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Case Report

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SARS-CoV-2 in a Pediatric Patient Requiring Mechanical Ventilation and Multi-Drug Therapy

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Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel viral pathogen that was found to disproportionately affect older adults, often sparing pediatric patients from moderate to severe illness. We report on a case of a 12-year-old patient admitted through the emergency department with bilateral pneumonia, thrombocytopenia and hematuria, who subsequently developed respiratory failure requiring intubation and mechanical ventilation. The patient was found to be SARS-CoV-2-positive. The patient's management strategy is discussed.

Keywords: Coronavirus; COVID-19; SARS-CoV-2; Pediatrics; Intubation; Mechanical ventilation

Introduction

Novel coronavirus disease 2019 (COVID-19), medically referred to as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a zoonotic viral illness, first identified in late December 2019 in Wuhan, China [1, 2]. Though exposure to wildlife accounts for less than 2% of documented cases, bats are initially believed to have been the host reservoir; however, direct person-to-person transmission has emerged as a more rapid transmission route [3]. The illness rapidly spreads between close contacts, presumably via aerosolized respiratory secretions, with precipitous spread from Asia to Europe and the Americas in rapid succession [1, 4]. Many patients present with several days of fever and dry cough, symptoms attributed to influenza or other respiratory pathogens [3]. Some patients present with abdominal pain, nausea, vomiting or diarrhea [5].

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A large-scale analysis of over 72,000 patient cases published in JAMA (February 2020) shows that less than 2% of cases occurred in patients under the age of 19 years, with fewer than 5% of cases deemed "severe" involving respiratory failure, septic shock, or multi-organ system failure [6].

We report a case involving a 12-year-old patient who presented on three occasions to the emergency department (ED) at a large urban hospital with subjective fever at home for 5 days. To our knowledge, this patient represents one of the first pediatric patients to require intubation and intensive care management following a diagnosis of SARS-CoV-2-induced pneumonia with subsequent respiratory failure.

Case Report

A 12-year-old, previously healthy female of African descent presented with her mother to the ED at a large urban children's hospital. Mother reported that the patient's symptoms began with subjective fever, controlled with acetaminophen in early-to-mid March. On day 2 of illness, after 36 h of fever to 39.6 °C (axillary), the patient was brought to the ED. At that time, the patient was found to be febrile to 39.6 °C without any other abnormality noted on exam (Table 1).

The patient was diagnosed with a non-specific viral illness. She was noted to be taking oral liquids without a problem following oral ondansetron (4 mg) administration. The patient stated that she "felt better" and agreed to symptomatic management with ondansetron, acetaminophen and oral fluid replacement at home.

On day 4 of illness, the patient returned to the ED with fever (maximum temperature at home: 106 °F axillary), new-onset non-productive cough and vomiting (Table 2).

At that time, a urinalysis obtained from a "dirty" catch demonstrated hematuria, mucus, bacteria and squamous epithelial cells without significant pyuria. Metabolic panel was within normal limits and rapid streptococcal testing was negative (Table 3). The patient received a normal saline bolus and was discharged home with recommendations for output primary care follow-up.

On her third visit to the ED, complaints consisted of persistent fever and emesis, with an absence of cough or difficulty breathing. At triage, vitals showed hypotension (blood pressure (BP) 90/71), pyrexia (39.6 °C) and hypoxia (SaO_2 89% on room air). Saturations improved to 92% on 2 L of oxygen by nasal cannula. Her respiratory rate ranged from 26 to 35 breaths per minute and she appeared intermittently

Table 1. Emergency Department Vital Signs and Examinations Results for Visit #1 Prior to Admission

