Received: 8 April 2020 | Revised: 9 April 2020 | Accepted: 9 April 2020

DOI: 10.1002/ajh.25833

IMAGES IN HEMATOLOGY

Rapid and severe Covid-19 pneumonia with severe acute chest syndrome in a sickle cell patient successfully treated with tocilizumab

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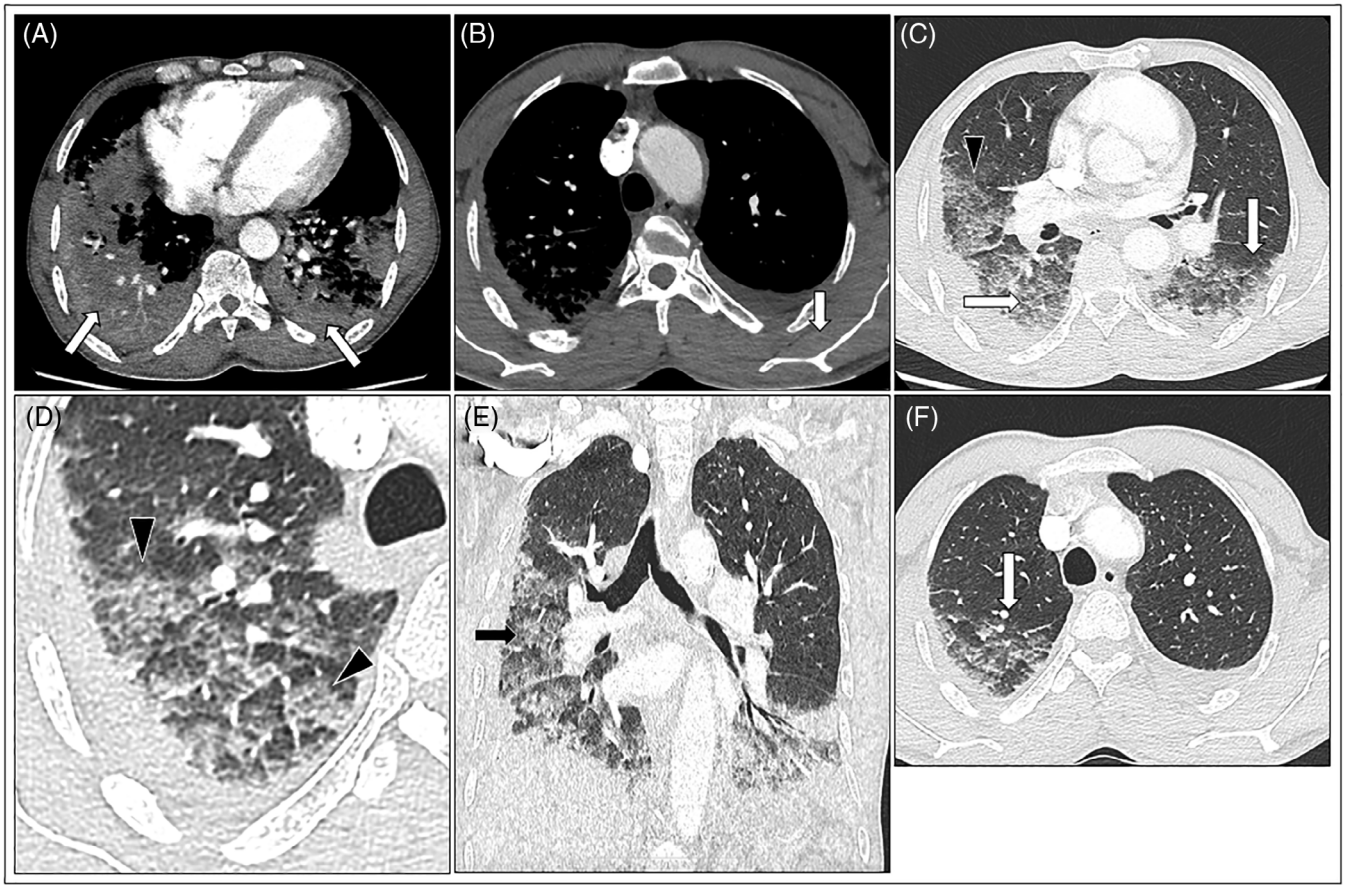

IMAGE 1 CT scan of the chest: Acute chest syndrome and Covid-19-induced pneumonia. A, Axial image of chest obtained with a soft-tissue windows at the level of the lower lobes evidenced areas of consolidation located at the posterior part of the lung (arrows). B, An axial image with the same windowing obtained at the upper part of the lungs showed a right small pleural effusion in the upper part of the great pleural cavity (arrow). C, Axial image located at the same level as A with lung windows evidenced areas of ground-glass opacities (arrows) in the lower lungs with regards to areas of consolidation, but also in the middle lobe (arrowhead) D, and in the upper right lobe. E, Coronal reconstruction confirmed areas of ground-glass opacities (arrow) and areas of consolidation with air bronchograms (arrowhead). F, Magnification of a CT image with lung windows acquired at the middle part of the lungs showing a crazy-paving pattern with ground-glass opacities and interlobar septal thickening (arrowhead)

