Unusual presentation of COVID-19 in a child complicated by massive acute pulmonary embolism and lung infarction

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Abstract

The Novel Coronavirus 2019 (SARS-CoV-2), which was first reported on in Wuhan, China, in late December 2019, causes a respiratory illness called COVID-19 Disease. COVID-19 is most likely causing a hypercoagulable state, however the prevalence of acute venothromboembolism is still unknown. Limited data suggest pulmonary microvascular thrombosis may play a role in progressive respiratory failure. Here, we report a case of a child with an unusual presentation of COVID-19 presented initially by dry cough without fever and complicated by massive acute pulmonary embolism and lung infarction and treated successfully by hydroxychloroquine and azithromycin, in addition to anticoagulant therapy.

Introduction

A pandemic coronavirus, termed SARS-CoV-2, causes a respiratory illness called COVID-19 (Corona Virus Disease 2019). COVID-19, first identified in December 2019 in Wuhan, China, has contributed at significant mortality in several countries with the number of infected cases increasing exponentially worldwide.[1,2] COVID-19 is a public health emergency of international concern. Currently, there is no known effective treatment or vaccination is available in spite of many studies are ongoing.[3] The main way of disease transmission from person to person is via respiratory droplets among close contacts.[4]

The real-time reverse transcriptase-polymerase chain reaction (rRT-PCR) of nasopharyngeal swabs is used to confirm the diagnosis of COVID-19 after clinical and radiological features had suspected the diagnosis. One of the most significant poor prognostic features in those patients is redevelopment of coagulopathy and elevated ferritin.[5,6] Elevated D-dimer are one of the commonest laboratory findings noted in COVID-19 patients requiring hospitalization.[6] Elevation of fibrinogen and other inflammatory markers is common as well. Lymphopenia has been reported in 30-50% of patients with COVID-19.[6]

Herein, we report an unusual case of a child confirmed COVID-19 presented initially by dry cough without fever and complicated by massive acute pulmonary embolism and lung infarction and treated successfully with hydroxylchloroquine and azithromycin, in addition to anticoagulant medication.

Case Report

A 12-year-old girl medically free presented with fever, loin pain and hematuria on February 26, 2020. Her laboratory work revealed anemia (hemoglobin level 8.4 g/dL, reference range: 11.5-15.5 g/dL) with normal platelets and white blood cells count.

Based on clinical presentation and laboratory data, diagnosed as urinary tract infection and iron deficiency anemia, she was discharged on cefprozil and oral iron supplements. Her other investigations showed normal chest x-ray (CXR) and negative urine culture.

After two weeks from initial presentation, she had developed dry cough and her family sought medical advice in many medical centers as her cough getting worse without improvement. On the 17th of March, the patient admitted to our institution complaining of worsening dry cough with no fever. Cough was associated with left sided chest pain, which increased with movement and deep breathing. She denied any history of contact with patient with confirmed COVID- 19 or any respiratory diseases. No history of travel or contact with any person with travel history. She had no gastrointestinal symptoms, joints pain, or skin rash. No family history of thrombosis or similar illness. On physical examination, the child was clinically stable with normal vital signs including body temperature as well as blood pressure. She was not in respiratory distress and saturated well in room air. Chest examination revealed normal contour, good air entry on the right side, and diminished air entry on the left side with no bronchial breathing or wheeze.

CXR showed opacity involving the left

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Informed consent: Informed consent was obtained from patient. The study was approved by the Research and Ethics Committee of PSMMC.

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lung base laterally with obliteration of the left costophrenic angle (Figure 1).

The laboratory investigations at admission are summarized in Table 1, showed mild lymphopenia and normal WBC, but later on she developed leukopenia and severe lymphopenia. Kidney and liver function were normal. On the next day of admission both D-dimer level and anti-Phosphatidylserine (IgG and IgM) were elevated whereas other thrombophilia panels were negative (D-Dimer: 4.590, reference range 0.000-0.500 ug/mL, IgG Anti-Phosphatidylserine: 39, reference range 0-1 U/mL, IgM Anti-Phosphatidylserine: 39, reference range 0-24 U/mL). Fibrinogen was normal: 3.8 (reference range 2.0-5.0 g/L). Procalcitoninwas elevated as well: 6.29 (reference range 0.10-0.49 ng/mL).

Because of CXR findings, computed tomography pulmonary angiography (CTPA) had been performed on the next day of admission and revealed extensive bilateral pulmonary embolisms (PE) with multiple peripheral subpleural infarctions and peripheral subpleural ground-glass opacity of the right upper lobe (Figure 2). The patient started initially from ceftriaxone and received a course of azithromycin as a treatment of atypical community acquired pneumonia with unusual PE for investigation.

