COVID-19 pneumonia successfully managed with high-flow nasal cannula in a 15-year-old boy

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SUMMARY

We report an otherwise healthy, fully immunised 15-year-old boy who was transferred to our Pediatric intensive care unit with 4 days of fever, dry cough, increased work of breathing and impending respiratory failure. Two days prior, amoxicillin/clavulanic acid was prescribed for lower airway symptoms resembling pneumonia. PCR of the nasopharyngeal swab revealed an active COVID-19 infection (Ct 19). The CT scan showed significant ground-glass opacities highly associated with COVID-19 (COVID-19 reporting and data system 4). Antibiotics were continued and chloroquine was given for 5 days. High-flow nasal cannula (HFNC) was started as respiratory support therapy with rapid decrease of tachypnoea and oxygen demand. HFNC was successfully stopped after 7 days. The patient made full clinical recovery. This case illustrates HFNC as a successful respiratory support therapy in a paediatric patient with an active COVID-19 pneumonia.

BACKGROUND

Approximately 1.2%–2% of all COVID-19 infections involve children. COVID-19 (SARS-CoV-2) affects all ages and shows no significant gender difference.[1–4] The signs of COVID-19 infection vary from a common cold to more severe disease consisting of bronchitis, pneumonia, severe acute respiratory distress syndrome (ARDS), multiorgan failure and even death. Severe COVID-19 pneumonia in children is rare. Dong *et al* published the largest COVID-19 retrospective case review of 2143 children, of which 4.4% were asymptomatic, 50.9% had mild symptoms and 38.8% had moderate disease, defined as pneumonia with fever and dry cough, but no obvious hypoxaemia. Severe symptoms were reported in 5,9% of the children.[2] The median time from illness onset to diagnosis was 2 days (range: 0–42 days).[2] Children with COVID-19 infection seem to be less affected compared with adults, showing milder symptoms and less progression to severe disease. Information about children requiring intensive care is limited. A study by Ong *et al* reported 5.2% children with respiratory distress and hypoxia, of which 0.6% progressed to ARDS.[4] Children under the age of 1 year are most vulnerable for severe disease. Dong *et al* reported 10.6% critical cases under the age of 1 year compared with 4.1% within the age group of 11–15 years.[2]

CASE PRESENTATION

An otherwise healthy 15-year-old boy was transferred from a regional hospital to our paediatric intensive care unit (PICU) with 4 days of fever (40°C), increased work of breathing, inability to speak, dry cough and impending respiratory failure, due to an active COVID-19 infection (Ct 19). His medical history was non-contributory, and he had no history of systemic illness. The general practitioner prescribed amoxicillin/clavulanic acid after diagnosing pneumonia 2 days earlier. His mother also experienced dry cough and shortness of breath. No other people in the surroundings had signs of active COVID-19 infection. He was living with his mother and sister during the COVID-19 pandemic. There was no history of recent travel to pandemic regions.

On examination, he was alert with a patent airway, breathing 31 times/min with chest retractions. He had a peripheral oxygen saturation of 91% with a non-rebreathing mask (15 L/min) and increased oxygen demand, heart rate 92 beats/min and blood pressure of 108/37 mm Hg. A chest X-ray showed a bilateral pneumonia with complete atelectasis of the left lung (figure 1). Subsequently, a chest CT was performed which showed significant ground-glass opacities in the left lung and some ground-glass opacities in the right lung (COVID-19 reporting and data system 4 (CORADS 4)), highly associated with severe COVID-19 infection (figure 2).

INVESTIGATIONS

At the time of hospitalization, blood cell count showed markedly elevated C reactive protein (CRP; 420 mg/L); thrombocytopenia (87×10^9/L); leucopenia (3.4×10^9/L) and lymphocytopenia (0.3×10^9/L) with an overload of young white blood cells. An elevated creatinine was also found (110 μmol/L), which improved after adequate fluid intake. Liver enzymes, electrolytes and glucose were normal. Coagulation parameters showed increased D-dimer (3.1 mg/L), prothrombin time (19.4 s) and activated partial thromboplastin time (58.4 s).

The PCR of the nasopharyngeal swab was negative for rhinovirus, influenza A/B, respiratory syncytial virus, human metapneumovirus, but was positive for COVID-19 (Ct 19). Bacterial culture of the throat was negative, and no blood cultures were taken. Before the administration of chloroquine, an ECG was performed which showed no prolonged QTc . No signs of pulmonary embolism were found on the chest CT.