Blood pressure (mm Hg)	-
Heart rate (beats per minute)	139
Respiratory rate (breaths per minute)	20
Temperature (°C)	39.6
Pulse Ox (%)	100% on room air
Weight (kg)	61
Constitutional	Active, no acute distress, alert, well hydrated
Head/ears/nose/throat	Bilateral tympanic membranes are normal without erythema or bulging. Oral mucosa is moist.
Eyes	Conjunctivae normal. Pupils are equal, round and reactive to light.
Neck	Musculoskeletal: normal range of motion and neck supple.
Cardiovascular	Rate and rhythm: normal rate and regular rhythm. Heart sounds: S1 normal and S2 normal.
Pulmonary	Pulmonary effort is normal. No respiratory distress or retractions. Normal breath sounds and air entry. No decreased air movement. No wheezing.
Abdominal	Bowel sounds are normal. There is no distension. Abdomen is soft and flat. There is no abdominal tenderness, guarding or rebound. No right lower quadrant tenderness. Able to hop, smiles while hopping.
Integumentary	Skin is warm and dry. Capillary refill takes less than 2 s. No petechiae or rash, purpura or mottling.
Neurological	Patient is alert with no focal neurologic deficits.

Table 2. Emergency Department Vital Signs and Examinations Results for Visit #2 Prior to Admission

Blood pressure (mm Hg)	116/79
Heart rate (beats per minute)	137
Respiratory rate (breaths per minute)	16
Temperature (°C)	39.5
Pulse Ox (%)	96% on room air
Weight (kg)	61
Constitutional	Active, in no acute distress. She is well-developed and well-groomed. She is not toxic-appearing.
Head/ears/nose/throat	Normocephalic and atraumatic. Right ear: tympanic membrane, ear canal and external ear normal. Left ear: tympanic membrane, ear canal and external ear normal. Nose: no congestion or rhinorrhea. Mouth: mucous membranes are moist. Pharynx: uvula midline. Pharyngeal swelling and posterior oropharyngeal erythema present. No oropharyngeal exudate or pharyngeal petechiae. Tonsils: 2+ on the right, 2+ on the left.
Eyes	General: visual tracking is normal. Lids are normal. Vision grossly intact. Right eye: no discharge. Left eye: no discharge. Conjunctiva/sclera: conjunctivae normal. Pupils: pupils are equal, round and reactive to light.
Neck	Full passive range of motion without pain, normal range of motion and neck supple. Normal range of motion. No neck rigidity or pain with movement.
Cardiovascular	Rate and rhythm: normal rate and regular rhythm. Pulses: normal pulses. Pulses are strong. Heart sounds: S1 normal and S2 normal. No murmur.
Pulmonary	Pulmonary effort is normal. No respiratory distress. Normal breath sounds. No stridor, decreased air movement or transmitted.
Abdominal	Bowel sounds are normal. There is no distension. Abdomen is soft. Abdomen is not rigid. There is no mass. There is no abdominal tenderness. There is no right costovertebral angle (CVA) tenderness, no left CVA tenderness, guarding or rebound.
Lymphadenopathy	Cervical: cervical adenopathy present. Right cervical: superficial cervical adenopathy present. Left cervical: superficial cervical adenopathy present.
Integumentary	General: skin is warm and moist. Capillary refill: capillary refill takes less than 2 s.
Neurological	Mental status: she is alert and oriented for age. Glasgow coma scale (GCS): eye subscore: 4. Verbal subscore: 5. Motor subscore: 6. No cranial nerve deficit. No sensory deficit.

Table 3. Emergency Department Visit #2 Laboratory Workup

Test	Result	Reference range
Sodium	135	134 - 143 mmol/L
Potassium	6.5[a]	3.4 - 5.1 mmol/L
Chloride	108	98 - 108 mmol/L
CO_2	21	21 - 31 mmol/L
Blood urea nitrogen	12	5 - 22 mg/dL
Creatinine	0.53	0.30 - 0.80 mg/dL
Glucose	88	70 - 110 mg/dL
Calcium	8.4	8.9 - 10.4 mg/dL
Anion gap	12.5	5.0 - 18.0 mEq/L
Red cell distribution width	13.1	11.5-14.5%
Streptococcus pyogenes group A PCr throat	Negative	Negative
Urinalysis	Specific gravity 1.032 Glu neg Bili neg Ketone trace Blood 3+ Protein 100 Nitrite neg Leukocyte esterase neg Urine red blood cell 193 Urine white blood cell 4 Urine bacteria 2+ Urine mucus 1+ Squamous epithelial cells 17	1.002 - 1.030 Negative Negative Negative Negative < 20 mg/dL Negative Negative 0 - 5/HPF 0 - 9/HPF None None 0/HPF
Urine culture	No growth	

[a]Grossly hemolyzed.

