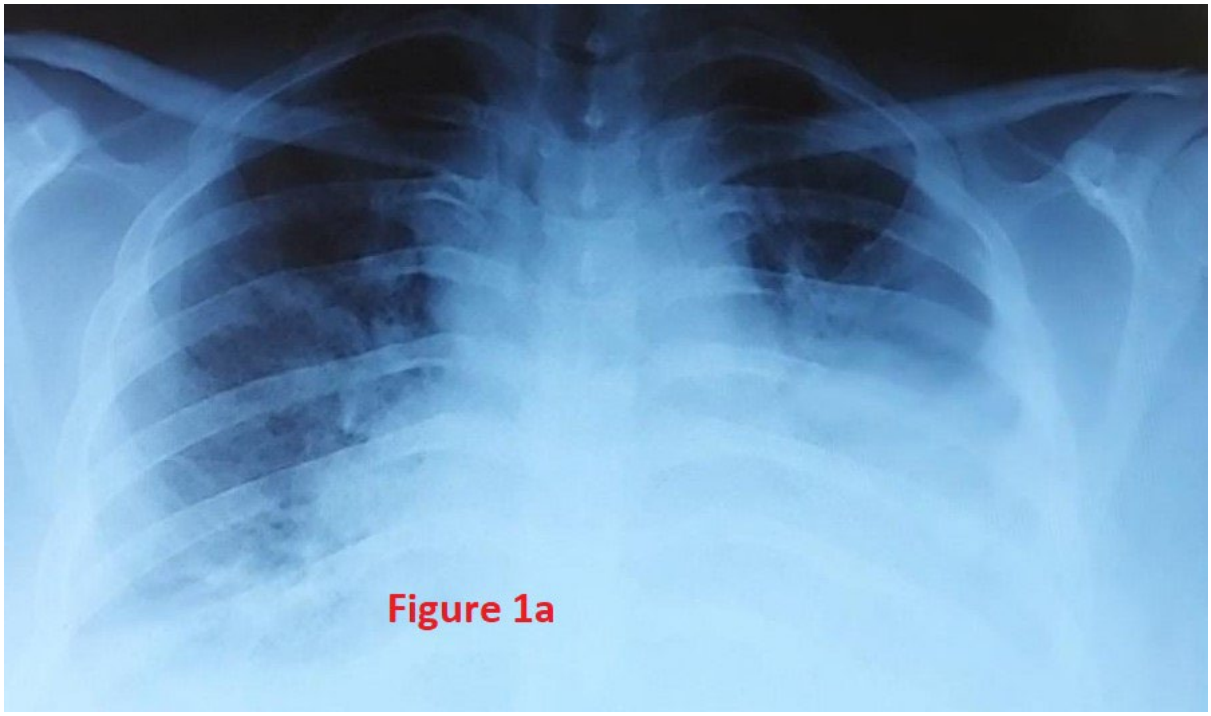

Figure 1a: Chest radiograph in anteroposterior view of patient 1 with bilateral infiltrates suggestive of COVID19 pneumonia.

Patient 2

A 32-year female patient, a known case of Down's syndrome, was admitted with tachypnoea and desaturation (SpO_2-85%). NIV was initiated (PS-12 cm of water, PEEP-12 cm of water, FiO_2 of 0.7). Her oxygen requirement kept increasing (P/F ratio consistently less than 100 for 2 days) and had no improvement in chest radiograph [Figure 1b]. After 4 days of NIV, she was intubated and ventilated. Prone ventilation was instituted as per international guidelines and neuromuscular blockade resorted to during prone position.[2] Fentanyl and midazolam infusions were used for sedo-analgesia. She was extubated after 5 days of mechanical ventilation and discharged on day 19.