Immediately, hematology and cardiology services evaluated the patient condition and documented the stability of the cardiorespiratory condition with no hematuria or potential risk of bleeding. To look for the source of PE, doppler ultrasonography of the lower limbs and echocardiography was reported as normal with no detected thrombi. Electrocardiogram testing was performed as well and revealed normal sinus rhythm with neither right ventricular hypertrophy nor ST segment abnormalities.

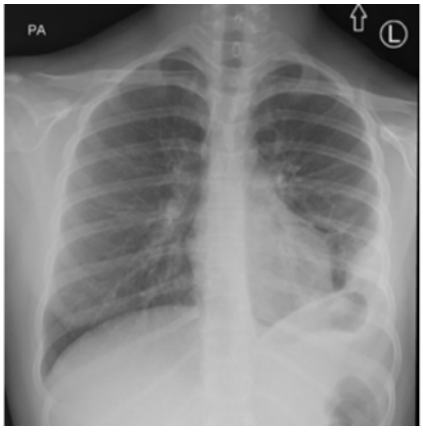

Figure 1. Frontal chest radiograph obtained at presentation shows left lung base pleural based opacity.

Multidisciplinary team decided to start the child from subcutaneous low molecular weight heparin (enoxaparin 1 mg/kg with a total dose of 30 mg subcutaneous every 12 hours). Based on the follow up of therapeutic anti-X level, enoxaparin adjusted to 40 mg s/c every 12 hours to keep the therapeutic level at the higher side 0.75-1.0 IU/mL.

On 25th of March, follow up CTPA showed the same features of PE and infarction as previous imaging. The child remains afebrile and clinically stable with no signs

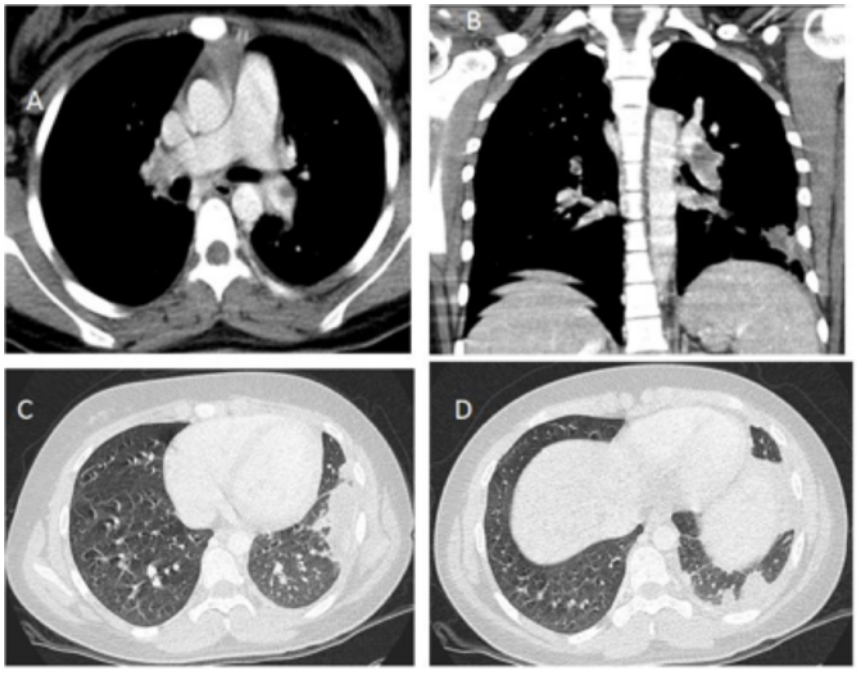

Figure 2. Contrast enhanced CT scan obtained on presentation shows multiple bilateral filling defects in distal pulmonary arteries and segmental branches more on the left consistent with pulmonary embolism A) axial, B), coronal. C, D) Axial lung windows show multiple peripheral wedge shaped left lower lobe opacities suggestive of pulmonary infarctions.

Table 1. Laboratory findings on admission.

