Received: 13 May 2022 | Accepted: 28 June 2022

DOI: 10.1002/ppul.26056

CLINICAL CORRESPONDENCE

PEDIATRIC PULMONOLOGY WILEY

COVID19-associated unilateral transient phrenic nerve palsy in a young child with respiratory failure

Pierre Goussard PhD[1] | Regan Solomons PhD[1] | Magriet van Niekerk FC Paed(SA)[1] | Noor Parker FC Paed(SA)[1] | Carien Bekker FC Paed(SA)[1] | Andre Gie PhD[1] | Marieke M. van der Zalm PhD[1] | Savvas Andronikou PhD[2,3] | Helena Rabie PhD[1] | Ronald van Toorn PhD[1]

[1]Department of Paediatrics and Child Health, Faculty of Medicine and Health Sciences, Stellenbosch University and Tygerberg Hospital, Cape Town, South Africa

[2]Department of Pediatric Radiology, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA

[3]Department of Radiology, Perelman School, of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania, USA

Correspondence: Pierre Goussard, Department of Paediatrics and Child Health, Faculty of Medicine and Health Sciences, Stellenbosch University, PO Box 241, Cape Town 8000, South Africa.
Email: pgouss@sun.ac.za

KEYWORDS
brachial plexopathy, lung collapse, SARS-COV-2, unilateral phrenic nerve paralysis

Funding information
None

We describe the case of a 4-year 11-month-old boy who presented to the emergency department with right-sided focal motor status epilepticus. The caregivers reported a normal birth and developmental history, no family history of epilepsy, no exposure to trauma, and no household tuberculosis or COVID contacts. Examination revealed that he was febrile; hypoxic and comatose (Glasgow Coma Scale of 7/15) which necessitated transfer to the pediatric intensive care unit for intermittent positive pressure ventilation. A low blood glucose level (1.3 mmol/L) required correction with intravenous dextrose infusion. There were no focal neurological signs, signs of raised intracranial pressure, or meningism. Respiratory examination revealed reduced ventilation in the right middle and lower lobes. Examination of the cardiovascular and abdominal systems proved unremarkable.

Blood investigations revealed normal full blood count and electrolytes, and slightly elevated C-reactive protein (27 mg/L). Cerebrospinal fluid (CSF) analysis revealed a clear and colorless macroscopic appearance with 20 lymphocytes/μl, no polymorphs, and normal biochemistry. CSF viral panel (including Herpes simplex polymerase chain reaction [PCR]) and CSF NMDA receptor antibodies proved negative. Chest radiography demonstrated atelectasis of the right lower and middle lobes (Figure 1A). Tracheal aspirate microbiological confirmation of *Mycobacterium tuberculosis* proved negative by Xpert MTB/RIF Ultra, microscopy, and culture. The SARS-CoV-2 PCR was indeterminate twice, but the SARS-CoV-2 IgG was positive. Contrasted cerebral computed tomography (CT) and subsequent magnetic resonance imaging proved normal.

Patient was empirically started on ceftriaxone (100 mg/kg/day), acyclovir (30 mg/kg/day), and antituberculous meningitis medication which included rifampicin (20 mg/kg/day), isoniazid (20 mg/kg/day), pyrazinamide (40 mg/kg/day), and ethionamide (20 mg/kg/day). Methylprednisolone (pulse therapy 30 mg/kg/day for 3 days) and intravenous immune globulin (IVIG) (2 g/kg over 2 days) were given to cover the possibility of autoimmune encephalitis.

On Day 3, the patient was extubated to high-flow nasal cannula oxygen but within hours required reintubation due to worsening respiratory distress and persistence of depressed consciousness. Bronchoscopy was performed with a 3.5-mm video bronchoscope due to the complete collapse of the right lung. (Figures 1B and 2A) The right main bronchus was completely obstructed with mucus, which was cleared. On Day 4 of ventilation, it was noted on the chest radiograph and subsequent lung ultrasound that the patient had a right upper lobe collapse consolidation and a very high right hemidiaphragm (Figure 1C).

