Case report

Atypical case of COVID-19 in a critically unwell 5-week old infant

Abirami Namasivayam, Than Soe, Jason Palman

Paediatrics, Princess Alexandra Hospital NHS Trust, Harlow, UK

Correspondence to
Dr Abirami Namasivayam; a.namasivayam@nhs.net

Accepted 30 July 2020

SUMMARY

The effect of COVID-19 by SARS-CoV-2 on the paediatric population remains an evolving mystery. Early reports from China stated that children seem to be unharmed by its dangerous effects, yet more recently there has been evidence of a systemic inflammatory response in a small number of children who are affected. We discuss a 5-week-old male infant who presented atypically with severe COVID-19 infection. To our knowledge, he is the youngest reported case in the UK to require mechanical ventilation and intensive care treatment as a direct result of COVID-19 following horizontal transmission. This case has generated several learning points with regard to atypical presentations of COVID-19 and identifying a potential cohort of 'at risk' infants. We also highlight a number of new challenges that have arisen for paediatricians and anaesthetists providing airway management for infants with SARS-CoV-2.

BACKGROUND

The world has unfortunately entered into a new challenge by facing the global pandemic of COVID-19. At the time of writing, more than 200 countries have been affected with over 16 million confirmed cases and over 650 000 deaths.[1] Even 6 months from the first reported case there remain vast uncertainties surrounding the virus. There has been extensive evidence which highlights the discriminatory nature of COVID-19. While the elderly, immunocompromised and black Asian and minority ethnic community remain its prime victims; children seem to be largely spared by its effects.[2] Why and how children have this tolerance are crucial unanswered questions.

Between December 2019 and February 2020, China reported a total of 31 211 cases of confirmed COVID-19.[3] Only nine of these cases were infants (aged 28 days to 1 year), none of whom required intensive care, mechanical ventilation or had severe complications.[3] Choi *et al* reviewed the epidemiology and clinical presentation of coronavirus in children as of March 2020, reporting 2.4% (0–18 years) in China, 3.6% (6 months to 17 years) in Singapore, 1.4% (0–18 years) in Italy, 1% (0–9 years) in Republic of Korea and 2.8% (0–9 years) in Australia.[4] A larger nationwide study investigating 134 paediatric cases across China reported that 76% cases had fever, 64.9% cases presented as acute upper respiratory tract infection, 26.9% as mild pneumonia and 1.5% cases were critical; unfortunately, the specific age groups and comorbidities were not reported.[4 5]

The Royal College of Paediatric Child Health has recently released evidence of children responding to COVID-19 with a systemic inflammatory response.[6] However, greater awareness and investigation for children with suspected infection is needed.

We report the case of a 5-week-old male infant who presented atypically to the commonly described features and deteriorated rapidly in our district general hospital (DGH). We explore the learning points from this case.

CASE PRESENTATION

A 34-day-old 2.1 kg ex-premature male infant was brought to the paediatric emergency department (PED) with reduced feeding and lethargy; he was 37^{+3} weeks corrected gestation at the time.

He was born at 32^{+4} weeks gestation via caesarean section due to maternal type 1 diabetes mellitus and was admitted to the neonatal unit for support of prematurity and respiratory distress. The antenatal history was unremarkable. He was the first child born to parents, both white Caucasian. Although maternal steroids were given, he required surfactant at 24 hours of age and mechanical ventilation for 12 hours before weaning to continuous positive airway pressure (CPAP) for 4 days, and later high flow nasal cannula (HFNC). Chest X-ray at day 1 of life is seen in figure 1. He was off all respiratory support by day 17 of life and quickly established breastfeeding. He was treated with antibiotics for 48 hours with suspected sepsis. He was discharged home at day 22 of life.

Since being discharged from the neonatal intensive care unit (NICU), he had been breastfeeding and thriving well with no other concerns. His mother brought him to PED because he had not fed well over the last 12 hours and his activity levels were reduced. He had no fever, no increased work of breathing and no cough.