Table 4. Emergency Department Vital Signs and Examinations Results for Visit #3 Prior to Admission

Blood pressure (mm Hg)	90/71
Heart rate (beats per minute)	129
Respiratory rate (breaths per minute)	26 - 35
Temperature (°C)	39.6
Pulse Ox (%)	89% on room air
Constitutional	Active. Not in acute distress. Non-toxic-appearing. Able to speak in full sentences.
Head/ears/nose/throat	Normocephalic and atraumatic. Right and left external ear normal. No congestion or rhinorrhea. Mucous membranes are moist. No oropharyngeal exudate or posterior oropharyngeal erythema.
Eyes	Right eye: no discharge. Left eye: no discharge. Extraocular movements intact. Conjunctiva/sclera: conjunctivae normal.
Neck	Normal range of motion and neck supple.
Cardiovascular	Regular rhythm. Tachycardia present. Pulses: normal pulses. Normal heart sounds.
Pulmonary	Tachypnea and respiratory distress present. No nasal flaring or retractions.
Abdominal	Abdomen is flat. Bowel sounds are normal. There is no distension or tenderness to palpation.
Lymphadenopathy	No cervical lymphadenopathy appreciated on exam.
Integumentary	Skin is warm and dry. Capillary refill takes 2 - 3 s.
Neurological	No focal deficit present. She is alert and oriented × 4. Mood normal. Thought content normal. Judgment normal.

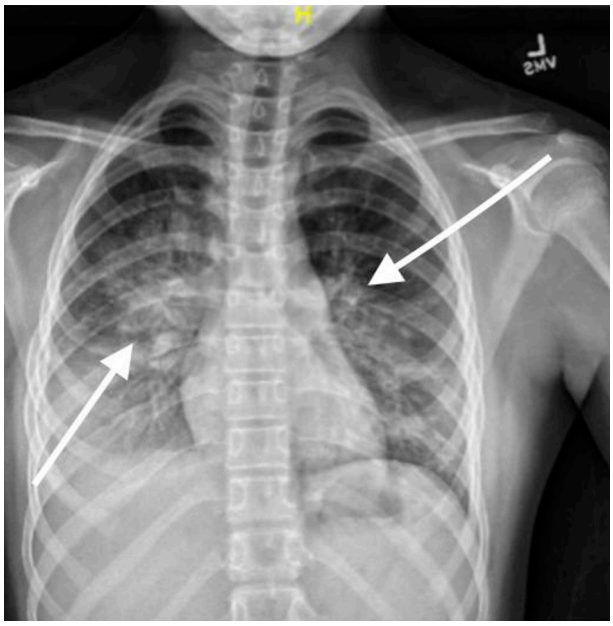

Figure 1. Chest X-ray, anteroposterior (AP) view on third presentation to emergency department showing signs of pneumonia with consolidation.

uncomfortable, though non-toxic. She was started on heated high flow oxygen, 10 L/FiO_2 35% and felt "more comfortable" (Table 4).

There was no history of recent travel in the 21 days preceding admission, sick contacts, or contacts with individuals with recent travel history or known COVID-19 exposures or diagnoses. However, the patient lives in a large urban center with known cases of COVID-19 and presented for evaluation following the closure of her county due to an outbreak of cases. Vaccinations were up to date, including against influenza A and B in August 2020. Of note, the patient's mother, father and 13-year-old brother are all healthy and developmentally appropriate, with no significant past medical history. Family history is significant for patient's maternal grandfather with medical history of diabetes mellitus.

Radiographic imaging revealed significant bilateral parahilar and basilar airspace opacities (right greater than left) consistent with pneumonia and atelectasis, as well as a right pleural effusion (Figs. 1, 2).

