

Croup and COVID-19 in a child: a case report and literature review

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SUMMARY

Croup (laryngotracheitis) is frequently encountered in the emergency department in a young child presenting with stridor. We describe a rare case of croup secondary to SARS-CoV-2 in an 18-month-old child who presented with stridor and respiratory distress and required urgent intubation. Subsequently, the child developed multisystem inflammatory syndrome in children (MIS-C). The child was monitored in paediatric intensive care unit. We would like to highlight that COVID-19 croup in children may be an indicator for MIS-C, and close monitoring is warranted as MIS-C is a life-threatening condition. Our limited experience suggests that COVID-19 croup especially if associated with MIS-C has an underlying more severe pathology and may require prolonged treatment in comparison with the typical croup or even COVID-19 croup. It is important to recognise this clinical entity during a time when most countries are in a third wave of COVID-19 pandemic.

BACKGROUND

The novel 2019 coronavirus SARS-CoV-2 responsible for COVID-19 was first identified in Wuhan, China, and has ever since swept across the globe. On 11 March 2020, the WHO declared COVID-19 a pandemic. Novel clinical presentations are being discovered daily. Croup (laryngotracheitis) traditionally has been linked to viral infection, notably, parainfluenza virus, respiratory syncytial virus, rhinovirus, enterovirus and others. To our knowledge, this is the first described case in the literature of croup in a child which turned out to be COVID-19 MIS-C. We would like to highlight that croup in a COVID-19 child may be an indicator for MIS-C.

CASE PRESENTATION

A previously healthy and immunised 18-month-child presented to the emergency department with a 1-day history of noisy breathing. According to the mother, the child was febrile at home for the past 2 days with reduced oral intake. There was no history of cough, choking or foreign body inhalation or recent contact with patients who are COVID-19-positive. Parents, however, claim that the child was recently brought to a crowded mall 2 days prior to symptoms.

On arrival, the child was tachypnoeic at 72 breaths per minute with deep subcostal and intercostal recessions and audible biphasic stridor (figure 1). His oxygen saturation was 76% under room air, the heart rate was 210 beats per minute and the recorded temperature was 39.7°C. Lung

auscultation revealed reduced air entry bilaterally with no crepitation. Nebulised budesonide and intravenous dexamethasone administered showed no improvement. Subsequently, he was given nebulised epinephrine. Unfortunately, he developed generalised tonic-clonic seizure midway through the nebulisation, possibly due to hypoxia which aborted with intravenous diazepam.

INVESTIGATIONS

Blood gas on high-flow oxygen of 15 L showed pH of 7.21, partial pressure of carbon dioxide of 65.9 mm Hg, partial pressure of oxygen of 71 mm Hg, bicarbonate of 21 mmol/L and base excess of -2 mmol/L. In view of type II respiratory failure, intubation was proceeded by the anaesthetist team with a 4.5 mm endotracheal tube assisted by video laryngoscope. His larynx appeared inflamed, and the supraglottic structures were not oedematous or obstructing the airway (figure 2). There was pooling of secretions below the vocal cords, and the subglottis looked oedematous.

Nasopharyngeal swab for SARS-CoV-2 PCR test was positive with cycle threshold value of 34.42, and the respiratory pathogen nucleic acid amplification panel was positive for respiratory syncytial virus as well. During the second day in paediatric intensive care unit (PICU), he developed seven episodes of loose watery stools which were negative for rotavirus and other organisms (*Shigella*, *Salmonella*, enteropathogenic *Escherichia coli*). Blood



Figure 1 Laboured breathing with recessions.



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Figure 2 Laryngoscopy showing inflamed supraglottis.

investigation showed haemoglobin was 10.2 g/dL, and white cell count was $14.7 \times 10^9/L$ with lymphocytopenia of $2.97 \times 10^9/L$. Inflammatory markers were raised with C reactive protein (CRP) of 13.8 mg/L, erythrocyte sedimentation rate of 45 mm/hour and fibrinogen of 5 g/L. There was also sign of coagulopathy evidenced by raised prothrombin time of 15 s and a positive D-dimer test of 1600–3200 ng/mL. He had elevated lactate dehydrogenase (LDH) of 385 U/L and low albumin of 26 g/L. Otherwise, his liver enzyme, kidney function and cardiac enzyme were normal (table 1). Bronchoalveolar lavage was positive for

respiratory syncytial virus but negative for SARS-CoV-2. Regrettably, no culture or viral immunofluorescence test was sent from vocal cord secretion. Blood cultures were normal. Chest X-ray showed relatively normal findings. SARS-CoV-2 antibody ELISA for qualitative detection of total antibodies in serum performed on day 8 of illness was found to be positive.

