

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active. 19 cohort as well as DISCOVERY trial strive to generate evidence to determine the optimal treatment of COVID-19.

The ongoing climate change, disruption of natural ecosystems, and human migration guarantee that we remain at risk of pandemics in the foreseeable future. Knowledge generated now will not only help us fight the current pandemic, but our lessons will also prepare us to prevent and maybe better coordinate our response for the future pandemics. Our reliance on evidencebased medicine generated through RCTs is critical to ensure that we are prepared for what comes next.

> Prakhar Vijayvargiya, MBBS Zerelda Esquer Garrigos, MD Natalia E. Castillo Almeida, MD Pooja R. Gurram, MBBS Ryan W. Stevens, PharmD Raymund R. Razonable, MD Mayo Clinic Rochester, MN

**Potential Competing Interests:** Dr Razonable serves as the principal investigator in clinical trials for tocilizumab and sarilumab. The other authors report no competing interests.

### ORCID

Prakhar Vijayvargiya: b https://orcid.org/0000-0002-7143-6886; Zerelda Esquer Garrigos: b https://orcid.org/0000-0003-4561-7883; Natalia E. Castillo Almeida: b https://orcid.org/0000-0002-9904-7137; Pooja R. Gurram: b https:// orcid.org/0000-0002-1211-0907; Raymund R. Razonable: b https://orcid.org/0000-0001-5248-0227

- Vijayvargiya P, Garrigos ZE, Castillo Almeida NE, Gurram PR, Stevens RW, Razonable RR. Treatment considerations for COVID-19: a critical review of the evidence (or lack thereof). *Mayo Clin Proc.* 2020;95(9):2037-2038.
- Tocilizumab improves significantly clinical outcomes of patients with moderate or severe COVID-19 pneumonia. APHP website. https://www.aphp.fr/ contenu/tocilizumab-improves-significantly-clinicaloutcomes-patients-moderate-or-severe-covid-19. Accessed April 4, 2020.
- Richardson P, Griffin I, Tucker C, et al. Baricitinib as potential treatment for 2019-nCoV acute respiratory disease. *Lancet*. 2020;395(10223):e30-e31.
- Stebbing J, Phelan A, Griffin I, et al. COVID-19: combining antiviral and anti-inflammatory treatments. *Lancet Infect Dis.* 2020;20(4):400-402.

- NIH clinical trial shows remdesivir accelerates recovery from advanced COVID-19. National Institute of Allergy and Infectious Diseases website. https://www.niaid.nih.gov/news-events/nih-clinicaltrial-shows-remdesivir-accelerates-recovery-advan ced-covid-19. Accessed April 29, 2020.
- Wang Y, Zhang D, Du G, et al. Remdesivir in adults with severe COVID-19: a randomised, doubleblind, placebo-controlled, multicentre trial. *Lancet.* 2020;395(10236):P1569-P1578.

https://doi.org/10.1016/j.mayocp.2020.05.016

Migratory Pulmonary Infiltrates in a Patient With COVID-19 Infection and the Role of Corticosteroids

To the Editor: The emergence of novel coronavirus disease 2019 (COVID-19) has led to a global pandemic and has threatened the lives of millions of people. This disease is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that results in respiratory failure, multiple organ dysfunction, and death.1 Little is known about the spectrum of clinical presentations of COVID-19 in cancer patients.<sup>2</sup> Herein, we present a patient with chronic lymphocytic leukemia (CLL) who developed organizing pneumonia (OP) as a late manifestation of COVID-19 after an initial improvement who was successfully treated with corticosteroids.

# **REPORT OF CASE**

A 62-year-old woman with CLL, hypertension, and type 2 diabetes mellitus presented with low-grade fever, cough, and shortness of breath of 1-week duration. Her CLL was treated with rituximab initially that was switched to ibrutinib 3 months earlier but was discontinued a few days before her hospitalization due to palpitations and arthralgia. On admission, she was hypoxic, requiring supplemental oxygen at 2 L/min to maintain oxygen saturation,  $SpO_2 >$ 93%, and in atrial fibrillation with no hemodynamic instability. Laboratory studies were significant only for elevated C-reactive protein at 74 mg/ L (normal <10 mg/L). Nasopharyngeal swab specimen for reverse transcriptase-polymerase chain reaction for SARS-CoV-2 was positive, but negative for other respiratory viruses. Computed tomography scan of the chest showed bilateral groundglass opacities (Figure A). The patient was enrolled in the Mayo Clinic COVID-19 expanded access program for convalescent plasma (CCP) on day 9 of her illness and received one dose of CCP. The patient's respiratory status rapidly improved the day following CCP transfusion, maintaining SpO<sub>2</sub> on room air. After 3 days, the patient developed daily low-grade fevers and increasing shortness of breath requiring supplemental oxygen via nasal cannula. Infectious disease workup including blood cultures and fungal serum markers were negative. A repeat chest computed tomography, on day 17 of illness (Figure B), revealed new and migratory ground-glass opacities in both lungs that were consistent with an OP pattern. The patient was started on intravenous methylprednisolone at 1 mg/kg/d, which resulted in improvement in oxygenation and resolution of fever. She was discharged in stable condition after 7 days of corticosteroids.