The patient's initial workup included a complete blood count with differential, blood culture, complete metabolic panel, inflammatory markers, respiratory viral panel, urinalysis and urine culture (Table 5).

Given the results showing a platelet count of 8 and a repeat count of 10, disseminated intravascular coagulation (DIC) panel, fibrinogen and ferritin were ordered. Initially, prolonged partial thromboplastin time (PTT) (49.5 (26 - 38 s)), elevated ferritin (481.05 (13.7 - 78.8 ng/mL)), normal PT (15.1 (12.6 - 15.9 s)), elevated D-dimer (432 (0 - 220 ng/mL)) and normal fibrinogen (376 (200 - 400 mg/dL)) were observed. However, through the course of hospitalization, the patients PT, PTT, D-dimer and fibrinogen all became elevated, well above reference ranges for the hospital laboratory.

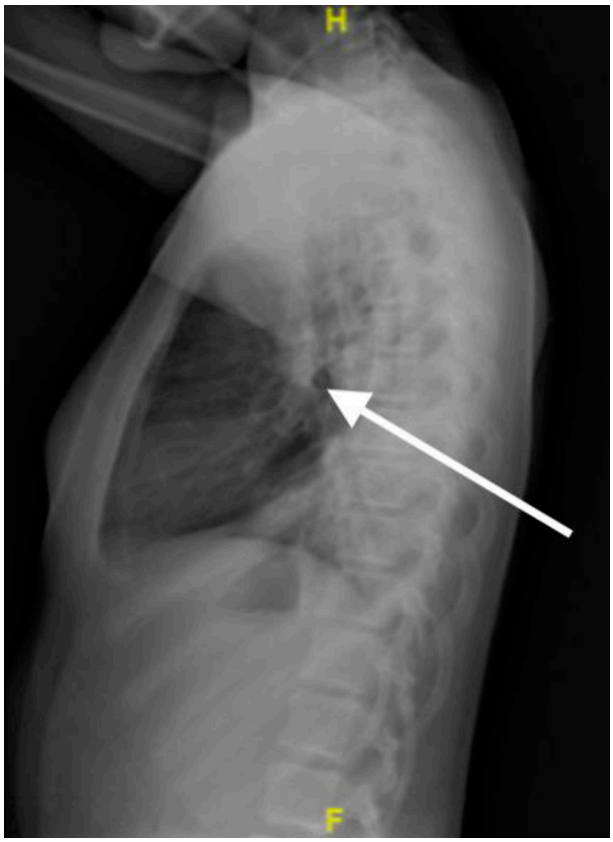

Figure 2. Chest X-ray, lateral view on third presentation to emergency department showing signs of pneumonia with areas of consolidation.

The patient received a normal saline bolus with improvement in her blood pressure. Ampicillin and ceftriaxone were administered. The patient was transferred in stable condition to the intensive care unit (ICU) for further care.

In the ICU, oxygen therapy was increased to 15 L/FiO_2 100% and subsequently bilevel positive airway pressure (BiPAP). The patient's chest radiographs continued to show worsening signs of acute respiratory distress syndrome (ARDS). Viral testing was obtained.

Through hospital day 1 and overnight into hospital day 2, the patient continued to require increasing levels of respiratory support, with worsening clinical picture (Fig. 3) necessitating intubation with mechanical ventilation and nitric oxide therapy. Antibiotic therapy was switched to rocephin and vancomycin on hospital day 2 and subsequently cefepime, azithromycin and clindamycin, in various combinations (Table 6).

Multiple doses of intravenous immune globulin (IVIG; 1 g/kg IV) were administered for severe thrombocytopenia, in addition to platelet transfusion, with minimal improvement. Solumedrol (100 mg IV for 1 day) was given in the treatment of presumptive immune thrombocytopenia. By hospital day 3, platelet count had improved to 34 and 151 by hospital day 8. On hospital day 4, immunologic workup was commenced, notable for elevated interleuken-6 (IL-6; 10 (< 5 pg/mL)).