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Funding information
This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

On 25 March 2020 presence of multifocal vaso-occlusive crises (VOC) for the past 24 hours was determined in a 45-year-old male patient with homozygous sickle cell disease (SCD) by the "DREPADOM" network. This was a phone consultation clinical monitoring and ambulatory care of SCD patients set up in our SCD referral center since the outbreak of the Covid-19 epidemic in France. Prior medical history included sickle cell nephropathy with tubular acidosis ischemic retinopathy priapism and cardiac remodeling. Past History for VOC or Acute Chest Syndrome (ACS) was negative for the past 10 years except for a brief hospitalization in February 2020 for sub-segmental pulmonary embolism secondary to ACS and treated with rivaroxaban. Hydroxyurea treatment was scheduled after sperm cryopreservation but had not yet started at the time of the Covid-19 hospitalization. After the DREPADOM screening he was admitted for multifocal VOC with normal pulmonary findings no dyspnea no diarrhea no anosmia no cough no fever and oxygen saturation (SpO2) at 98%. On day 1 of hospitalization the patient developed fever (38.5°C) and SpO2 dropped to 91% with crackles at pulmonary auscultation. Antibiotic therapy was immediately started with amoxicillin-clavulanic acid and the patient received supplemental oxygen through a nasal cannula at a rate of 3 L/min. Hydroxychloroquine treatment at a dosage of 200 mg orally every 8 hours was instituted while results of the real-time reverse-transcription-polymerase-chain-reaction (RT-PCR) assay were still pending. The electrocardiogram showed a QT interval at 390 ms. On day 2 the patient's general condition rapidly deteriorated and SpO2 dropped to 80%. Supplemental oxygen through Venturi mask at a rate of 15 L/min and a 100% fraction of inspired oxygen maintained the SpO2 at 91%. Surprisingly the patient presented a respiratory rate of 19 breaths/min. Notable laboratory values were; hemoglobin 7 g/L reticulocytes 8.4% leucocytes 20 Giga/L C-reactive protein at 189 mg/L serum ferritin 3271 μg/L and creatinine clearance (DFG CKD EPI) 120 mL/min/1.73 m^2. Computerized tomography (CT) of the chest displayed abnormalities consistent with a Covid-19-induced pneumonia and ACS. (Image 1). The RT-PCR assay for the Covid-19 diagnosis was positive. Treatment with one pulse of intravenous tocilizumab at a dosage of 8 mg/kg was administered. On day 3 a clear improvement of the patient's general condition was observed with a SpO2 at 97% by supplemental oxygen through a nasal cannula at a rate of 3 L/min and no fever. On day 4 blood transfusion was performed due to the ACS condition. On day 5 the patient was discharged and referred back for ambulatory care to the DREPADOM structure

Sickle cell disease is a serious genetic condition that shortens life expectancy. It affects more than 30 000 people in France, 50% of whom are located in the Ile de France region.[1] A severe complication of SCD is ACS, that can be triggered by infectious complications.[2] The Influenza H1N1 epidemic had a 17% rate of hospitalization in intensive care units for the SCD population.[3,4] Covid-19 and the associated acute respiratory distress syndrome (ARDS), represent a significant mortality risk for SCD patients. Extracorporeal membrane oxygenation (ECMO), which is often required in ARDS, is associated in SCD patients with catastrophic prognosis (70% mortality rate).[5] Note, IL-6 is a multifunctional cytokine that plays a central role in host defense mechanisms. Abnormally high plasma values of IL-6 have been reported in SCD patients at steady (healthy) state.[6] Both IL-6 and C reactive protein are elevated during VOC. Inflammation contributes to the sickle red blood cells adhesion process involved in vaso-occlusive pathophysiology.[7] The SARS-CoV S protein induces direct up-regulation of IL-6,[8] IL-1 and TNFα, some of the most potent pro-inflammatory cytokines. Tocilizumab (TCZ) is an anti-human IL-6 receptor monoclonal antibody that inhibits signal transduction by binding sIL-6R and mIL-6R. Despite the lack of clinical trials on TCZ efficacy and safety for Covid-19 treatment, it was recently approved in China for patients affected by severe Covid-19 pulmonary complications. Preliminary data from an observational study conducted in China on 21 severe cases receiving TCZ,[9] showed improvement of clinical and radiological outcomes. Early antiviral strategies at the onset of the infection should be considered for

high risk patients. For critically ill patients, therapy directed toward the chemokine release syndrome is required. For our patient, given the prior history of severe SCD and the potential risks, treatment with hydroxychloroquine and TCZ were initiated, with a positive resolution. More studies are needed to determine the proper therapy for COVID-19 in patients affected by SCD.

CONFLICT OF INTEREST

Bartolucci reports being a consultant for F. Hoffmann-La Roche. No other potential conflict of interest relevant to this letter was reported.

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How to cite this article: De Luna G, Habibi A, Deux J-F, et al. Rapid and severe Covid-19 pneumonia with severe acute chest syndrome in a sickle cell patient successfully treated with tocilizumab. *Am J Hematol*. 2020;95:876–878. https://doi.org/10.1002/ajh.25833