Laboratory findings	Results
WBC (4.5-13.5, 10^9/L)	8.4
Hemoglobin (11.5-15.5 g/dL)	7.1
Platelets (150-45, 10^9/L)	166
Neutrophils (1.4-7.5, 10^9/L)	6.3
Lymphocytes (1.9-7.6, 10^9/L)	1.4
Monocytes	0.6X
Eosinophils (0.0-0.8, 10^9/L)	0.1
Basophils (0.0-0.2, 10^9/L)	0.0
Anti-muclear antibodies	Positive
Ferritin (7-84 ng/mL)	142
Lactate dehydrogenase (120-300 U/L)	385
CRP (0-6 mg/L)	39
Respiratory syncytial virus	Negative
Influenza A & B Virus (PCR)	Negative
C3 (0.79-1.52 g/L)	1.21
C4 (0.16-0.40 g/L)	0.12
Prothrombin time (11.5-14.5 sec)	15.4
Activated partial- thromboplastin time (30-41 sec)	38
The international normalized ratio (0.9-1.3 IU)	1.2
Erythrocyte sedimentation rate (0-15 mm/hr)	80

of respiratory distress until 28th of March (11 days after admission) when she started to have frequent spikes of fever up to 39.5°C with no respiratory distress and her laboratory testing revealed leucopenia and severe lymphopenia (0.6×10^9/L). Although she had been on broad-spectrum intravenous antibiotics, which were escalated to a combination of tazocin and vancomycin, her body temperature continued to spike daily. Antimicrobials therapy was stopped after the microbiological laboratories had reported negative blood cultures on multiple occasions.

Due to the clinical manifestations of persistent fever and dry cough, radiological features of ground glass appearance and PE, in addition to laboratory testing of progressive leucopenia and lymphopenia, COVID-19 was suspected. On March 31st, COVID-19 testing was performed by (rRT-PCR) of nasopharyngeal swab. While waiting the COVID-19 rRT-PCR result, the patient was started on daily oral hydroxylchloroquine 200 mg as a suspected with antiphospholipid syndrome because of PE and associated elevation of both antinuclear and antiphospholipid antibodies with elevated ESR and CRP

Three days later, COVID-19 rRT-PCR results reported as positive which led to the addition of azithromycin to hydroxychloroquine. The child remained clinically stable , afebrile, and on room air without any cardiorespiratory assistance. After two COVID-19 negative serial RT-PCR for SARS-CoV-2 RNA from the nasopharyngeal swab, she was discharged home from anticoagulant therapy in a good condition with a repeat of CTPA in two weeks from discharge for evaluation of her clinical condition.

Discussion

COVID-19 is a public health emergency of international concern.[3] The symptomatology of COVID-19 was discussed in detail in WHO-China joint report on COVID-19.[7] Although patients with COVID-19 present with fever in 85% of cases, however, only 45% of cases experience fever at early presentation.[8] At the beginning of the pandemic, it was thought to spare children and adolescents as a very smaller number of cases have been reported in the pediatric population in comparison to adults, however, later on many cases are reported.[9]

Here we report a pediatric patient from Saudi Arabia, presenting with persistent dry cough without fever and dyspnea at presentation secondary to COVID-19 confirmed with rRT-PCR of nasopharyngeal swabs. To the best of our knowledge, no pediatric cases reported from Saudi Arabia in the literate, our patient is interesting as she is presented without fever initially and developed fever after 11 days of admission and complicated by massive acute bilateral PE and lung infarction, in spite of that, she surprisingly clinically stable on room air without cardiopulmonary instability. Although few cases of bilateral massive PE are reported with COVID-19.[10] However no case is reported without any without cardiopulmonary support and clinically stable. After the diagnosis of PE, the patient was started on LMWH as recommended.

As reported previously,[11] the clinical suspicion of COVID-19 was based on CXR and CT findings of PE and ground-glass opacities. The CXR and CT chest can make an early diagnosis of COVID-19 in case of unusual presentation as in our case study. Our patient started on hydroxyl chloroquine before the diagnosis of COVID-19 due to suspicious of antiphospholipid syndrome. The association of Viral infections and antiphospholipid antibodies was previously reported and recently few cases were reported in patients with COVID-19.[12,13]

Our patient is discharged after remained stable, afebrile without cough for more than 3 days, in addition to negativity of two serial RT-PCR for SARS-CoV-2 RNA from the nasopharyngeal.

Furthermore, the association with the thrombosis she developed and it was also reported to result in thrombosis/pulmonary embolism in children and adolescents as in the following reference:

Conclusions

We report the first case in the Saudi Arabia, of a 12 years old female previously healthy present only by dry cough at early presentation without fever. chest X-ray and CT-chest making an early diagnosis of COVID-19 through the identification of PE and ground-glass opacities. The utilization of the CT scan would prevent an infected patient from being discharged back to the community when an unusual clinical presentation.

Cases of pediatric with COVID-19 positive are not as rare as they might have been thought. The association of antiphospholipid antibodies in patients with COVID-19 had been recently reported.

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