Table 5. Emergency Department Visit #3 Laboratory Workup

White blood cell	5.47	4.5 - 13.5 × 10^3/µL
Red blood cell	4.43	3.80 - 5.00 × 10^6/UL
Hemoglobin	12.3	12.0 - 16.0 g/dL
Hematocrit	35.4 (L)	37.0-45.0%
Mean corpuscular volume	79.8	78.0 - 102.0 fL
Mean corpuscular hemoglobin	27.7	26.0 - 32.0 pg
Mean corpuscular hemoglobin concentration	34.8	31.0-37.0%
Red cell distribution width	13.1	11.5-14.5%
Platelet count	< 10 (LL)	150 - 450 × 10^3/µL
Mean platelet volume	15.1 (H)	7.5 - 9.3 fL
Automated absolute neutrophil	4.60	1.80 - 7.97 × 10^3/µL
Band	13.0 (H)	0-11%
Segmented neutrophils	70.0 (H)	40.0-59.0%
Lymphocyte	13.0 (L)	33.0-48.0%
Monocyte	4.0	0.0-6.0%
Absolute neutrophil manual	4.54	1.80 - 7.97 × 10^3/µL
Red blood cell morphology	Normal	
C-reactive protein	11.5	
Urinalysis	Specific gravity 1.009 Glu neg Bili neg Ketone 1+ Blood 3+ Nitrite neg Leukocyte esterase neg Urine red blood cell 14 Urine white blood cell 2	
Urine culture	No growth	
Respiratory viral panel (RVP)	Negative	Ref range
Adenovirus PCr	Negative	Negative
Coronavirus 229E PCr	Negative	Negative
Coronavirus HKU1 PCr	Negative	Negative
Coronavirus NL63 PCr	Negative	Negative
Coronavirus OC43 PCr	Negative	Negative
HMPV PCr	Negative	Negative
Rhinovirus/enterovirus PCr	Negative	Negative
Influenza A PCr	Negative	Negative
Influenza B PCr	Negative	Negative
Parainfluenza 1 PCr	Negative	Negative
Parainfluenza 2 PCr	Negative	Negative
Parainfluenza 3 PCr	Negative	Negative
Parainfluenza 4 PCr	Negative	Negative
RSV PCr	Negative	Negative
Chlamydia pneumoniae PCr	Negative	Negative
Mycoplasma pneumoniae PCr	Negative	Negative

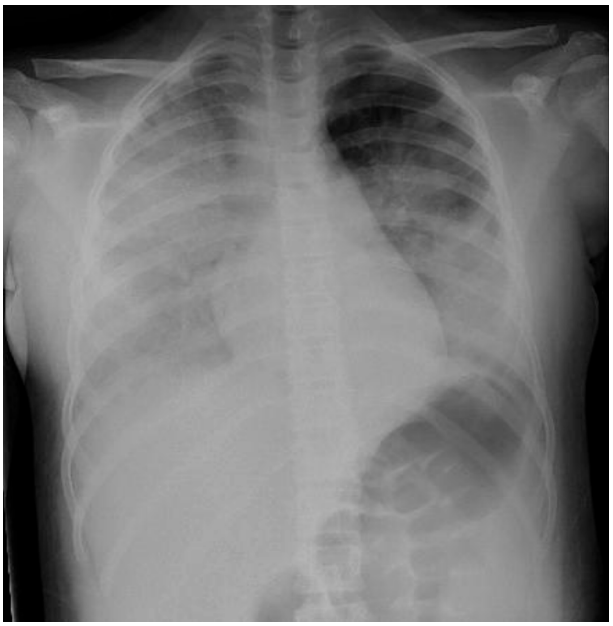

Figure 3. Chest X-ray, hospital day 1 showing signs of worsening acute respiratory distress syndrome (ARDS).