TREATMENT

Initially, bacterial pneumonia was considered, and amoxicillin/clavulanic acid was continued intravenously due to the combination of respiratory

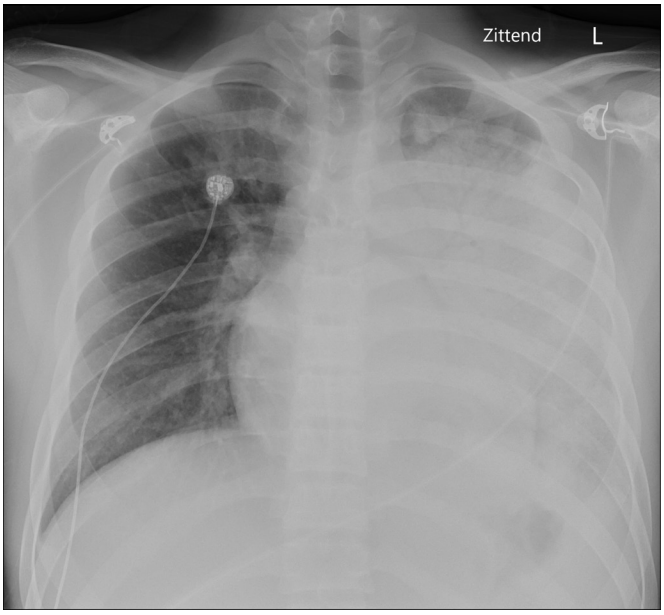

Figure 1 Chest X-ray at hospitalisation which shows bilateral pneumonia with complete atelectasis of the left lung.

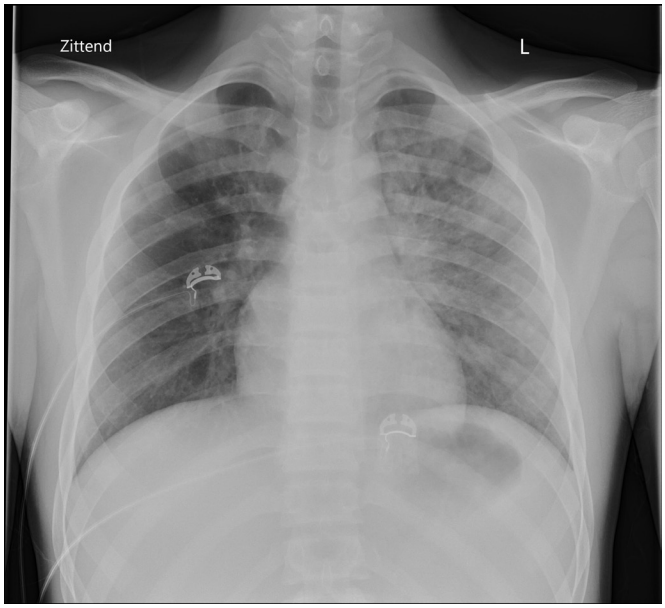

Figure 3 Chest X-ray after 7 days of hospitalisation, showing total recovery of infiltration, atelectasis and ground-glass opacities.

distress and fever for 14 days. Chloroquine was administered for a total of 5 days. High-flow nasal cannula (HFNC) was immediately started (50 L/min) with initial oxygen administration of 70%, with the aim of avoiding intubation and to diminish work of breathing. Physiotherapy was started to stimulate coughing and later to support his muscle weakness. Prone position was not necessary in this patient because of his fast recovery after starting HFNC.

OUTCOME AND FOLLOW-UP

In the first hours after starting HFNC, the patient showed clinical improvement with reduced work of breathing. Because of fast improvement after starting HFNC, there was no immediate need for intubation. The inflammation decreased as shown by normalisation of the temperature and lowering of CRP. Breathing exercises resulted in a productive cough and mobilisation of mucus. With clinical improvement, his appetite increased. After 7 days, the chest X-ray showed no signs of infiltration or atelectasis (figure 3). HFNC was discontinued after 7 days and he was transferred to the medium care unit with low-flow oxygen therapy (2 L/min). After 9 days of hospitalisation, he made a full clinical recovery and was discharged home without supplemental oxygen. Amoxicillin/clavulanic acid was continued for a total of 14 days.

Follow-up is arranged after 3 months in our outpatient clinic, where a chest CT will be performed to evaluate his pulmonary condition.