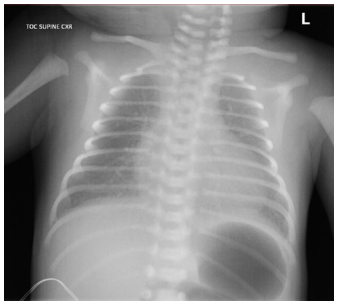

Figure 1 Chest X-ray on day 1 of life.

To cite: Namasivayam A, Soe T, Palman J. *BMJ Case Rep* 2020;**13**:e237142. doi:10.1136/bcr-2020-237142

Table 1 Blood gases over the course of the admission in the emergency department

Blood gases	pH	PCO_2	PO_2	HCO_3-	Base excess	Lactate	Glucose
Initial presentation	7.3	8.52	4.2	31.2	2.7	1.25	3.9
After unresponsive episode	7.21	7.67	–	22.5	−5.8	0.75	3.4
Post intubation	7.5	4.12	6.08	24	1.6	1.15	3.3
Mechanically ventilated	7.4	5.66	6.96	27	2.9	1.3	5.4

On initial assessment, he was alert but quiet. His heart rate was 125 bpm, his respiratory rate was 26/min, his saturations were 80% and despite being fully dressed, he was hypothermic with an unrecordable axillary temperature.

High flow facial oxygen was given which improved his oxygen saturations to above 97%. Although his respiratory rate was reduced, there were no other clinical signs of respiratory distress—no grunting, no recessions and his chest was clear with good air entry. He was haemodynamically stable with capillary refill time under 2 s. Intravenous access was obtained to deliver ceftriaxone and amoxicillin for suspected sepsis; his blood gas at this time showed a partially compensated respiratory acidosis (table 1). During this period he remained alert but was particularly quiet with minimal response to the interventions being performed.

Shortly after achieving intravenous access, the infant unexpectedly became unresponsive and bradycardic with heart rate reducing to 40–50 bpm with minimal respiratory effort.

Effective bag valve mask (BVM) ventilation was established and an intravenous fluid bolus was given. The heart rate rapidly improved on warming with a Bair Hugger and warmed intravenous fluids. During rewarming he became increasingly alert and responsive, however, his respiratory effort gradually deteriorated with tachypnoea, grunting, nasal flaring and intercostal recession. Chest auscultation remained clear, heart sounds were normal with palpable femoral pulses and no hepatomegaly. The decision for CPAP escalated to mechanical ventilation as he then developed frequent apnoeas. His rapid clinical decline within a short time frame and a suspicious chest X-ray raised the likely possibility that this was all attributed to COVID-19 (figure 2).

As per national and local resuscitation guidelines,[7 8] minimal staff all wearing full personal protective equipment (PPE), were present during intubation. A size 3 cm endotracheal tube was used; however, ventilation was more difficult than anticipated reflecting a rapidly evolving acute respiratory distress syndrome (ARDS). To improve ventilation, the infant was mechanically ventilated using a BVM which maintained stable observations.

INVESTIGATIONS

Haematological markers revealed thrombocytopenia; platelets 48×10^9/L while the haemoglobin concentration was 134 g/L, white cell count 5.6×10^9/L, neutrophils 1.7×10^9/L and lymphocytes 3.3×10^9/L. His renal function and electrolytes were normal; his albumin was low at 25 g/L with a raised alanine aminotransferase of 78 IU/L and raised C reactive protein (CRP) of 23 mg/L. His clotting studies were normal. Table 1 demonstrates his progressive blood gases.

His initial chest X-ray showed bilateral consolidation of the lung parenchyma and the subsequent X-ray performed after intubation showed bilateral ‘ground-glass infiltration’. The worsening radiological findings correlate to the clinical deterioration of the patient and illustrate evidence of evolving ARDS. His nose and throat swabs for coronavirus PCR returned after 24 hours as strongly positive for SARS-CoV-2 RNA.

