Adult sickle cell disease and SARS-CoV-2: an increasingly common comorbidity for a rare disease

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Table S1. Medical history, current medications, presenting symptoms, and hemoglobin values.

Reference	History	Current medications	Presenting symptoms	Hemoglobin	Hemoglobin F/hemoglobin S
Chen *et al.*,[59] 30-year-old, M	-HbSS -Recurrent VOCs -11-year history of cigarette smoking -Sepsis with acute hypoxic respiratory failure -Cholecystectomy	-Cyclobenzaprine 10 mg as needed -Hydroxyurea 1000 mg/ daily -Oxycodone 30 mg every four hours as needed for pain -Oxycodone 80 mg extended release every 12 hours	In ER: -Right lower extremity pain following vehicle collision On admission: -Continued right lower extremity pain -Suspected COVID-19 -Reported decreased oxygen saturation	In ER: -8.9 g/dL On admission: -8.9 g/dL Day two of hospitalization: -6.7 g/dL	In ER: -N/S On admission: -N/S Day two of hospitalization: -N/S
Chen *et al.*,[59] 49-year-old, F	-HbSC -Avascular necrosis of right hip -Rheumatoid arthritis -Daily chronic musculoskeletal pain -Bilateral retinopathy	-One lifetime blood transfusion -Baclofen 5 mg orally every 8 hours as needed for muscle spasm -Ergocalciferol 1.25 mg/weekly -Folic acid 1 mg/daily -Hydrocodone-Acetaminophen 10 to 325 mg every 8 hours as needed for pain -Promethazine HCl 25 mg twice daily as needed for nausea/vomiting	One week prior to telehealth appointment: -Fever, 38.1°C -Diarrhea -Loss of taste and smell -Cough -10/10 pain severity in both arms, both legs, and chest wall -Advised to go to ER In ER: -Cough -Fever -Pain in the arms	In ER: -N/S	In ER: -N/S

		-Tofacitinib XR 11 mg/daily	and chest wall		
Chen *et al.*,[59] 23-year-old, M	-HbSS -3-4 VOCs per year requiring hospitalization -Multiple episodes of ACS -Priapism -Bilateral avascular necrosis of the humeral heads -Hypertension -MDD	-Hydroxyurea 1500 mg/daily -Lisinopril 10 mg/daily -Duloxetine 60 mg/daily -Naproxen 500 mg every 8 hours for pain -Hydromorphone HCl 4 mg orally every 6 hours as needed for severe pain	5 days prior to ER visit: -Chronic back pain -pain in both arms -Icteric sclera In ER: -Pain severity 9/10 -SOB and cough -Dry mucosal membranes -Rales bilaterally with normal respiratory effort Day two of hospitalization: -Cough -SOB Day three of hospitalization: -Cough	In ER: -7.8 g/dL Day one of hospitalization/ following transfusion: -8.8 g/dL Day three of hospitalization: -9.2 g/dL	In ER: -N/S Day one of hospitalization: -N/S Day three of hospitalization: -N/S
Chen *et al.*,[59] 25-year-old, F	-HbSS -Appendectomy -Cholecystectomy -Pain crises -Migraine headaches -Benign cyst in left breast	-Hydroxyurea 1000 mg/daily	-Nasal congestion -Loss of taste -Intermittent frontal headache -Intermittent musculoskeletal pain	Telehealth appointment with Hematology: -N/S	Telehealth appointment with Hematology: -N/S

Teulier *et al.*,[60] 33-year-old, M	-HbSS -Mild episodes of VOC -2 episodes of ACS -Goldberg's stage III retinopathy -GFR 120 mL/min -Microalbuminuria 0.75 g/L	N/S	In ER: -Febrile dyspnea -Cough -Headache -Fever, 39°C -Acute respiratory distress	Baseline: -11.5 g/dL	Baseline: -HbF: 2.5% -HbS: 87%

HbSS, hemoglobin SS; VOC, vaso-occlusive crises; ER, emergency room; N/S, not specified; ACS, acute chest syndrome; MDD, major depressive disorder; SOB, shortness of breath; XR, extended release; GFR, glomerular filtration rate.

Table S2. Vital signs.

