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Reply to Morán-Mendoza and Khalil: Are Ground Glass Opacities on HRCT a Manifestation of Airway Disease?

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However, mosaic attenuation is not specific for air trapping, because it can be due to GGOs, particularly in the setting of HP; therefore, to avoid confusion, would it not be better to use either air trapping or mosaic attenuation due to air trapping on expiratory CT images as a criterion for small airway disease?

Finally, in their Table 6 the authors included GGOs as an abnormality indicative of small airway disease in a “fibrotic typical HP” pattern on CT. However, they stated in their Table 4 that GGOs reflect an infiltrative lung disease, which is in agreement with the Fleischner Society, which considers GGOs to be caused by partial filling of airspaces, interstitial thickening (due to fluid, cells, and/or fibrosis), partial collapse of alveoli, increased capillary blood volume, or a combination of these (2). We would appreciate clarification of the seemingly contrasting definition of GGOs. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

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References

1. Raghu G, Remy-Jardin M, Ryerson CJ, Myers JL, Kreuter M, Vasakova M, et al. Diagnosis of hypersensitivity pneumonitis in adults: an official ATS/JRS/ALAT clinical practice guideline. *Am J Respir Crit Care Med* 2020;202:e36–e69.
2. Hansell DM, Bankier AA, MacMahon H, McLoud TC, Müller NL, Remy J. Fleischner Society: glossary of terms for thoracic imaging. *Radiology* 2008;246:697–722.

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Reply to Morán-Mendoza and Khalil

From the Authors:

We thank Dr. Morán-Mendoza and Dr. Khalil for their important comments regarding the interpretation of high-resolution computed tomography (HRCT) images in nonfibrotic and fibrotic forms of hypersensitivity pneumonitis (HP). We proposed specific combinations of HRCT findings most suggestive of typical HP in Tables 5 and 6, further explained in the text, and clarified the radiological terms used for description of

heterogeneous lung attenuation in Table 4 of the guideline document (1). These terms were derived from the Fleischner Society glossary of terms (2).

The points raised by Dr. Morán-Mendoza and Dr. Khalil give us the opportunity to clarify some potential difficulties regarding the descriptions of lung infiltration and ground-glass opacities (GGOs) in HP.

The first point concerns the features of lung infiltration in the typical nonfibrotic HP pattern for which they propose to use either GGOs or mosaic attenuation due to GGOs as the sole criterion for lung infiltration. Whereas we agree that in mosaic attenuation of HP there is a variable degree of infiltration (and thus, GGOs), the most striking feature may be the “hypoattenuated” zones (due to vasoconstriction in the areas of bronchiolitis), seen in the vicinity of lung zones interpreted as having a “normal” attenuation on inspiratory images. This highlights the difficulty of interpreting relative enhancement and/or decrease in attenuation in the lung parenchyma. Because we can observe both aspects in the mosaic attenuation of nonfibrotic HP, we opted to separate the two HRCT findings, reflecting variants in the visual depiction of lung infiltration on HRCT images.

The second point concerns the proposed combination of HRCT features to characterize fibrotic HP. Although there is no apparent concern with the description of HRCT features suggestive of lung fibrosis in HP, questions are raised regarding the HRCT features indicative of small airway disease. Drs. Morán-Mendoza and Khalil interpreted the list as “ill-defined centrilobular nodules and/or GGOs, or mosaic attenuation”; however, the intent of the guideline was “ill-defined centrilobular nodules and/or GGOs, and/or mosaic attenuation.” In fibrotic HP, we listed three features of heterogeneous lung attenuation that could indicate the presence of small airway disease in the background of fibrosis; they are presented from the less specific (i.e., mosaic attenuation) to the most suggestive (i.e., air trapping) HRCT sign, detectable on inspiratory and expiratory images.

The third point deals with the inclusion of GGO in the list of abnormalities indicative of small airway disease in Table 6 of the published document (1). This assumption does not contradict the description proposed by the Fleischner Society as the inflammatory component in HP is located around the bronchioles and also extends into surrounding alveoli; thus, it is responsible for lesions of bronchioloalveolitis. In the context of bronchioloalveolar infiltration, highly profuse centrilobular nodules lead to a uniform ground-glass appearance in the lung parenchyma where both the bronchiolar and alveolar components are mixed. This pathologic-HRCT situation is frequently encountered in clinical practice, for example, in patients with smoking-related abnormalities, and chest radiologists are used to associating extensive GGOs to underlying bronchioloalveolar changes.

We thank Dr. Morán-Mendoza and Dr. Khalil for giving us the opportunity to clarify these different situations with GGOs in HP. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

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*K.C.W. and G.R. are the cochairs of the official American Thoracic Society Document entitled “Diagnosis of Hypersensitivity Pneumonitis in Adults: An Official ATS/JRS/ALAT Clinical Practice Guideline.”

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2. Hansell DM, Bankier AA, MacMahon H, McLoud TC, Müller NL, Remy J. Fleischner Society: glossary of terms for thoracic imaging. *Radiology* 2008;246:697–722.

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Erratum: Single-Cell RNA Expression Profiling of ACE2, the Receptor of SARS-CoV-2

There is an error in the affiliation section in the letter by Zhao and colleagues published in the September 1, 2020, issue of the *Journal* (1). The affiliation for Drs. Yu Zhao, Zixian Zhao, Wang, Zhou, and Zuo that currently appears as “Tongji University,

Shanghai, China” is incorrect; it should be “Shanghai East Hospital, Shanghai, China.” For the convenience of our readers, the *Journal* is replacing the online version of the article with a corrected one. ■

Reference

1. Zhao Y, Zhao Z, Wang Y, Zhou Y, Ma Y, Zuo W. Single-cell RNA expression profiling of ACE2, the receptor of SARS-CoV-2. *Am J Respir Crit Care Med* 2020;202:756–759.

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Erratum: Immunomodulators in COVID-19: Two Sides to Every Coin

There is an error in the letter by Snow and colleagues (1), published in the November 15, 2020, issue of the *Journal*. In Figure 1, the drug PUL-042 is incorrectly indicated as an inhibitor of Toll-like receptors 2/6/9 (TLR-2/6/9), when in fact it is comprised of agonists of the TLR-2/6 heterodimer and the TLR-9 homodimer. A corrected version of the figure is included here.

The authors thank Drs. Scott E. Evans, Jezreel Pantaleón García, and Burton F. Dickey from the University of Texas MD Anderson Cancer Center, who alerted the *Journal* to the error. ■

Reference

1. Snow TAC, Singer M, Arulkumaran N. Immunomodulators in COVID-19: two sides to every coin [letter]. *Am J Respir Crit Care Med* 2020;202:1460–1462.

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