## DISCUSSION

Our case may present a rare clinical course of COVID-19. Given the radiological appearance of migratory lung infiltrates and rapid improvement with corticosteroids, we hypothesize that this is OP due to the associated hyper-inflammation phase commonly seen in the later stages of COVID-19.<sup>3</sup> Moreover, acute fibrinous and OP (a subtype of OP) are

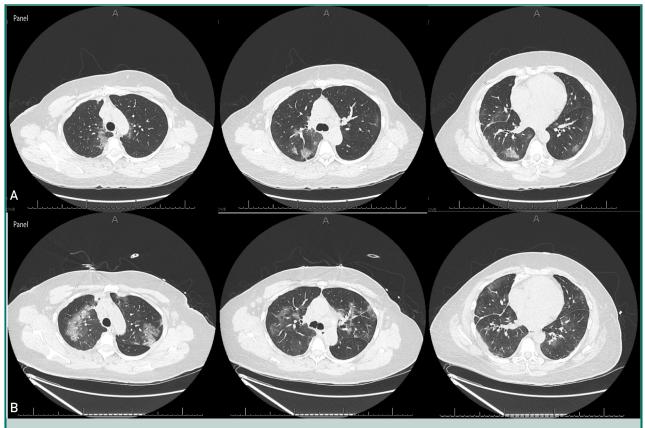


FIGURE. Axial computed tomography chest images on day 7 (day of admission, A) and day 17 after symptom onset (B), showing new and migratory lung infiltrates suggestive of organizing pneumonia.

described in COVID-19, which could be the case in our patient, although it cannot be confirmed without a tissue biopsy.<sup>4</sup> Although we conjecture that this is likely the explanation in our case, other plausible mechanisms of OP in our patient are 1) an immune activation-like phenomenon following cessation of ibrutinib or 2) augmentation of immune response by convalescent plasma.<sup>5</sup> Bruton's tyrosine kinase inhibitors are involved in toll-like receptor-mediated signaling and triggering of inflammatory cytokine and chemokine release.<sup>6</sup> Ibrutinib, a highly potent inhibitor of Bruton's tyrosine kinase, is considered to protect against lung injury in COVID-19.6

Corticosteroids are not currently recommended in the management of hospitalized patients with COVID-19 unless there is a separate indication such as asthma or chronic obstructive pulmonary disease or in intubated patients with acute respiratory distress syndrome.<sup>7</sup> Organizing pneumonia as a delayed presentation of COVID-19 for which corticosteroids have significant benefit should be considered. Moreover, given the increasing use of convalescent plasma, OP as a possible downstream consequence should be investigated.

Teny M. John, MD Alexandre E. Malek, MD Victor E. Mulanovich, MD Javier A. Adachi, MD Issam I. Raad, MD Alexis Ruth Hamilton, PA-C Department of Infectious Diseases, Infection Control and Employee Health

Control and Employee Health The University of Texas MD Anderson Cancer Center Houston, TX

### Elizabeth J. Shpall, MD Katayoun Rezvani, MD, PhD

Department of Stem Cell Transplantation and Cellular Therapy The University of Texas MD Anderson Cancer Center Houston, TX

### Samuel L. Aitken, PharmD

Department of Infectious Disease The University of Texas MD Anderson Cancer Center Houston, TX

### Nitin Jain, MD

Department of Leukemia The University of Texas MD Anderson Cancer Center Houston, TX

> Kimberly Klein, MD; Fernando Martinez, MD, MScPH

Department of Pathology and Laboratory Medicine The University of Texas MD Anderson Cancer Center Houston, TX

### Ceena N. Jacob, MD

Department of Internal Medicine Cleveland Clinic

Cleveland, OH

# Sujith V. Cherian, MD

Division of Critical Care, Pulmonary and Sleep Medicine University of Texas Health Science Center at Houston Houston, TX

### Joanna-Grace M. Manzano, MD, MPH Mayoora Muthu, DO

Department of General Internal Medicine The University of Texas MD Anderson Cancer Center Houston, TX

#### Robert Wegner, MD

Division of Anesthesiology, Critical Care and Pain Medicine The University of Texas MD Anderson Cancer Center Houston, TX

**Grant Support:** The EAP Convalescent Plasma Program is supported by the US Department of Health and Human Services (HHS), Biomedical Advanced Research and Development Authority (BARDA) contract 75A50120C00096 (PI: Michael J. Joyner, MD). The funding source did not have any involvement in the collection, analysis, and interpretation of data, writing of the report, and submitting the letter for publication.