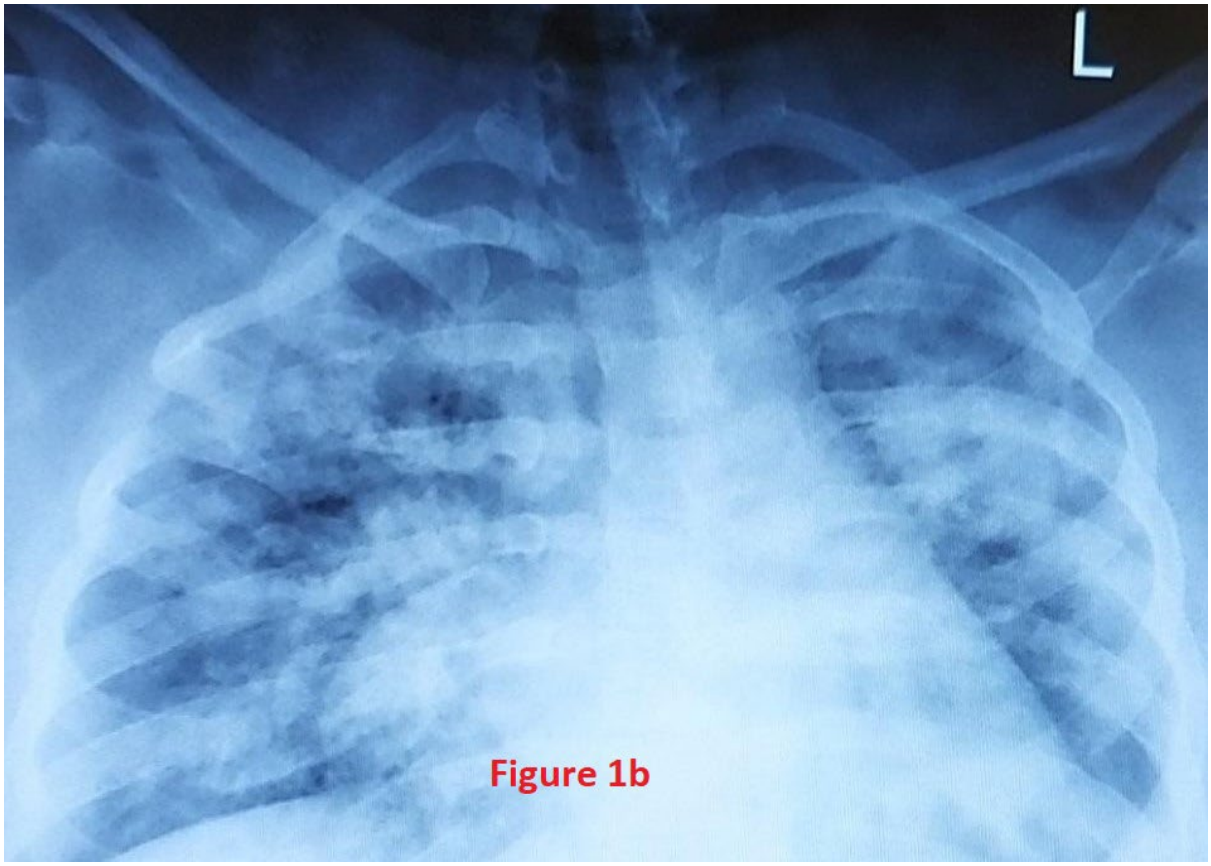

Figure 1b: Chest radiograph in anteroposterior view of patient 2 with bilateral infiltrates suggestive of COVID19 pneumonia.

Patient 3

A 24-years old male patient, a known case of Down's syndrome, admitted to COVID19 ICU was initiated on NIV (PS of 8 cm of water, PEEP 10 cm of water, FiO_2 1) in view of tachypnoea and desaturation (SpO_2- 87%). Chest radiograph showed bilateral infiltrates consistent with COVID19 pneumonia [Figure 1c]. Although respiratory distress settled with above ventilatory settings, P/F ratio remained low for 2 days (lowest being 61). Invasive ventilation was started and prone ventilation was initiated as mentioned above. In view of leukocytosis and presence of multi-drug resistant bacteria in tracheal secretion culture, broad spectrum intravenous antibiotics were started based on sensitivity report. Serial chest radiographs and arterial blood gas analysis showed consistent improvement. Trachea was extubated after 9 days of mechanical ventilation and thereafter managed with NIV for another 2 days followed by oxygen therapy. Patient was discharged from the hospital on day 19.