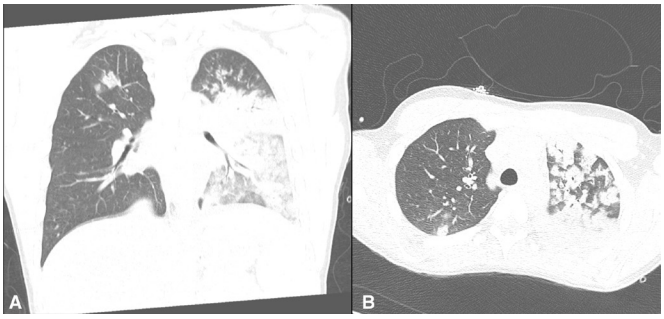

Figure 2 (A, B) Chest CT which showed significant ground-glass opacities in the left lung and a couple of ground-glass opacities in the right lung (COVID-19 reporting and data system 4).

DISCUSSION

The symptoms of paediatric COVID-19 infection vary widely and resemble symptoms of an acute upper respiratory tract infection such as fever, fatigue, cough, sore throat, rhinorrhoea and shortness of breath.[1] In rare severe cases, patients can progress to respiratory failure, shock, coagulation dysfunction and renal injury.[5]

Why adults are more severely affected by the COVID-19 virus is topic of discussion. One of the theories suggests that secondary haemophagocytic lymphohistiocytosis (sHLH), an uncontrolled and hyperinflammatory syndrome triggered by an infection (like COVID-19), plays a role. sHLH is characterised by a fulminant hypercytokinaemia with multiorgan failure. Untreated sHLH is fatal, but even when treated, mortality is high. Pulmonary involvement (including ARDS) occurs in approximately 50% of adult patients with hypercytokinaemia.[6] A cytokine profile resembling sHLH is associated with COVID-19 disease severity, characterised by increased interleukins (IL-2, IL-7, granulocyte colony-stimulating factor, interferon-Y and tumour necrosis factor-alpha).[6 7]

In adult patients with COVID-19, a dysregulation of the immune response is described due to suppressed T cells, resulting in a delayed immune response and uncontrolled viral replication and hyperinflammatory response of the body.[8] Children do not have a similar tendency toward immune dysregulation. Diagnostic findings like elevated inflammatory markers and lymphocytopenia are less common in children. Lu *et al* described 171 children with COVID-19 infection, of which 3.5% showed lymphocytopenia.[9] Bai *et al* reported 25 paediatric COVID-19 cases and described no abnormalities in absolute lymphocyte counts and CRP in mild to severe cases.[10] Children are possibly less susceptible to severe COVID-19 disease due to decreased expression of ACE-2.[4] COVID-19 enters respiratory epithelial

cells by attaching to ACE-2 receptors. Affinity of COVID-19 for ACE-2 receptor is approximately 10–20 times higher than other coronaviruses.[11] Another hypothesis to why children are less affected is the relation between the vaccination status (especially the measles, mumps and rubella (MMR)) and the severity of the COVID-19 symptoms. The fusion proteins in this vaccine share structural similarities with the spike glycoproteins of COVID-19. The MMR vaccination was introduced in the mid 1970s, which may be one of the reasons why adults of higher age and therefore no prior MMR vaccination have a higher risk of developing severe symptoms of COVID-19 infection.[12]

Most of the typical findings on chest CT start with unilateral lesions with rapid evolution into diffuse bilateral ground-glass opacities with air bronchograms within 1–3 weeks after the onset of symptoms. Abnormal lung CT findings can even be present in asymptomatic patients.[13–15] Old age, male sex, underlying comorbidities and progressive radiographical deterioration on follow-up CT might be risk factors for poor prognosis, ARDS and even death in patients with COVID-19 pneumonia.[15] Ai *et al* reported 1014 adult patients, of which 59% had positive PCR results and 88% had positive chest CT scans. In patients with negative PCR results, 75% had positive chest CT findings, indicating that a chest CT not only has a high sensitivity, but could be also an important complement to the PCR test.[13] In accordance with the conclusion of Ai *et al*, the chest CT in our case was performed in addition to the positive PCR result. The CORADS classification is a standardised classification system for radiologists in the Netherlands for patients with suspected COVID-19 infection.[12] Based on the CT findings, the level of suspicion of COVID-19 infection is graded from very low (CORADS 1) up to very high (CORADS 5). Our patient had a CORADS 4 classification, which correlates with a high level of suspicion of COVID-19 infection.[14–16]

