


INSTRUCTIVE CASE

First paediatric COVID-19 associated death in ItalyFederico Mercolini ¹, Daniele Donà,² Ylenia Girtler,¹ Konrad Anton Mussner,³ Paolo Biban,⁴ Andrea Bordugo⁵ and Grazia Molinaro⁶

¹Department of Pediatrics, Hospital of Bolzano, ³Department of Pediatrics, Hospital of Vipiteno, ⁶Pediatric Palliative Care, Pain Service, Bolzano Hospital, Bolzano, ²Division of Paediatric Infectious Diseases, Department of Woman's and Child's Health, Padua University Hospital, Padua, ⁴Department of Neonatal and Pediatric Critical and Emergency Care, and ⁵Inherited Metabolic Disease Unit, Department of Pediatrics, Azienda Ospedaliera Universitaria Integrata Verona Sede di Borgo Trento, Verona, Italy

Since December 2019, a novel, highly infective coronavirus has emerged in Wuhan, China, rapidly spreading around the world. In the last few months, several studies on paediatric COVID-19 have been published,^{1–4} highlighting the less aggressive clinical course observed in children compared to adults. However, there is limited evidence regarding the impact of COVID-19 in paediatric patients with chronic or degenerative diseases.

Case Report

We report the case of a 5-year-old girl with mucopolysaccharidosis type II (mutation of both GNPTAB genes: c.3503_3504delTC) who died from COVID-19 pneumonia complicated by acute respiratory distress syndrome (ARDS).

She had growth retardation (weight, height and head circumference < 3rd percentile) and neurological impairment. Since 2018, she developed hypertrophic cardiomyopathy, with thickening of the mitral and aortic valves. Despite this, cardiac and pulmonary function remained stable, with no need for respiratory support or pharmacological therapy.

On 25 March, 2020, she had fever of 39.5°C and rhinorrhoea, with overall good clinical condition. At that time, some members of her family presented symptoms suggestive of SARS-CoV-2 infection. Her mother had anosmia without respiratory symptoms; one aunt had a febrile respiratory infection; and two grandparents had fever, cough and fatigue. Oral broad-spectrum

antibiotic therapy was started due to persistent fever; a nasopharyngeal swab for detecting SARS-CoV-2 was performed. Two days later, the young child became symptomatic with moderate dyspnoea (respiratory rate 30/min, mild intercostal retractions) and needed supplemental oxygen. Meanwhile, positivity for COVID-19 was confirmed. Although the parents were initially keen to keep their child at home, hospitalisation was necessary. On admission, chest X-ray showed marked bilateral opacification (Fig. 1). Her serum C-reactive protein was 17.3 mg/dL, lactate dehydrogenase 700 U/L and interleukin-6 78.3 pg/mL (normal 5–15), with normal blood cell count and renal and liver function tests.

Parenteral hydration, intravenous antibiotics (ceftriaxone and azithromycin) and corticosteroid therapy (methylprednisolone 1 mg/kg/day) were started. In less than 24 h, mask oxygen requirement increased to 7–8 L/min. We considered therapy with hydroxychloroquine, but this was not administered due to her rapid deterioration.

Parents and doctors, in consideration of the patient's underlying disease, agreed not to proceed with invasive ventilatory



Fig. 1 Chest x-ray showing widespread opacification of both lungs.

Key Points

- 1 Children show a milder course of COVID-19 infection than adults.
- 2 The impact of COVID-19 infection in paediatric patients with chronic or degenerative diseases is not known.
- 3 Dedicated guidelines should be developed for these patients and their families.

Correspondence: Dr Federico Mercolini, Department of Pediatrics, Hospital of Bolzano, 39100 via L. Bohler 5, Bolzano, Italy. Fax: +39 0471 908656; email: federico.mercolini@sabes.it

Conflicts of interest: None declared.

Accepted for publication 20 May 2020.

support. The patient passed away in her mother's arms in the following days.