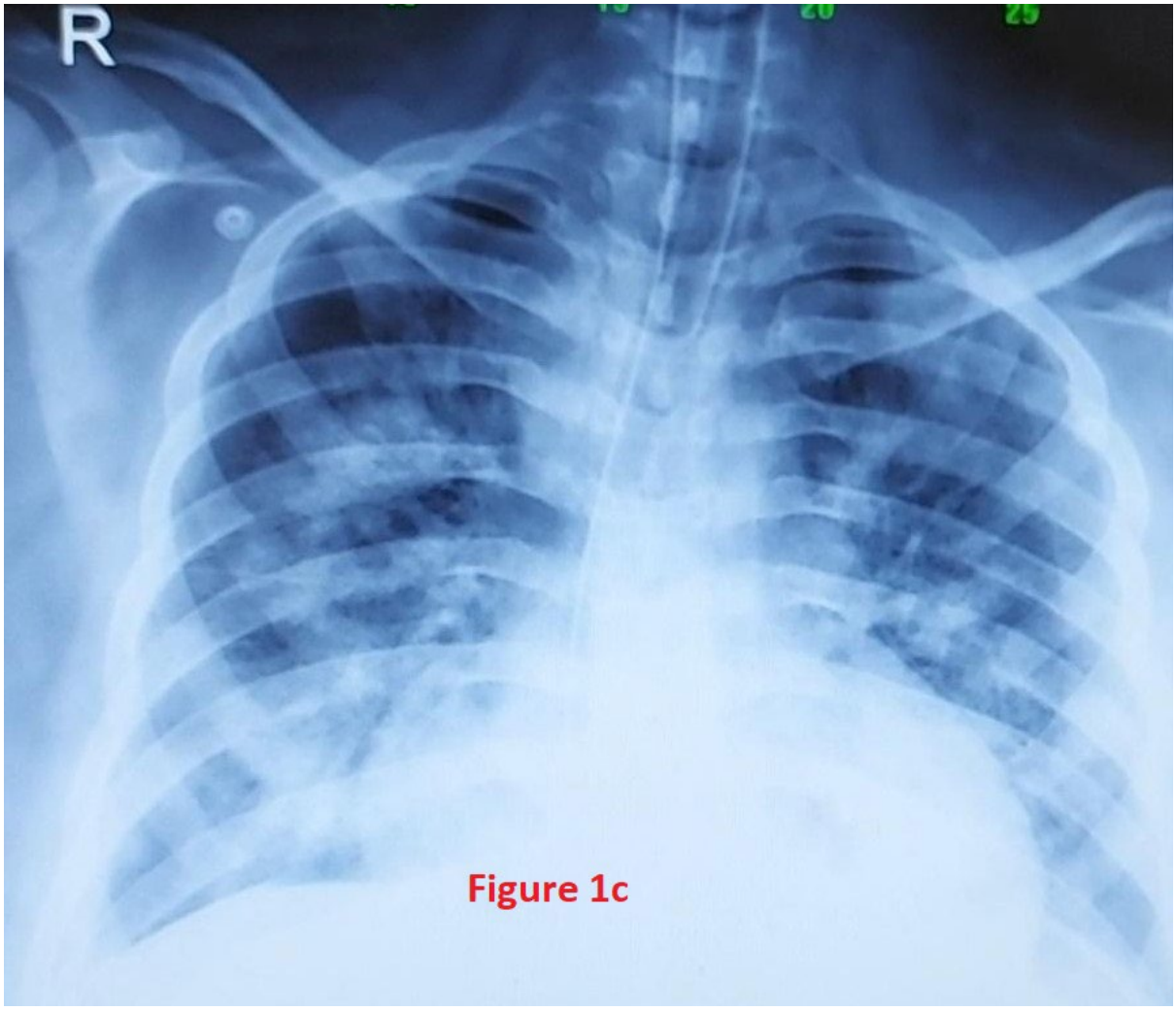

Figure 1c: Chest radiograph in anteroposterior view of patient 3 with bilateral infiltrates suggestive of COVID19 pneumonia.

Demography details, duration of ventilation, adverse events, inflammatory markers, relevant investigations, medications used, and duration of hospital stay have been summarized in table 1a and 1b.

Table 1a: Demographic data, relevant investigations and inflammatory markers.

S.no.	Age (years)	Weight (kg)	Associated problems	WBC count (2.2-10)10*3/uL Arrival/ Highest	Neutrophils (1-5) 10*3/uL Arrival/ Highest	Lymphocytes (1.2-4) 10*3/uL Arrival/ Lowest	CRP: mg/L Arrival/ Highest	Ferritin 18-323 ng/ml Arrival/ Highest	D-dimer: 0-0.55 mg/L Arrival/ Highest	LDH 125-240 iU/L Arrival/ Highest
Case 1	37	69	Hypothyroid	6.92 16.07	4.79 9.8	1.65 1.65	51.39 51.39	1458 1629	0.46 0.46	471 471
Case 2	32	80	Hypothyroid	9.95 29.39	8.41 25.36	1.00 0.7	18.8 109		0.45 1.20	344 488
Case 3	24	105	Hypothyroid	6.71 17.38	5.97 14.75	0.5 0.5	152 152	20374	1.99	1552

WBC- White blood cells, CRP: C-reactive protein, LDH- lactate dehydrogenase.