#### ORCID

Teny M. John: b https://orcid.org/0000-0002-2675-1529; Samuel L. Aitken: b https://orcid.org/0000-0002-8659-4238; Sujith V. Cherian: https://orcid.org/0000-0003-0177-9979

- Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020; 323(13):1239-1242.
- Liang W, Guan W, Chen R, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. Lancet Oncol. 2020;21(3):335-337.
- Wu Y, Xie Y, Wang X. Longitudinal CT findings in COVID-19 pneumonia: case presenting organizing pneumonia pattern. *Radiol Cardiothorac Imaging*. 2020;2(1):e200031.

- Copin M-C, Parmentier E, Duburcq T, et al. Time to consider histologic pattern of lung injury to treat critically ill patients with COVID-19 infection. *Intensive Care Med.* 2020. Epub ahead of print https://doi.org/10.1007/s00134-020-06057-8.
- Shaz B, Dunbar C, Hillyer C. COVID-19 and Convalescent Plasma: Frequently Asked Questions. American Society of Hematology. https://www. hematology.org/covid-19/covid-19-and-convalescent-plasma.2020. Accessed May 25, 2020.
- Treon SP, Castillo J, Skarbnik AP, et al. The BTKinhibitor ibrutinib may protect against pulmonary injury in COVID-19 infected patients. *Blood*. 2020; 135(21):1912-1915.
- Bhimraj A, Morgan RL, Shumaker AH, et al. Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19. *Clin Infect Dis.* 2020. Epub ahead of print https://doi.org/10.1093/cid/ciaa478.

https://doi.org/10.1016/j.mayocp.2020.06.023

Association of Obesity With More Critical Illness in COVID-19

*To the Editor*: In follow-up to a recent major state-of-the-art review on obesity and outcomes in severe acute respiratory syndrome corona-virus 2 (SARS-CoV-2) (coronavirus disease 19 [COVID-19]),<sup>1</sup> we have additional data regarding the relationship of obesity with outcomes in patients with COVID-19. Clearly, obesity and metabolic syndrome affect both innate and adaptive immunity, leading to increased infection severity.<sup>1,2</sup>

This association is very important because current statistics indicate that three-fourths of the US population are either overweight or obese by body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) criteria, and currently over 42% meet criteria for obesity by a BMI of 30 kg/ m<sup>2</sup> or greater. More alarmingly, currently over 9% of the US population meet criteria for severe or morbid obesity (class III obesity) by a BMI of 40 kg/m<sup>2</sup> or greater.<sup>1,2</sup> Certainly, many other countries across the globe are experiencing marked increases in the prevalence and severity of obesity,<sup>1,2</sup> which may be particularly problematic in COVID-19 and other such pandemics. We performed a rapid review and meta-analysis to evaluate whether obesity is associated with worse outcomes in patients with COVID-19.

The present study was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. We performed a comprehensive search in the MEDLINE and medRxiv.org databases for studies published between January 1, 2019, and May 31, 2020. The following key words were used for the search in different combinations: coronavirus 2019, Covid-19, SARS-CoV2, obesity, body mass index, and outcomes. Studies reporting the relationship between BMI (nonobese vs obese) and outcomes among hospitalized patients with COVID-19 were included for analysis. Three reviewers (A.S., A.G., A.R.) screened the study titles and abstracts for relevance, followed by full manuscript evaluation. The following data were collected from included studies: baseline characteristics, proportion of patients classified by BMI categories (<30 kg/m<sup>2</sup> vs >30 kg/m<sup>2</sup>), and percentage of hospitalized patients. The primary outcome was critical illness (need for intensive care unit [ICU] admission, invasive mechanical ventilation [IMV], or mortality) as defined per individual study protocol. We used Cochrane Review Manager 5.3 (Cochrane Collaboration) for study analysis. Pooled odds ratios and 95% CIs were calculated using random-effects models and the Mantel-Haenszel method. Heterogeneity was assessed using the  $I^2$  statistic. The initial search resulted in 266