OUTCOME AND FOLLOW-UP

The patient was transferred to a tertiary unit where he required high frequency oscillation ventilation for 48 hours with a trial of inhaled nitric oxide and intermittently kept in prone position. He was conventionally ventilated for a further 4 days before weaning to CPAP and later HFNC; he was off respiratory support by day 11. He was given a 10-day course of remdesivir along with cefotaxime, clarithromycin and acyclovir and had been on ionotropic support via a peripherally inserted central catheter line. His echocardiogram was structurally normal with normal ventricular function. He unfortunately developed a femoral thrombus for which he remains on dalteparin. He has been discharged from hospital, is developing well and being regularly monitored by the local DGH.

DISCUSSION

At present there are few reports of paediatric patients requiring intensive care support with confirmed COVID-19. To the best of our knowledge, this is the youngest reported case of SARS-CoV-2 following horizontal transmission in the UK.

On presentation to PED the patient had no cough or fever symptoms which have been extensively reported as common clinical manifestations of COVID-19.[8] Similarly, the distinguishing biochemical abnormalities associated with COVID-19 positive patients, specifically leucopenia[9] and significantly elevated CRP,[10] were not observed in our case. As noted in table 1, the initial blood gas of the infant demonstrates a mixed acidosis and metabolic alkalosis. A plausible explanation for this could be that the infant had been in respiratory distress prior to presentation. This may also account for his hypothermia, lethargy and subsequent apnoeas; all of which suggest some neurological involvement. This case demonstrates the need for vigilance in considering COVID-19 infection in infants presenting with less discriminatory symptoms such as lethargy or reduced feeding.

In adults, comorbidities such as cardiovascular disease, diabetes and hypertension are associated with significant morbidity when infected with COVID-19.[9] It remains a challenge to identify the most vulnerable groups among children. Dong *et al* report a case series of 2135 paediatric patients with confirmed and suspected coronavirus; infants (<1 year) were noted to be particularly vulnerable. Thirteen cases were ‘critical’—quickly progressing to ARDS±shock, encephalopathy, myocardial injury, heart failure, coagulation dysfunction and acute kidney injury—seven of whom were less than 1 year of age.[11] The authors did not report the patient’s comorbidities.

There is evidence that the respiratory tract of premature babies has an immature mucosal barrier with a reduced mucociliary clearance, increasing their vulnerability to pulmonary infections.[12] Although our patient was corrected to 37 weeks at presentation, his prematurity may have contributed to the increased risk of contracting the virus and the cascading response that followed.

Hong *et al* hypothesised that the reason for the small number of infants affected by the virus was because of their low risk of

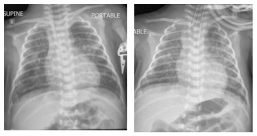

Figure 2 Chest X-rays of the patient pre and post intubation 3.5 hours apart, showing the transition from bilateral consolidation to bilateral ground glass infiltration due to evolving ARDS. ARDS, acute respiratory distress syndrome.

exposure to the virus.[13] Since the infant was discharged from the neonatal unit 12 days before presenting to the emergency department he was within the 2–14 day incubation period for COVID-19.[14 15] We must therefore consider the possibility of exposure before discharge from the neonatal unit, especially since he had remained at home isolating with his parents following his discharge. However, it is also important to note that there is no substantive evidence for vertical transmission from COVID-19 positive mothers to their baby, and therefore neonatal units are considered a low risk area to COVID-19.[16 17] It would have been valuable to have identified sources of potential exposure with contact testing and tracing. It is unfortunate that at the time of presentation, the 'NHS Test and Trace' service had not been implemented in the UK and therefore the route of transmission and acquisition of COVID-19 remains unsolved.

COVID-19 is highly contagious and there is a large concern for healthcare staff involved in airway management for patients with the virus. Guidance released by The Resuscitation Council UK and Cook *et al* is being used to maintain the safety of staff while performing high risk aerosol generating procedures including intubation[7 8]; however, the guidance remains quite limited for infants. There are also challenging non-technical factors to consider when providing advanced airway management for an infant with suspected COVID-19. These factors included designating the most appropriate person to carry out intubation, use of cuffed endotracheal tubes, the number and selection of health professions involved during intubation, and communication barriers with full PPE and designated contained areas for managing the patient.