On hospital day 5, COVID-19 PCR was detected; the patient was SARS-CoV-2-positive. Given anecdotal reports of hydroxychloroquine in patients with COVID-19, this therapy was trialed on hospital days 6 through 8, without signs of improvement. The patient was started on tocilizumab for its anticytokine effects, to dampen hyper-inflammation associated with sepsis, and due to emerging trials showing success in patients with ARDS due to COVID-19. On hospital day 7 (Fig. 4), approval for trial with remdesivir was obtained, which was started on hospital day 8 (Table 6; Fig. 5).

The patient's repeat chest radiograph showed signs of improvement on hospital day 8, with weaning of ventilator settings through hospital day 15 (Figs. 6-8).

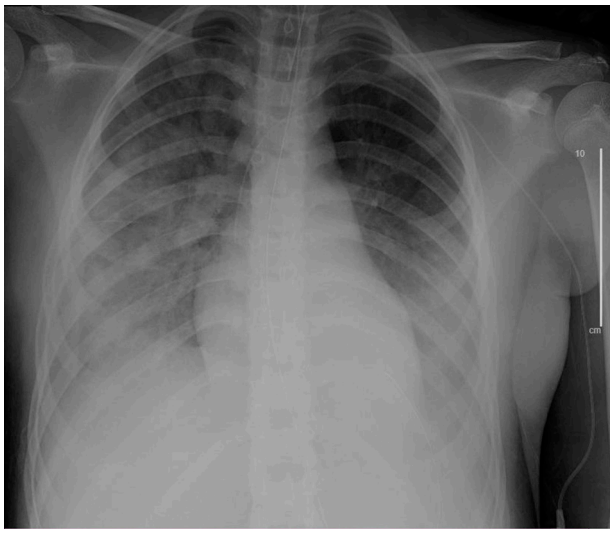

Figure 4. Chest X-ray, anteroposterior (AP) view on the day prior to start of remdesivir trial (hospital day 7).

The patient remained intubated on a ventilator for 13 days before extubation to high flow nasal cannula for 2 days and nasal cannula for 1 day. She then received 9 days of inpatient rehabilitation therapies due to global weakness, requiring extensive speech, physical and occupational therapy prior to discharge home.

Discussion

This previously healthy, 12-year-old female with no significant past medical history, presented with a 5-day history of fever

Table 6. Antibiotic, Antimicrobial and Antiviral Therapy Received During Hospitalization in Chronological Order as Medication Was Added to Treatment Plan

Therapy	Dosage	Route of administration	Frequency	Duration of treatment	Days received
Ceftriaxone	2 g	IV	Daily	7 days	Admission - HD 3
Ampicillin	2 g	IV	Daily	1 day	Admission - HD 1
Albuterol	2.5 g	Inhaled nebulizer therapy	Every 3 h PRN	14 days	Admission - HD 17
Vancomycin	20 mg/kg	IV	Every 8 h	5 days	HD 2 - 6
Cefepime	2 g	IV	Every 8 h	7 days	HD 3 - 10
Azithromycin	10 mg/kg	IV	Daily	2 days	HD 3 - 4
Azithromycin	5 mg/kg	IV	Daily	3 days	HD 5 - 7
Tocilizumab	600 mg	IV	Daily	1 day	HD 7
Tocilizumab	600 mg	IV	Every 12 h	1 day	HD 8
Hydroxychloroquine	400 mg	IV	Twice daily	3 days	HD 6 - 8
Clindamycin	10 mg/kg	IV	Every 8 h	3 days	HD 7 - 9
Remdesivir	200 mg	IV	Daily	1 day	HD 8
Remdesivir	100 mg	IV	Daily	9 day	HD 9 - 17