Discussion

There is strong evidence that COVID-19 infection is generally milder in children than adults.^{1–4} The cause for this difference in incidence and severity is still not known. Many hypotheses have been formulated so far, including differences in the immune response, different ACE2 receptor expression and/or lower risk of developing ARDS.⁵

The largest paediatric case series described patients with a median age ranging from 6.7 to 8.3 years.^{2–4} Qui *et al.* reported 36 hospitalised children, of whom 53% had moderate pneumonia, 19% had dry cough only, and 28% had mild symptoms or were asymptomatic.² In a cohort of 171 paediatric patients, Lu *et al.* reported cough and pharyngeal erythema as the most common symptoms, associated with fever in less than half of patients.³ Chest-X-ray showed ground-glass opacity in 32.7%, patchy local shadowing in 18.7% and patchy bilateral shadowing in 12.3% of patients. Only three patients needed invasive ventilation, one of whom had leukaemia on maintenance chemotherapy, one had hydronephrosis and one had intussusception. Dong *et al.*⁴ described 2143 paediatric patients: 731 laboratory-confirmed cases and 1414 suspected cases. Unlike adult patients, only 5% of symptomatic children had dyspnoea or hypoxia, and only 0.6% progressed to acute respiratory distress syndrome.

Ludvigsson analysed data from 45 scientific papers and letters on COVID-19 in children, confirming the milder disease course and better prognosis in children than adults.⁶ The proportion of all cases that were paediatric ranged between 1 and 5%, with a much lower rate of severe pneumonia, lymphopenia and raised inflammatory biomarkers.⁶ However, there are less data on COVID-19 in children with comorbidities such as cancer or chronic or degenerative diseases. Sinha *et al.*⁷ recommend that these patients should be considered at higher risk for complicated disease. Interestingly, Bouffet *et al.*⁸ recently provided some recommendations regarding the optimal management of children with cancer. Ideally, these patients should be admitted to COVID-19-free hospital sites with dedicated health-care providers. In addition, if at all possible, they should be managed at home, observing general infection prevention rules and appropriate use of personal protection equipment (PPE) by health-care personnel and by other care givers in close contact with the patient, while maintaining a strict clinical monitoring and ongoing communication with the hospital team.

A similar level of protection may need to be adopted for children with metabolic conditions. The use of PPE even at home by family members, a scrupulous education of care givers in the prevention of transmission and the strengthening of telemedicine for early recognition of alarming situations could improve the management, quality of life and outcome of these fragile patients.

Conclusions

We report the first paediatric death in Italy of a young child with a severe metabolic disorder. Our case emphasises that some children with chronic medical conditions may have a worse prognosis with COVID-19 infection. This has implications for prevention. Health-care providers should provide special support and guidance to these patients and their families.

Acknowledgement

The authors thank the child's parents for approving the publication of this case.

References

- 1 Cai J, Xu J, Lin D *et al.* A case series of children with 2019 novel coronavirus infection: Clinical and epidemiological features. *Clin. Infect. Dis.* 2020; ciaa198. <http://dx.doi.org/10.1093/cid/ciaa198>.
- 2 Qiu H, Wu J, Hong L, Luo Y, Song Q, Chen D. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: An observational cohort study. *Lancet Infect. Dis.* 2020; **20**: 689–696. [https://doi.org/10.1016/S1473-3099\(20\)30198-5](https://doi.org/10.1016/S1473-3099(20)30198-5).
- 3 Lu X, Zhang L, Du H *et al.* SARS-CoV-2 infection in children. *N. Engl. J. Med.* 2020; **382**: 1663–1665. <https://doi.org/10.1056/NEJMc2005073>.
- 4 Dong Y, Mo X, Hu Y *et al.* Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China. *Pediatrics* 2020; **145**: e20200702. <https://doi.org/10.1542/peds.2020-0702>.
- 5 Brodin P. Why is COVID-19 so mild in children? *Acta Paediatr.* 2020; **109**: 1082–1083. <https://doi.org/10.1111/apa.15271>.
- 6 Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. *Acta Paediatr.* 2020; **109**: 1088–95.
- 7 Sinha IP, Harwood R, Semple MG *et al.* COVID-19 infection in children. *Lancet Respir. Med.* 2020; **8**: 446–447. [https://doi.org/10.1016/S2213-2600\(20\)30152-1](https://doi.org/10.1016/S2213-2600(20)30152-1).
- 8 Bouffet E, Challinor J, Sullivan M, Biondi A, Rodriguez-Galindo C, Pritchard-Jones K. Early advice on managing children with cancer during the COVID-19 pandemic and a call for sharing experiences. *Pediatr. Blood Cancer* 2020; **2**: e28327. <https://doi.org/10.1002/pbc.28327>.