Understanding the clinical course of COVID-19 in the paediatric population is continually evolving. Although cases of critically unwell infants remain uncommon, this particular group may be more vulnerable. An appreciation for early identification of subtle symptoms, such as reduced feeding, lethargy and hypoxia in the absence of respiratory distress, will enable prompt escalation of care and appropriate stabilisation. Although there is no specific guidance on airway management for infants with suspected COVID-19, it is important to keep up-to-date with local and national guidance to ensure patient and staff safety. Further epidemiological reports will hopefully uncover the vast expanse of symptomology of the heterogenic COVID-19 positive paediatric cohort and the optimal management of the virus.

Learning points

- COVID-19 may present as subtly as lethargy and poor feeding in infants.
- Infants may present with hypoxia in the absence of respiratory distress.
- More understanding on the effects of COVID-19 in infants, especially premature infants is required.

Contributors AN contributed to the concept, write up and literature search of the case as well has being involved in the patient's initial care. TS was the consultant involved in the patient's care. JP reviewed, revised and edited the manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Parental/guardian consent obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1 World Health Organization. Coronavirus disease (COVID-19) situation report, 2020. Available: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports
2 Morand A, Fabre A, Minodier P, *et al*. COVID-19 virus and children: what do we know? *Arch Pediatr* 2020;27:117–8.
3 Wei M, Yuan J, Liu Y, *et al*. Novel coronavirus infection in hospitalized infants under 1 year of age in China. *JAMA* 2020;323:1313–4.
4 Choi S-H, Kim HW, Kang J-M, *et al*. Epidemiology and clinical features of coronavirus disease 2019 in children. *Clin Exp Pediatr* 2020;63:125–32.
5 Society of Pediatrics, Chinese Medical Association. Editorial board, Chinese Journal of pediatrics. *Zhonghua Er Ke Za Zhi* 2020;58:E004.
6 Royal College of Paediatrics and Child Health. Guidance—Paediatric multisystem inflammatory syndrome temporally associated with COVID-19 2020.
7 Resuscitation Council. Resuscitation Council UK statement on COVID-19 in relation to CPR and resuscitation in paediatrics, 2020. Available: https://www.resus.org.uk/media/statements/resuscitation-council-uk-statements-on-covid-19-coronavirus-cpr-and-resuscitation/covid-paediatrics/
8 Cook TM, El-Boghdadly K, McGuire B, *et al*. Consensus guidelines for managing the airway in patients with COVID -19. *Anaesthesia* 2020;75:785–99.
9 Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, *et al*. Clinical, laboratory and imaging features of COVID-19: a systematic review and meta-analysis. *Travel Med Infect Dis* 2020;34:101623.
10 Riphagen S, Gomez X, Gonzalez-Martinez C, *et al*. Hyperinflammatory shock in children during COVID-19 pandemic. *Lancet* 2020;395:1607–8.
11 Wang E, Brar K. COVID-19 in children: an epidemiology study from China. *J Allergy Clin Immunol Pract* 2020.
12 Collins A, Weitkamp J-H, Wynn JL. Why are preterm newborns at increased risk of infection? *Arch Dis Child Fetal Neonatal Ed* 2018;103:F391–4.
13 Hong H, Wang Y, Chung H-T, *et al*. Clinical characteristics of novel coronavirus disease 2019 (COVID-19) in newborns, infants and children. *Pediatr Neonatol* 2020;61:131–2.
14 Lauer SA, Grantz KH, Bi Q, *et al*. The incubation period of coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases: estimation and application. *Ann Intern Med* 2020;172:577–82.
15 Linton NM, Kobayashi T, Yang Y, *et al*. Incubation period and other epidemiological characteristics of 2019 novel coronavirus infections with right truncation: a statistical analysis of publicly available case data. *J Clin Med* 2020;9:538.
16 Chen H, Guo J, Wang C, *et al*. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet* 2020;395:809–15.
17 Lu Q, Shi Y. Coronavirus disease (COVID-19) and neonate: what neonatologist need to know. *J Med Virol* 2020;92:564–7.