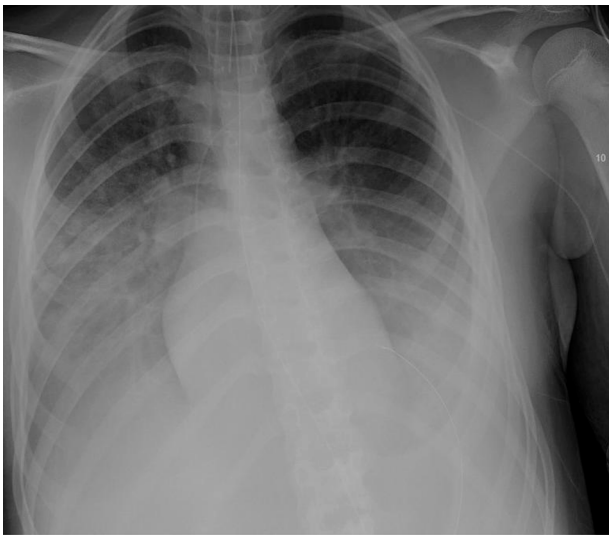

Figure 5. Chest X-ray, anteroposterior (AP) view on the day with remdesivir trial commenced (hospital day 8).

followed by abdominal pain, vomiting and increased work of breathing, found to have significant thrombocytopenia, bilateral pneumonia and respiratory failure as a result of COVID-19.

To our knowledge, this is the first pediatric patient in a large urban city in North America to fall critically ill due to this disease process, requiring mechanical ventilation, intensive care management and rehabilitation services prior to discharge home.

Recent reports suggest that less than 10% of children experience severe illness. When compared with adults, only one-third as many children have become critically ill [1, 7]. Studies report that remarkably fewer children present acutely ill. Viral tests demonstrate that children may be asymptomatic carriers [1]. Virologists have hypothesized that the difference between adults and children stems from the fact that

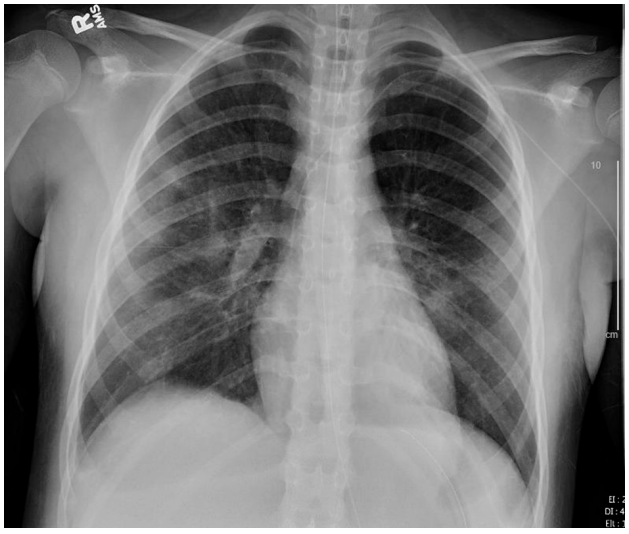

Figure 6. Chest X-ray, anteroposterior (AP) view on the day following start of remdesivir (hospital day 9).

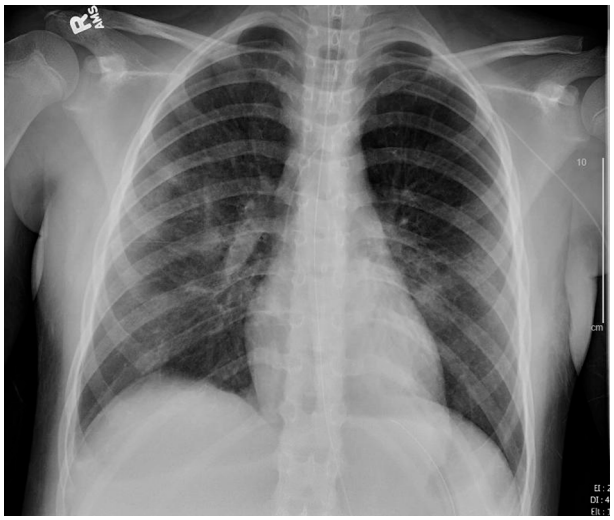

Figure 7. Chest X-ray, anteroposterior (AP) view after 2 days of remdesivir therapy (hospital day 10).

an adult's immune system has been exposed to more pathogens and mounts a hyper-exaggerated inflammatory immune response which in turn may damage the host [8]. Similarly, hyper-inflammation mediated by significant cytokine release has been noted in patients who have COVID-19: "cytokine profile resembling (secondary HLH) is associated with COVID-19 disease severity" [9]. It was noted that patients with significantly elevated IL-6 and ferritin carried a poor prognosis [9].