Reference	Pulse oximetry (SpO2)	Blood pressure	Heart rate	Respiratory rate
Chen *et al.*,[59] 30-year-old, M	In ER: 89% on room air On admission: -96%	In ER: 106/61 mmHg On admission: -106/55 mmHg	In ER: 100 bpm On admission: -77 bpm	In ER: 18 breaths per minute On admission: -18 breaths per minute
Chen *et al.*,[59] 49-year-old, F	In ER: -98%	In ER: -N/S	In ER: -N/S	In ER: -N/S
Chen *et al.*,[59] 23-year-old, M	In ER: -88% on room air Day one of hospitalization: -94%	In ER: -N/S Day one of hospitalization: -N/S	In ER: -124 bpm Day one of hospitalization: -N/S	In ER: -26 breaths per minute Day one of hospitalization: -N/S
Chen *et al.*,[59] 25-year-old, F	Telehealth appointment with hematology: -N/S	Telehealth appointment with hematology: -N/S	Telehealth appointment with hematology: -N/S	Telehealth appointment with hematology: -N/S
Teulier *et al.*,[60] 33-year-old, M	In ER: -88%	In ER: -134/82 mmHg	In ER: -106 bpm	In ER: -36 breaths per minute

ER, emergency room; bpm, beats per minute; N/S, not specified.

Table S3. Relevant hematologic values, D-dimer levels, and total bilirubin.

Reference	Hematocrit	Reticulocytes	Lymphocytes	Platelets	Total bilirubin	D-dimer levels
Chen *et al.*,[59] 30-year-old, M	In ER: -N/S On admission: -24.9% Day two of hospitalization: -17.6%	In ER: -9.5% On admission: -N/S Day two of hospitalization: -N/S	In ER: -N/S On admission: -10.4 K/CMM Day two of hospitalization: -12.7 K/CMM	In ER: -N/S On admission: -369 K/CMM Day two of hospitalization: -309 K/CMM	In ER: -N/S On admission: -5.4 mg/dL Day two of hospitalization: -N/S	In ER: -N/S On admission: -N/S Day two of hospitalization: -N/S
Chen *et al.*,[59] 49-year-old, F	In ER: -N/S	In ER: -N/S	In ER: -N/S	In ER: -N/S	In ER: -N/S	In ER: -N/S
Chen *et al.*,[59] 23-year-old, M	In ER: -N/S Day one of hospitalization: -25.5% Day three of hospitalization: -N/S	In ER: -N/S Day one of hospitalization: -N/S Day three of hospitalization: -N/S	In ER: -3.8 K/CMM Day one of hospitalization: -2.2 K/CMM Day three of hospitalization: -2.4 K/CMM	In ER: -237 K/CMM Day one of hospitalization: -267 K/CMM Day three of hospitalization: -278 K/CMM	In ER: -7.3 mg/dL Day one of hospitalization: -N/S Day three of hospitalization: -N/S	In ER: -10.12 µg/mL Day one of hospitalization: -N/S Day three of hospitalization: -3 µg/mL
Chen *et al.*,[59] 25-year-old, F	Telehealth appointment with Hematology: -N/S	Telehealth appointment with Hematology: -N/S	Telehealth appointment with Hematology: -N/S	Telehealth appointment with Hematology: -N/S	Telehealth appointment with Hematology: -N/S	Telehealth appointment with Hematology: -N/S
Teulier *et al.*,[60] 33-year-old, M	In ER: -N/S	In ER: -N/S	In ER: -N/S	In ER: -N/S	In ER: -N/S	In ER: -N/S

ER, emergency room; N/S, not specified.

Table S4. Imaging and testing results and SARS-CoV-2 reverse transcription polymerase chain reaction testing results.

Reference	Chest X-ray results	CT results	Other imaging/testing results	SARS-CoV-2 RT-PCR test (positive/negative)
Chen *et al.*,[59] 30-year-old, M	In ER: -No acute cardiopulmonary findings On admission: -No acute cardiopulmonary findings	On admission: -Showed basilar atelectasis bilaterally with some plate-like atelectasis in the bases without consolidation or cardiomegaly	On admission: -Ventilation/ perfusion scan showed no evidence of pulmonary embolism -Ultrasound of leg was negative for deep vein thrombosis	-Positive on final day of hospitalization
Chen *et al.*,[59] 49-year-old, F	In ER: -N/S	In ER: -N/S	In ER: -N/S	-Positive one week prior to ER visit
Chen *et al.*,[59] 23-year-old, M	In ER: -Consistent with ACS -Multifocal airspace opacities most consistent with pneumonia	In ER: -N/S	In ER: -N/S	In ER: -Positive
Chen *et al.*,[59] 25-year-old, F	Telehealth appointment with Hematology: -N/S	Telehealth appointment with Hematology: -N/S	Telehealth appointment with Hematology: -N/S	-Positive
Teulier *et al.*,[60] 33-year-old, M	In ER: -Bilateral alveolar and interstitial infiltrates predominating in the middle lobe	In ER: -N/S	Blood analysis: -Moderate anemia -Reticulocytopenia -Moderate hemolysis -Lymphocytopenia -Major inflammatory	Day one of Hospitalization: -Positive

			syndrome Day three of hospitalization: -Bone marrow aspiration revealed normal structure and cytology without bone marrow necrosis Day four of hospitalization: -Cardiac ultrasound revealed a thrombus of the inferior vena cava Day 19 of hospitalization: -Thoracic angioscanner no longer revealed this thrombus Day 16 of hospitalization: -BAL performed, showing lymphocytic alveolitis Due to increased inflammatory markers and clinical deterioration, a protected distal sampling allowed for the diagnosis of pneumopathy acquired under late mechanical ventilation	