DIFFERENTIAL DIAGNOSIS

Epiglottitis presents with inspiratory stridor and fever. However, pathognomic findings of thumb sign are found in lateral soft tissue neck radiograph. In bacterial tracheitis, the child presents with expiratory stridor with no classical radiographic findings. However, tracheoscopy will reveal inflamed and oedematous mucosa overlying the tracheal wall with positive bacterial culture. The child with foreign body inhalation may present with expiratory stridor but without a history of fever or upper respiratory

Table 1 Blood investigation trend

			2/2/2021	1/2/2021	31/1/2021	30/1/2021	29/1/2021
Liver function test	Units	Reference range					
Albumin (serum)	g/L	32–48	L 28	L 27	L 28	L 26	
Total bili (serum)	μmol/L	<17	3	3	3	3	
ALP (serum)	U/L	54–369	113	112	118	129	
ALT (GPT) (serum)	U/L	10–49	40	36	41	38	
Gamma GT (serum)	U/L	<73	26	29	26	22	
Calcium (corrected)	mmol/L	2.20–2.60	2.48	2.54	2.44	2.47	
Calcium (serum)	mmol/L	2.20–2.60	2.24	2.28	2.20	L 2.19	
Phosphate (serum)	mmol/L	0.78–1.65	1.4	1.4	1.1	1.3	
AST (GOT) (serum)	U/L	<34	H 45	H 41	H 50	H 41	
CKMB (mass)							
C kinase (serum)	U/L	46–171	101	86	146	H 356	
CKMB mass (serum)	ng/mL	<5.0	1.2	1.0	1.9	H 6.2	
RI			1.19	1.16	1.30	1.74	
Troponin I (plasma)	ng/mL	<0.06	0.04	0.02	0.04	0.05	
LDH (serum)	U/L	120–246	H 448	H 467	H 461	H 385	
Complete blood count							
HB	g/L	94.0–130.0	L 108.0	L 109.0	L 104.0	L 102.0	
HCT	L/L	0.30–0.38	0.32	0.32	0.31	0.30	
RBC	$10^{12}/L$	3.10–4.30	4.05	4.05	L 3.86	L 3.77	
MCV	fL	72–84	78	79	80	80	
MCH	pg	25.0–29.0	26.7	26.9	26.9	27.1	
MCHC	g/L	320–360	341	340	335	339	
RDW	%	11.6–14.0	L 11.4	11.6	11.9	12.1	
WBC	$10^9/L$	5.0–15.0	8.7	10.5	9.0	L 5.5	
Platelet	$10^9/L$	200–550	H 561	449	343	307	
ESR	mm/hour	<21	H 45	H 42	H 27	H 34	H 28
Serum ferritin	μg/L	22.0–322.0	94.2	114.4	133.0	132.3	
Coagulation screen							
PT							
PT-patient	s	10.8–12.4	H 13.1	H 12.6	H 13.4	H 15.0	
PT ratio	Ratio	0.93–1.07	H 1.2	H 1.1	H 1.2	H 1.4	
PT INR	INR		1.2	1.1	1.2	1.4	
Fibrinogen	g/L	1.78–3.96	H 4.00	3.90	3.61	H 4.60	
APTT							
APTT-normal	s	24.9–34.1	29.5	29.5	29.5	29.5	
APTT-patient	s	24.9–34.1	26.9	28.2	25.8	33.5	
D-dimer	ng/mL		Positive (200–400)	Positive (400–800)	Positive (1600–3200)	Negative	Negative

ALP, alkaline phosphatase; ALT, alanine aminotransferase; APTT, activated partial thromboplastin time; AST, aspartate transaminase; CKMB, creatine kinase myocardial band; ESR, erythrocyte sedimentation rate; HB, haemoglobin; HCT, haematocrit; INR, international normalised ratio; LDH, lactate dehydrogenase; MCH, mean corpuscular haemoglobin; MCHC, mean corpuscular haemoglobin concentration; MCV, mean corpuscular volume; PT, prothrombin time; RBC, red blood cells; RDW, red cell distribution width; RI, renal insufficiency; WBC, white blood cells.

tract infection. In addition, bouts of cough and choking along with witnessed foreign body inhaled have been reported.

TREATMENT

Due to the possibility of multisystem inflammatory syndrome in children (MIS-C), the child was started on low-dose intravenous methylprednisolone (1.25 mg/kg/day) for 5 days in addition to intravenous ceftriaxone.

OUTCOME AND FOLLOW-UP

The child responded to treatment and was extubated after being ventilated for a total of 7 days. He was discharged well without complications. The child subsequently defaulted follow-up. Telephone conversation with his parent revealed that the child was active and thriving well without alarming symptoms.

