Asthma phenotypes, comorbidities and disease activity in COVID-19: the need of risk stratification Reply to Morais-Almeida

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Reply to Morais-Almeida.

To the Editor,

We appreciate Dr. Morais-Almeida’s comments ¹ about our Letter to the Editor, presenting additional literature about asthma prevalence in severe COVID-19 patients and highlighting data that contrasts our hypothesis that asthma, particularly type 2 asthma, may be protective against severe disease.

The data that protection may be dependent on type 2 immunity is derived from the higher percentage of asthmatics being atopic², also reflected in the series of ~2,500 patients regularly followed up in our Allergy Unit. Yu et al. ³ provided preliminary evidence about this in a single-center retrospective study, where COVID-19 atopic patients had less severe infections, milder lung damage compared to age- and gender-matched COVID-19 controls.

ACE-2, the SARS-CoV-2 receptor, is linked to type 1 and 2 interferon signatures, and found to be overexpressed in type 2-low asthmatics⁴. Nevertheless, different outcomes in distinct asthma phenotypes still need to be addressed in COVID-19 studies.

Besides Italy and China, reports from Russia ⁵ on ~1,300 intensive care unit patients with SARS-CoV-2 infection confirm the observation of a low prevalence of chronic lung diseases (i.e. asthma as well as COPD).

Although preliminary data on the first COVID-19 cases in the US⁶ seem to contrast these observations, the higher prevalence of asthma in US COVID-19 hospitalised patients should be considered alongside a higher overall prevalence in these countries compared to Europe and China, as well as on the influence of other comorbidities (i.e. obesity) and host factors (i.e. age, race: 33% were non-Hispanic black patients in the study by Garg et al.) impacting COVID-19 outcomes. Another report from Sweden ⁷ highlights the association between severe asthma and severe COVID-19.

The severe asthma phenotype is often characterized by mixed granulocytic populations (neutrophilic and eosinophilic), prevalent type 1 inflammation, increased IFN-γ levels in the airways and ineffectiveness of ICS. This severe phenotype by itself, although accounting for less than 5% of asthmatic patients, would justify the CDC (and other institutions) including asthma as a risk factor for COVID-19. Data from the UK ⁸, apart from confirming the role of additional comorbidities, draw attention to the recent use of oral steroids, which, indeed, may be a clue for uncontrolled and/or severe asthma.

Uncontrolled asthma is a risk factor for viral exacerbations and hospitalizations and we embrace the opportunity to stress the importance of optimal adherence to asthma controlling medications, regular follow-up
and specialist-assessment of disease activity. Moreover, treatable comorbidities, which may impair asthma control, should always be managed. Promoting vaccination for preventable respiratory infections (i.e. Influenza and Pneumococcal pneumonia) is also advisable. Future studies may help better distinguishing the impact of different asthma phenotypes and comorbidities on COVID-19 outcome.

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Conflicts of interests
Dr. Carli, Dr. Cecchi, Prof. Parronchi, and Dr. Farsi have nothing to disclose. Prof. Stebbing’s conflicts of interest can be found at https://www.nature.com/onc/editors and none are relevant here.

References

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