The patient required ventilator support for 9 days followed by two further days of supplementary nasal cannula oxygen. With the

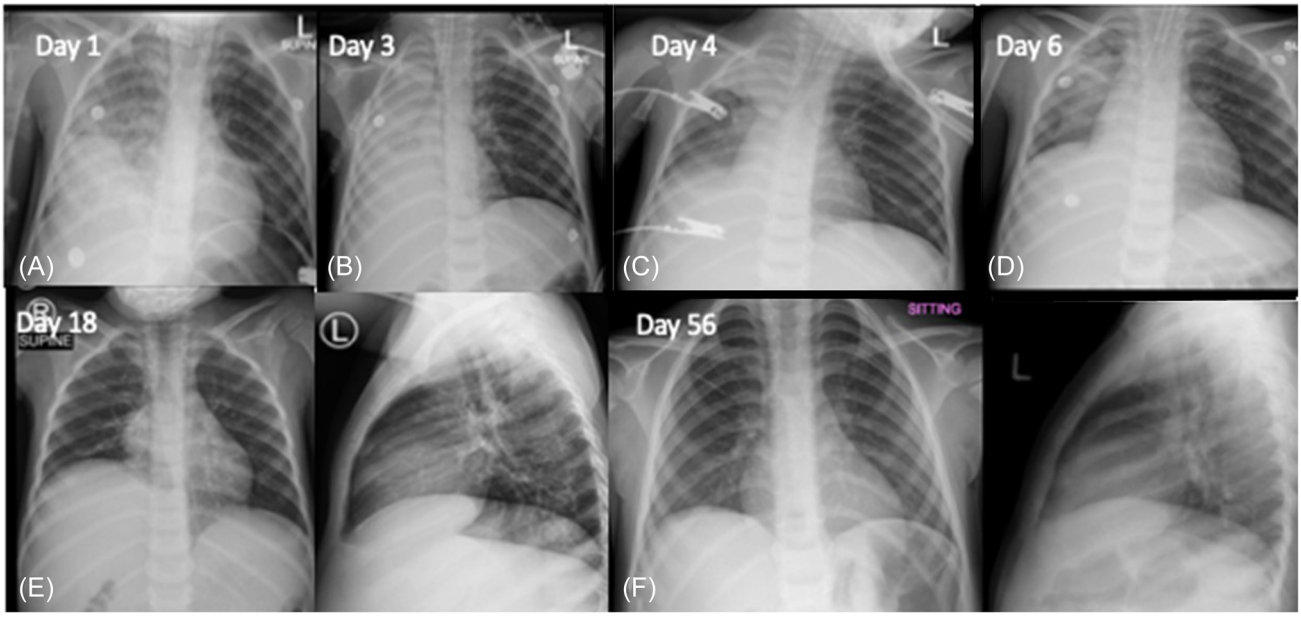

FIGURE 1 (A–F) Chest radiograph series in a 4-year 11-month-old boy with COVID-19 encephalitis who was admitted to ICU with depressed conscious and requiring ventilation. Frontal chest radiographs from Day 1 of presentation to Day 6 of presentation demonstrate, in sequence, atelectasis of the right lower and middle lobes, atelectasis of the whole right lung, and then atelectasis of the right upper lobe and right lower lobe, all while the patient was intubated with appropriate positioning of the tip of the endotracheal tube, above the level of the carina. The right hemidiaphragm is not visible on these radiographs. Frontal and lateral chest radiographs on Day 18 demonstrate an "apparently" elevated right hemidiaphragm, in keeping with phrenic nerve palsy, while a follow-up chest radiograph on Day 56 demonstrates a normal position of the right hemidiaphragm, indicating resolution. [Color figure can be viewed at wileyonlinelibrary.com]