CT, computed tomography; RT-PCR, reverse transcription polymerase chain reaction; ER, emergency room; ACS, acute chest syndrome; BAL, bronchoalveolar lavage; N/S, not specified.

Table S5. Complications during hospitalization and treatment.

Reference	Complications during hospitalization	Treatment
Chen *et al.*,[59] 30-year-old, M	No significant complications during hospitalizations	-Started on prophylactic enoxaparin to prevent DVT -Simple transfusion of 1 unit of packed red blood cells for treatment of hypoxia and pain -Advised to self-quarantine following positive COVID-19 test
Chen *et al.*,[59] 49-year-old, F	No significant complications during hospitalizations	-Albuterol MDI -Dextromethorphan 20 mg every 4 hours as needed for cough -Lidocaine patch as needed for pain
Chen *et al.*,[59] 23-year-old, M	No significant complications during hospitalizations other than VOC pain fluctuations	<u>In ER:</u> -4 L O2 via nasal cannula -Azithromycin -Ceftriaxone -I.V. Morphine -Dexamethasone -Enoxaparin 80 mg for 12 hours for thrombosis prophylaxis because of high D-dimer levels <u>Day one of hospitalization:</u> -Transfusion of 1 unit packed red blood cells -Switched from I.V. morphine to home regimen of oral morphine IR 15 mg every four hours and ibuprofen 600 mg every 8 hours <u>Day two of hospitalization:</u> -Pain levels increased, switched back to I.V. morphine <u>Day three of hospitalization:</u> -decreased to 1 L of O2 via nasal cannula

		-Returned to home oral pain management regimen -Prophylactic dose of enoxaparin 40 mg subcutaneous injection daily <u>Final day of hospitalization:</u> -Weaned to oral acetaminophen 325 mg/ hydrocodone 10 mg every 8 hours as needed for pain -Morphine IR 15 mg by mouth every 4 hours as needed for severe pain -Enoxaparin 40 mg/0.4 mL subcutaneous injection
Chen *et al.*,[59] 25-year-old, F	Never hospitalized	-Pain management with OTC analgesics
Teulier *et al.*,[60] 33-year-old, M	<u>Day one of hospitalization:</u> -Respiratory condition worsened, requiring ICU admission and intubation with mechanical ventilation <u>Day three of hospitalization</u>: -Bone marrow aspiration performed because of severe ACS associated with a drop in reticulocytes and mild thrombocytopenia suggesting a spinal thrombosis -Bone marrow aspiration revealed normal structure and cytology without bone marrow necrosis <u>Day four of hospitalization:</u> -D-dimer levels increased markedly <u>Day 19 of hospitalization:</u> -Respiratory condition worsened, progressed to severe COVID-19 with ARDS -Worsening pulmonary infiltrates and	<u>Day one of hospitalization:</u> -Hemolysis worsened, prompting blood exchange transfusions (3 sessions) to maintain HbS below 40% <u>Day four of hospitalization:</u> -Anticoagulation was switched from prophylactic to therapeutic dose (I.V. unfractionated heparin with a ratio of activated partial thromboplastin time target between 2 and 2.5) <u>Day five of hospitalization:</u> -ECMO was installed and removed 10 days later <u>Day 16 of hospitalization:</u> -Treated with antibiotics <u>Day 25 of hospitalization:</u> -Patient was extubated and treated with corticosteroid aerosol due to laryngeal edema <u>Day 27 of hospitalization:</u> -Patient was discharged from ICU

	major hypoxemia Day 25 of hospitalization: -Laryngeal edema complicated extubation	Day 34 of hospitalization: -Patient was discharged from hospital

DVT, deep vein thrombosis; VOC, vaso-occlusive crises; ER, emergency room; MDI, metered-dose inhaler; I.V., intravenous; IR, immediate release; ICU, intensive care unit; ACS, acute chest syndrome; ECMO, venovenous extracorporeal membrane oxygenation; ARDS, acute respiratory distress syndrome; OTC, over the counter; N/S, not specified.