In our patient's case, identifiable host factors have been limited. With seemingly no past medical history, it is hypothesized that she may have been exposed to novel pathogens in her native country or more distant travels, a pathogen that may have been similar to SARS-CoV-2 or mimicking its effect, resulting in an exaggerated immune response.

Adult patients infected with SARS-CoV-2 frequently present with lymphopenia and mild thrombocytopenia with a platelet count rarely less than 100 [10]. Significant thrombocy-

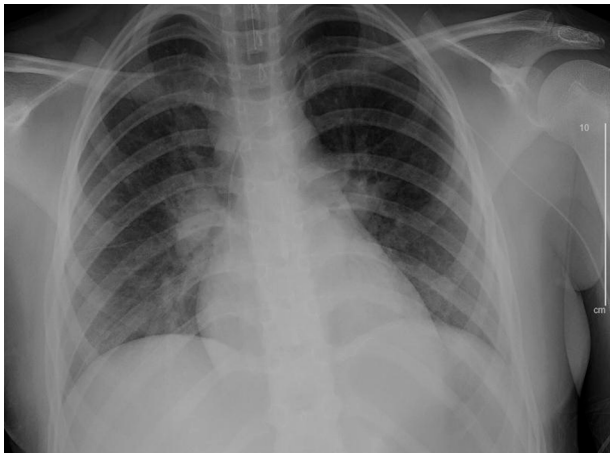

Figure 8. Chest X-ray, anteroposterior (AP) view after 7 days of remdesivir therapy (hospital day 15).

topenia has been deemed a worse prognostic indicator in these patients, denoting more severe disease and increased mortality [10, 11]. Our patient was admitted after approximately 5 days of illness. It is likely that 5 - 10 days prior to presentation she contracted SARS-CoV-2 and was asymptomatic while the virus replicated and her body mounted a response. It is common for patients who are admitted to intensive care settings to present with thrombocytopenia as a direct result of platelet and complement activation or immune consumption [12, 13].

In general, patients with SARS-CoV-2 are found to have ground glass opacities in peripheral or basilar lung fields on chest radiographs. Disease severity has been associated with greater lung segment involvement [14]. Dense consolidation and pleural effusions are uncommon, with pleural effusion accounting for less than 1% of all computed tomography (CT) findings [15, 16]. Additionally, bilateral lung involvement was seen in the vast majority of patients presenting in the late stages of disease, with consolidation clearing several weeks following illness [15]. In our patient's case, it is probable that she was asymptomatic with significant disease progression before presenting to the ED.

Hematuria has been described in the limited literature in older patients with COVID-19 with renal insufficiency and increased mortality [17]. Adult urine specimens often reveal asymptomatic microscopic hematuria with one systematic review of 80,000 patients, citing the prevalence as high as 31% of cases [18]. This pediatric patient presented with microscopic hematuria several days prior to admission, which was believed to be an innocuous finding warranting outpatient follow-up.

This case presents an important reminder that all symptoms, physical exam findings and laboratory data must be utilized in the evaluation and management of patients, even those that appear to be insignificant. Taken together, the sum of the pieces may represent a different clinical picture than each piece evaluated separately. The disease impact of SARS-CoV-2 is such that even when patients recover from the acute physiologic derangements associated with this virus, extensive rehabilitation services may be necessary in order to return the patient to baseline functioning.

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Financial Disclosure

None to declare.

Conflict of Interest

Neither Dr. Gordon nor Dr. Dinerman has any conflict of interest to report.

Informed Consent

None to declare.

Author Contributions

Dr. Gordon researched, drafted and edited the report. Dr. Dinerman edited and provided guidance and mentorship in the drafting of the report.

Data Availability

The authors declare that data supporting the findings of this study are available within the article.

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