Chloroquine was successfully used during the SARS pandemic, and is therefore considered as potentially beneficial in the treatment of patients with COVID-19.[17] Chloroquine is primarily used to prevent and treat malaria, and is efficacious as an anti-inflammatory agent for the treatment of rheumatoid arthritis and lupus erythematosus. Wang *et al* revealed that it also has potential broad-spectrum antiviral activities by increasing endosomal pH required for virus/cell fusion, because low pH is necessary for cell fusion of COVID-19, as well as interference with glycosylation of cellular receptors of SARS-CoV.[18] Nevertheless (hydroxy)chloroquine is not useful in the treatment of COVID-19. Horby *et al* and Axfors *et al* described no positive effect in the treatment in adult patients with COVID-19.[19 20] However, because of the limited scientific evidence and the possible side effects, chloroquine should be prescribed with caution in children with COVID-19 virus infections.[21] In our case, chloroquine was given early in the COVID-19 pandemic without the availability of the literature as cited above.

The Dutch paediatric guidelines recommend intubation with rapid sequence induction to avoid an unanticipated need for intubation with increased risk of respiratory arrest and increased risk of aerosol exposure to the intubating team in patients with COVID-19 with mild to severe respiratory distress.[20] However, clinicians experienced that mortality of invasively ventilated patients was high and it was not easy to extubate many of these patients.[22] This raised the question whether HFNC could be a good alternative additional respiratory support therapy in paediatric patients with COVID-19. Some hospitals discourage the use of non-invasive modalities such as HFNC, others such as Surviving Sepsis/Society of Critical Care Medicine Guidelines advocate it as the first-line approach.[22] Opponents are afraid that aerosol-generating procedures, including intubation and HFNC, could lead to aerosol dispersion and places healthcare workers at increased risk of contracting COVID-19. However, the fear of increased infection risk of healthcare workers is questionable. There is little data to prove that HFNC results in dispersion of viral particles. Li *et al* investigated the differences between exhaled smoke dispersion in different devices with 10 L/min and 60 L/min and no differences in dispersion of virus particles between oxygen masks/venturi masks and HFNC were found.[23] Our patient was admitted in a negative pressure isolation room on the PICU and personal protective equipment was used. Nobody was infected with COVID-19 after taking care of the patient.

HFNC refers to high-flow oxygenated gas heated and humidified to body condition, and delivered via nasal cannula. It may provide specific positive end-expiratory pressure and improves inspiratory peak flow by reducing the inspiratory resistance/bronchoconstriction. Heated and damp air through the nasal pharynx makes it tolerable and reduces the metabolic work and anatomical dead space by the washout of CO_2 from the upper airways. The heat and humidification also help to maintain hydration and mobility of secretions and preserve mucociliary function.

Despres *et al* described six adult patients with severe COVID-19 disease, all of whom were successfully managed with HFNC in the prone position and avoided the need of invasive ventilation.[24 25] Raoof *et al* revealed that the respiratory status of approximately 20%–25% of patients with COVID-19 stabilised by using different modalities such as HFNC, non-invasive ventilation and awake proning. The fact that prone position improves oxygenation in patients with ARDS is well known and could also benefit patients with COVID-19 while using HFNC.

HFNC is a good respiratory support therapy, but strict evaluation of the clinical condition is essential and should never delay intubation if the patient deteriorates. With the use of HFNC, the risk of permanent damage to the lung epithelium due to ventilator-induced lung injury may be avoided, but also potentially associated harms such as sedation and prolonged ICU stay.[25]

In conclusion, HFNC can be safely used as respiratory support therapy in paediatric patients with COVID-19 with the use of aerosol mitigating interventions considered. Re-evaluation of the clinical status is essential to prevent delay in the notification of

Learning points

- High-flow nasal cannula can be safely used as respiratory support therapy in paediatric patients with moderate-to-severe COVID-19 pneumonia.
- Aerosol-mitigating interventions, such as negative pressure rooms, high efficiency particulate air filters and adequate personal protective equipment, are sufficient to protect healthcare workers.
- Severe COVID-19 pneumonia in children is rare; most of the children have mild respiratory symptoms and fever.
- Elevated inflammatory markers and leucopenia are seen in adults with COVID-19 pneumonia but are rare in children.
- Combining the assessment of CT imaging features (COVID-19 reporting and data system classification) with clinical and laboratory findings could facilitate early diagnosis of COVID-19 pneumonia.

respiratory deterioration while using HFNC but could prevent ventilator-induced lung injury and prolonged ICU stay.

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