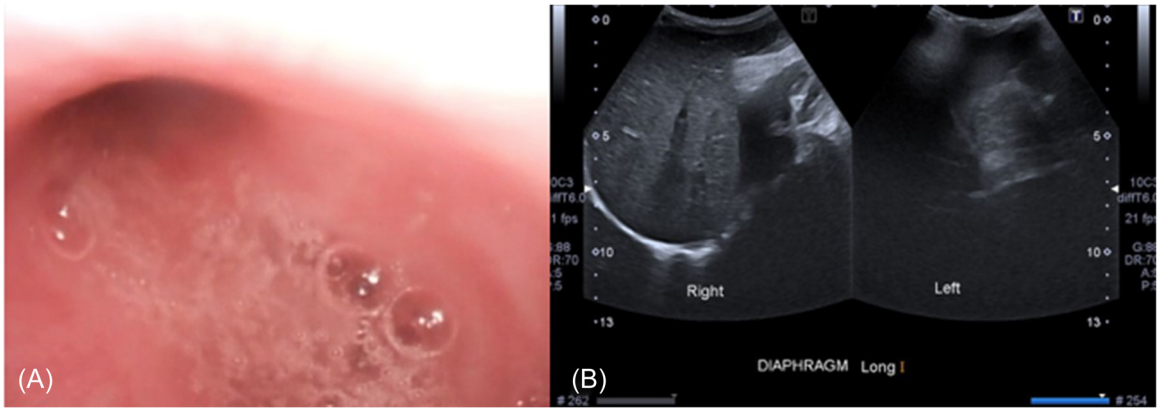

FIGURE 2 (A and B) Bronchoscopic image at the opening of the right main bronchus demonstrating complete obstruction with mucus, Ultrasound image demonstrating right-sided hemidiaphragm paralysis [Color figure can be viewed at wileyonlinelibrary.com]

normalization of consciousness, it became apparent that the child also exhibited right upper arm and shoulder weakness (grade 3/5) of a lower motor neuron nature. Grasp was preserved. The right arm weakness responded favorably to physiotherapy and full recovery of power was noted after 17 days in the hospital. Phrenic nerve conduction studies were planned but canceled after the complete recovery. Repeat chest radiography and ultrasound before discharge on Day 20 revealed persistence of the right-sided hemidiaphragm paralysis (Figures 1E and 2B). Clinical and radiological review 56 days after presentation revealed complete resolution of the right hemidiaphragm (Figure 1F).

The parents gave consent for the publication of this case report. The study was approved by the Stellenbosch University Health Research Ethics Committee (N20/04/013_COVID-019).

Case reports and case series exist that report phrenic palsy-related diaphragmatic weakness in adults with acute COVID-19 infection-related pneumonia.[1,2] Abdeldayem et al. reported incidental unilateral diaphragmatic paralysis in 1.5% (23/1527) on CT scans in adult patients with COVID-19 pneumonia. Twenty-one patients had shown complete recovery of the associated diaphragmatic paralysis at follow-up chest CT.[2]

Phrenic nerve palsy should also be excluded in adults with long COVID-19 suffering from prolonged dyspnea.[2] The case reported is unique as it involves a child with unilateral phrenic nerve paralysis without any cardiac, pleural, parenchymal, or vascular pulmonary abnormalities. In addition to the phrenic nerve palsy, the child also exhibited other COVID-19-related neurological symptoms which included encephalitis with seizures and ipsilateral shoulder and upper limb weakness secondary to an associated brachial plexopathy.

The neurological features of the SARS-CoV-2 virus are highly variable, involving the central and peripheral nervous system, both through acute infection or post-infectious inflammation pathways. Neurological manifestations described in children include meningitis/encephalitis/encephalopathy; seizures, stroke, and loss of smell and taste (anosmia and ageusia). Peripheral nerve manifestations include Guillain–Barré syndrome, cranial nerve palsies (facial and abducens), optic neuritis, and unilateral vocal cord paralysis.[3,4] It is likely that the diaphragmatic paralysis and ipsilateral shoulder and upper limb weakness in this patient can be attributed to a brachial plexopathy. The phrenic nerve originates mainly from the fourth cervical nerve, but also receives contributions from the third and fifth cervical nerves. The fever, seizures, depressed level of consciousness, inflammatory CSF response, and normal neuroimaging suggest the presence of concomitant encephalitis.