Table 1b: Details of ventilatory support, oxygenation, duration of hospital stay, supportive treatment.

S.no.	IV/NIV	No. of days of ventilation (IV/NIV)	Extubation	Adverse events	Discharge from hospital	P/F ratio (lowest)	Highest PEEP required (cm H2O)	Supportive treatment
Case 1	NIV	6	NA	NONE	Day 13	120	10	Convalescent plasma, Dexamethasone, Broad spectrum antibiotics, Favipiravir. LMWH
Case 2	NIV and IV	NIV- 4+3 IV-5	After 5 days	NONE	Day 21	90	14	Tocilizumab, Dexamethasone, Broad spectrum antibiotics, Favipiravir, LMWH
Case 3	NIV and IV	NIV-2+2 IV-9	After 9 days	NONE	Day 19	61	14	Favipiravir, Dexamethasone, Tocilizumab, Broad spectrum antibiotics

NIV: non-invasive ventilation, IV: invasive ventilation, NA-not applicable, P/F- PaO_2/FiO_2, LMWH- low molecular weight heparin, PEEP- positive end expiratory pressure

Discussion

Intellectual impairment, disorders of cardiovascular system, dependency on family members, and immune dysregulation are the associated factors which further predispose these patients to adverse pulmonary complications. The proposed mechanism of immune dysregulation is that several genes encoded in chromosome 21 are over-expressed in patients with DS. Hence these patients have increased circulating cytokines like tumor necrosis factor-α, interleukin (IL)-β and IL-λ levels along with an altered cell-mediated immunity. Therefore, these patients tend to have exaggerated inflammatory responses and infectious diseases tend to be more severe. The disease course in patients with DS affected with COVID19 is expected to be stormy due to various factors. These are mental retardation, abnormalities of upper airway predisposing to frequent respiratory tract infections, immune dysregulation- all of which can lead to a severe course of illness. [3] Underlying pulmonary hypertension, obstructive sleep apnea, and chronic lung disease resulting from chronic respiratory tract infections also make the disease process tempestuous for these patients. These patients are more susceptible for secondary bacterial infections due to underlying chronic lung disease. [4]

Patients with DS have unfavorable characteristics like mental retardation, attention problems, cognitive dysfunction, tantrums all of which make them unsuitable for NIV. Due to these issues, previous papers have shown that these patients have worse outcomes. [5] In Sultanate of Oman, the birth prevalence of DS is 2.4 in 1000 which translates to about 120 affected births / year. [6]

In a retrospective study by Pérez-Padilla et al, authors presented their data derived from a national database of 60 patients with DS who were admitted during the H1N1 pandemic (2009). On analysis authors concluded that patients with DS had an increased propensity for hospitalization, endotracheal intubation, and death due to pulmonary complications when compared with patients without DS. [7] Even if they are successfully weaned off mechanical ventilation, it is difficult to expect assisted respiratory exercises like incentive spirometry from these patients. Underlying compromised cardiopulmonary status predisposes these patients to a serious course of viral illness. They also have an exaggerated cytokine storm due to underlying immune dysregulation. Vita et al have suggested early vaccination in this high-risk category of patients in view of above-mentioned issues and possibility of a stormy course of disease.[8]

In an international online survey performed by Hüls et al, authors identified 1046 patients with DS from a total of 59,025 hospitalized patients with a mortality of 13% in DS patients. The authors suggested that patients with DS should be considered a priority group for COVID-19 vaccination. [9] The mortality in hospitalized DS patients is higher than that of the mortality in general population of patients admitted due to COVID19 infection. [10] Hence, we also suggest that all DS patients should be considered a priority group for vaccination.

Conclusion

Patients with DS with COVID19 disease and presenting with hypoxic respiratory failure should be closely monitored clinically. Managing NIV is challenging in these patients due to underlying intellectual problems and their dependency on family members. If managing with NIV is difficult, early invasive ventilation should be considered if clinical course is expected to worsen based on inflammatory markers, chest radiograph, P/F ratio and clinical signs.

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