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CORRESPONDENCE

COVID-19 pneumonia as a cause of acute chest syndrome in an adult sickle cell patient

To the Editor:

As the coronavirus disease 2019 (COVID-19) pandemic continues, there is an increasing focus on the impact of patient comorbidities on disease presentation and clinical course. Patients with sickle cell disease (SCD) who are infected with COVID-19 may have a significant risk of developing acute chest syndrome (ACS), a potentially life-threatening complication. We report on the first documented case of a hospitalized patient with SCD who developed ACS with COVID-19.

A 21-year-old man with a history of SCD (HbS/β^0-thalassemia) on maintenance hydroxyurea therapy presented to our emergency department, with worsening left hip pain over four months. His prior history was notable for an episode of ACS two years before presentation requiring simple blood transfusion, plus multiple pain crises and septic arthritis of the right hip. After an MRI showed evidence of avascular necrosis of the left hip, he was admitted for pain control. On hospital day five, the patient developed a new-onset fever of 38.6°C. A chest X-ray showed minimal linear atelectasis in the right lower lung, and joint aspiration of his left hip was negative for septic arthritis. Despite starting an empiric course of ceftriaxone and azithromycin his fever persisted. Influenza A/B/RSV PCR swab, urine legionella antigen, and blood cultures were negative. Procalcitonin was normal at 0.19 ng/mL.

On hospital day ten, he developed a new cough and hypoxia with SpO_2 82% correcting with two liters/minute of supplemental O_2. His labs began to show evidence of systemic hemolysis with a decrease in hemoglobin of 2g/dL, and an increase in LDH from 302 to 664 U/L. His white blood cell count was 6000/μL with an absolute lymphocyte count of 1400/μL. A repeat chest X-ray showed multifocal ill-defined opacities in the left mid-lung, retro-cardiac portion of the left lower lobe and right lung base (Figure 1). Given his new cough, hypoxia, and infiltrates on chest X-ray, he met criteria for moderate ACS and received a simple blood transfusion of one unit packed red blood cells, which increased his hemoglobin from 8.6 to 9.2 g/dL. His oxygen saturation improved from 82% to 90% after simple transfusion. The SARS-CoV-2 PCR nasopharyngeal swab testing was sent and returned positive on hospital day eleven after which the patient was started on hydroxychloroquine for severe COVID-19 pneumonia.

On hospital day eleven, the patient experienced new pleuritic chest pain and dyspnea, with continued high fevers and an increasing oxygen requirement to 4 liters/minute. An EKG showed sinus tachycardia without ischemic changes and troponin enzymes were undetected, however an interval chest X-ray showed worsening diffuse ground-glass and reticular opacities. Given his worsening respiratory and clinical status, he underwent same-day urgent exchange transfusion with reduction in hemoglobin-S fraction from 87.8% to 18.1%. After exchange transfusion, chest pain, dyspnea and hemolysis improved, room air oxygen saturations remained around 90% and fevers continued. On hospital day fourteen the patient received an investigational product (possibly placebo) as part of a research study. Fevers resolved the next day and room air saturations increased to above 95%. He was discharged home on hospital day sixteen.

Viral pathogens are a common cause of ACS in pediatric sickle cell patients. The incidence of viral infections inciting ACS in adult sickle cell patients, however, has been reported to be seen in less than 10% of cases.[1] Viral pandemics are of particular risk to vulnerable SCD patients given lack of past immunity in a population with an already weakened immune response. However, data from previous pandemics is both limited and conflicting. No published evidence about SCD patients and the 2002-2003 SARS-CoV outbreak currently exists, and evidence regarding SCD patient outcomes during the 2009 H1N1 influenza pandemic is sparse. Previous small cohort studies from the 2009 H1N1 influenza pandemic within pediatric SCD populations have suggested that SCD patients may be at risk for developing more complications. In one study of 48 patients, 10 (21%) patients had initial diagnoses of ACS, nine patients received a simple transfusion, and only one patient required an exchange transfusion and ICU-level monitoring. However, this study combined both seasonal influenza (13) and H1N1 (35) in the analysis, and other studies reported more severe findings with H1N1.[2] In a cohort of 21 pediatric patients with SCD and H1N1, 11 patients (52.3%) received blood transfusions for ACS or worsening anemia, and one patient required mechanical ventilation.[3] A larger retrospective cohort of 123 SCD patients (94 with influenza versus 29 with H1N1) found that 34% of patients developed ACS with H1N1, as compared to only 13% with influenza. They also noted that those with H1N1 more frequently required simple transfusion, exchange transfusion, and mechanical ventilation.[4]

As COVID-19 remains an emerging disease, there is a paucity of data on how the pandemic may complicate SCD in both pediatric and adult patients. During the first two months of the COVID-19 outbreak in China, approximately 15% of diagnosed patients with severe disease developed acute respiratory distress syndrome (ARDS), and 6% of all patients received mechanical ventilation.[5] A study involving 201 COVID-19 patients in Wuhan found that older age, higher inflammatory markers (IL-6, CRP, ferritin) and co-morbidities as hypertension and diabetes were significantly associated with progression to ARDS and death.[6]