Multiple mechanisms of neurological involvement by the virus have been postulated, including direct neuroinvasion (attachment to the neuronal ACE-2 receptors, via the olfactory nerve) or immune-mediated pathogenesis (impairment of function by proinflammatory cytokines).[5] We postulate that the neurological manifestations of COVID-19 in our patients are likely a consequence of immune-mediated phenomena. This is supported by the favorable response and full recovery following administration of high-dose corticosteroids and intravenous immunoglobulins and the presence of SARS-CoV IgG. The absence of anosmia and dysgeusia also argues against direct viral invasion. CSF SARS-CoV-2 and CSF cytokine analysis was not performed on this patient. The majority of adults with COVID-19-related phrenic nerve palsy spontaneously recover.

We describe a case of unilateral phrenic nerve palsy due to SARS-COV-2 in a young child, which led to prolonged and complicated ventilation. The child was treated with methylprednisolone and IVIG, which led to a complete recovery of phrenic function. Temporary involvement of the phrenic nerve should be considered in children infected with SARS-COV-2 requiring prolonged ventilation. The phrenic nerve palsy is postulated to be due to peripheral nerve involvement by SARS-CoV-2. In South Africa, children under 12 years of age are not prioritized for SARS-CoV-2 vaccination. This case reiterates that even though SARS-CoV-2 disease is mild in the vast majority of children there are more severe presentations that, in low- or middle-income countries, might even go unrecognized.

AUTHOR CONTRIBUTIONS

Pierre Goussard: Conceptualization; methodology; investigation; supervision; writing–original draft; writing–review and editing. **Regan Solomons:** Methodology; supervision; writing–review and editing; writing–original draft. **Magriet van Niekerk:** Data curation; writing–original draft; investigation. **Noor Parker:** Data curation; formal analysis; writing–original draft. **Carien Bekker:** Data curation; formal analysis; investigation; methodology; writing–original draft. **Andre Gie:** Writing–original draft; methodology; data curation. **Marieke M. van der Zalm:** Data curation; supervision; writing–original draft. **Savvas Andronikou:** Formal analysis; supervision; investigation; writing–original draft. **Helena Rabie:** Data curation; formal analysis; visualization; supervision; writing–original draft. **Ronald van Toorn:** Writing–original draft; formal analysis; supervision; investigation.

ACKNOWLEDGEMENT

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

None.

ORCID

Pierre Goussard http://orcid.org/0000-0003-1146-1307

REFERENCES

1. Abdeldayem EH, Abdelrahman AS, Mansour MG. Recognition of phrenic paralysis as atypical presentation during CT chest examination of COVID-19 infection and its correlation with CT severity scoring: a local experience during pandemic era. *Egypt J Radiol Nucl Med*. 2021;52:156.
2. Maurier F, Godbert B, Perrin J. Respiratory distress in SARS-CoV-2 without lung damage: phrenic paralysis should be considered in COVID-19 infection. *Eur J Case Rep Intern Med*. 2020;7(6):001728.
3. Paliwal VK, Garg RK, Gupta A, Tejan N. Neuromuscular presentations in patients with COVID-19. *Neurol Sci*. 2020;41(11):3039-3056.
4. Korkmaz MÖ, Güven M. Unilateral vocal cord paralysis case related to COVID-19. *SN Compr Clin Med*. 2021;3(11):2319-2321.
5. Chen T, Wu D, Chen H, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. *BMJ*. 2020;368:m1091.

How to cite this article: Goussard P, Solomons R, Niekerk M, et al. COVID19-associated unilateral transient phrenic nerve palsy in a young child with respiratory failure. *Pediatric Pulmonology*. 2022;57:2565-2567. doi:10.1002/ppul.26056