DISCUSSION

Although a common presentation, croup in children during the COVID-19 period requires thorough assessment. To date, only two articles (a case series and a case report) have been reported on croup with COVID-19 in paediatric patients.^{1,2} All the four patients described required ward admission for nebulisation and dexamethasone in addition to close observation for stridor.^{1,2} Only one patient required non-invasive ventilation along with heliox in the PICU. Our patient demonstrated the stormiest clinical course among the other children with croup as he developed MIS-C. In retrospect, case 2 in the case series by Venn *et al*¹ had a history of maculopapular rash, while in the case report by Pitstick *et al*,² there was fever with high CRP, which if evaluated further could have fitted into the definition of MIS-C. It is imperative to be aware that croup in paediatric patients could be secondary to COVID-19 and croup in COVID-19 era may be an indicator for MIS-C.

Earlier, COVID-19 among children was associated with milder symptoms and presentations compared with adults.³ Surveillance from various countries reported that children typically account for up to 13% of confirmed COVID-19 cases.⁴ Despite the increasing number of COVID-19 hospitalisation, only a minority of children require admission. In the USA, the rate of hospitalisation was between 2.5% and 4.1%.⁵ Among them, approximately 33% required intensive care and 6% needed invasive ventilation.⁶ Clinical findings of COVID-19 in children are diverse, and the most common reported symptoms are fever or chills and cough.⁵ Our child presented with febrile stridor and rapid breathing due to laryngotracheitis. It is possible that COVID-19 croup has an underlying more critical pathophysiology compared with the usual croup.¹

The incidence of MIS-C is still uncertain, and different case definitions have been described in varying studies. As growing evidence is emerging daily, it is coming to light that there is a wide spectrum of disease severity in MIS-C.⁷ In our child, he presented with severe respiratory distress with type II respiratory failure, gastrointestinal symptom of diarrhoea on days 4 and 5 of illness requiring fluid correction, and neurocognitive complication of seizure. Our patient had mild anaemia, lymphocytopenia, raised inflammatory markers, coagulopathy and raised LDH with low albumin. His chest X-ray was normal, and surprisingly, both parents were tested negative for SARS-CoV-2. This suggests that the immune dysregulation is from an abnormal immune response to the virus.⁷ As serial monitoring of his cardiac enzymes was normal, he was given echocardiogram appointment on discharge. Fortunately, he responded well to low-dose

intravenous methylprednisolone without immunoglobulin or antiviral therapy.

WHO has established a preliminary set of case definition for MIS in children and adolescents. The listed criteria include fever for 3 or more days; two of the following: rash or bilateral non-purulent conjunctivitis or mucocutaneous inflammatory signs; hypotension or shock; heart abnormalities from echocardiogram or elevated troponin/N-terminal pro-hormone brain natriuretic peptide; evidence of coagulopathy; acute gastrointestinal pathology; elevated inflammatory markers (CRP, ESR or procalcitonin); and no other obvious microbial cause of inflammation and evidence of COVID-19 (PCR antigen or serology positive). In our patient suspected with MIS-C, we monitored his progress while under intubation by charting his inflammatory markers, D-dimer, ferritin, coagulation profile and cardiac enzyme to determine the need for immunoglobulin and further cardiac evaluation.

A multicentre study on paediatric patients hospitalised with severe acute COVID-19 and MIS-C also distinguished the differing patterns of presentation between the two.⁸ Most patients with MIS-C had multiple organ involvement, more commonly cardiovascular, mucocutaneous and gastrointestinal involvement, whereas severe acute COVID-19 had more severe pulmonary disease without cardiovascular involvement. In addition, MIS-C commonly has markedly raised CRP (>100 mg/L), lymphopenia and thrombocytopenia. While it is premature to claim that croup may be an indicator of MIS-C based on limited case reports, further studies are needed to establish this link.

Patient's perspective

As the child is a minor, his parents were filled with guilt when he was diagnosed with SARS-CoV-2. Later, they were perplexed as to why their child had such life-threatening events while they both tested negative for SARS-CoV-2.

Learning points

- ▶ COVID-19 in children may present as croup, also known as acute laryngotracheobronchitis.
- ▶ COVID-19 and croup in children can be an indicator of MIS-C (multisystem inflammatory syndrome in children).
- ▶ SARS-CoV-2 and respiratory syncytial virus can exist together and lead to more severe and acute presentation refractory to initial treatments.
- ▶ Corticosteroid remains a more accessible and viable armamentarium in the treatment of suspected MIS-C.
- ▶ More studies are needed to establish the natural history and optimal treatment of presumed COVID-19 croup with MIS-C.

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