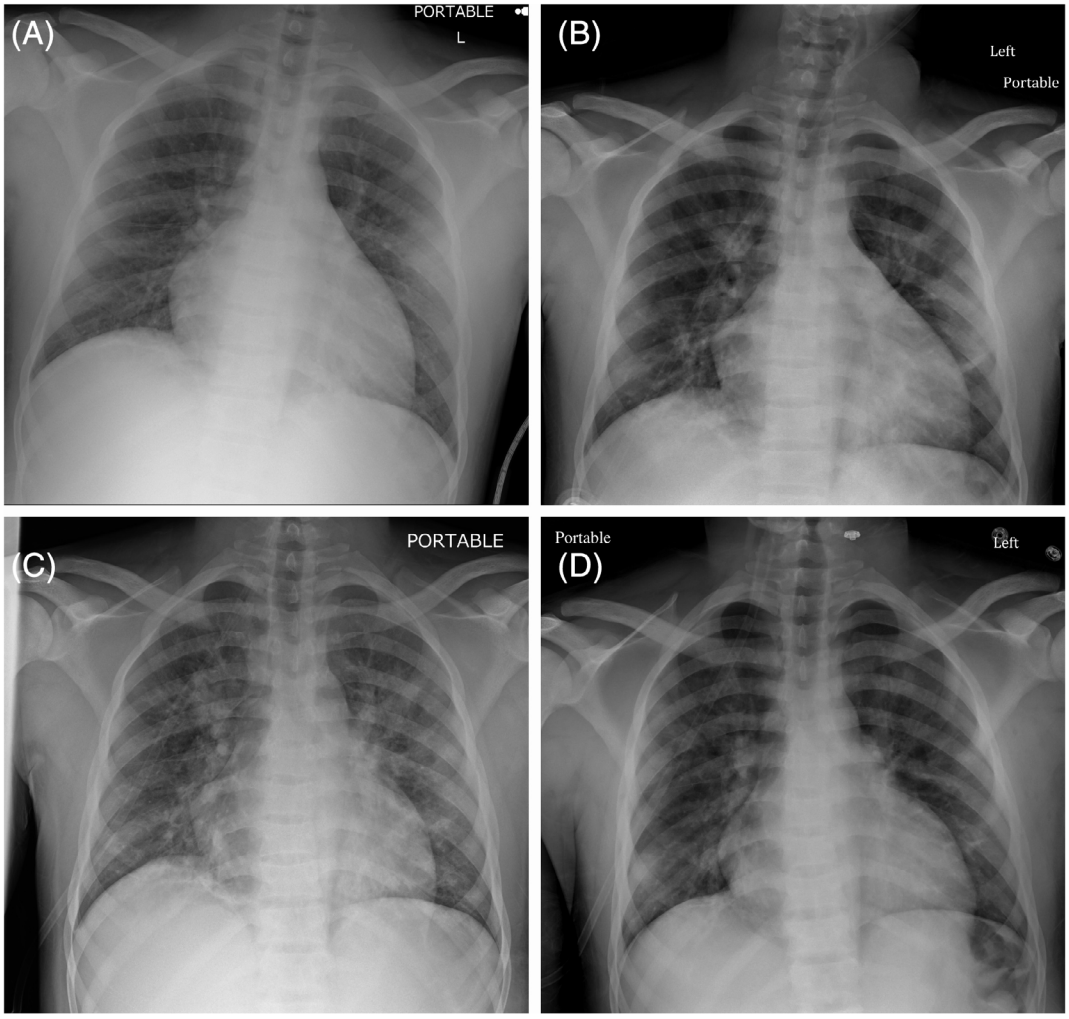

FIGURE 1 Progression of COVID-19 pneumonia to acute chest syndrome and response to exchange transfusion. A, Chest X-ray on hospital day 5 without evidence of pneumonia. B, Chest X-ray on hospital day 10 with multifocal ill-defined opacities in the left mid-lung, retro-cardiac portion of the left lower lobe and right lung base. C, Chest X-ray on hospital day 11 with worsening diffuse ground-glass- and reticular opacities. D, Chest X-ray on hospital day 13 status post exchange transfusion with improvement in diffuse ground glass opacities

Given the higher likelihood of ACS and respiratory complications amongst SCD patients during the H1N1 outbreak, it is possible that SCD patients are also at higher risk of such complications from COVID-19, particularly those with a history of pulmonary comorbidities. However, it is unclear if the SARS-CoV-2 pandemic will lead to increased rates of ACS for sickle cell patients. Still, hospitalized sickle cell patients should be monitored closely for development of ACS and if this occurs, exchange transfusion should be promptly initiated.

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