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.

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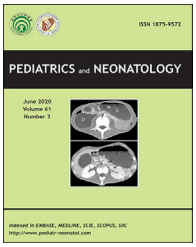

Letter to the Editor

Role of thymopoiesis and inflamm-aging in COVID-19 phenotype

Dear Editor:

We have read the article by Hong H. et al. with interest in which the authors highlighted that SARS-CoV-2 pneumonia is reported in fewer cases of children and that pediatric clinical manifestations are relatively milder compared with those of adult patients.[1]

This point is of valuable interest. Among the causes, the most important mechanisms underlying severe adult COVID-19 pneumonia cases are a reduction in CD4+ and CD8+ T cells and a decrease in regulatory T cells. These decreases are probably due to the high expression of proinflammatory cytokines, such as tumor necrosis factor (TNF)-α, interleukin (IL)-1, and IL-6, in COVID-19 patients.[2]

Furthermore, it is known that characteristic changes occur in the T cell compartment with age and these contribute to the increased incidence and severity of infections in elderly subjects. The production of naïve T cells is severely impaired due to a decreased output of lymphoid cells from the involution of the thymus.[3]

The thymus is a central lymphoid organ, which is responsible for the generation of T lymphocytes under the control of the local cellular microenvironment, mainly represented by thymic epithelial cells (TEC).[4]

Thymopoiesis leads to the maturation of peripheral naïve T cells with diverse recognition capacity against various microorganisms, such as RNA viruses, and subsets of Tregs to inhibit overactive immune responses. One of the most important age-related immune changes is the impaired generation of primary T cell responses against infection.[3,4]

Further, adult patients with severe case of COVID-19 had a cytokine release storm with an increase of several proinflammatory molecules, including TNF-α, IL-1, and IL-6.[2]

Not surprisingly, a progressive propensity toward a proinflammatory phenotype, identified as inflamm-aging, plays a key role in the remodeling of the immune system at older ages, with evidence pointing to an inability to fine-control inflammation.[5]

Thus, in our opinion, the role of the thymus could be crucial in the modulation of the immune response toward SARS-CoV-2 leading to a less severe phenotype in children when compared with those in adult COVID-19 patients. On the other hand, inflamm-aging associated with the absence of thymopoietic mechanisms could be a predisposing condition that sustains the cytokine release storm as is most often reported in adult COVID-19 subjects, especially in the older COVID-19 patients.

Further studies are needed to clarify the impact of thymopoiesis and inflamm-aging on COVID-19 phenotypes. These studies could be useful not only for considering new therapeutic strategies but also for better addressing the studies that focus on inflammatory profiles and biomarkers of COVID-19 patients for pneumonia risk stratification.

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Declaration of Competing Interest

The authors declared that there are no conflicts of interests.

References

1. Hong H, Wang Y, Chung HT, Chen CJ. Clinical characteristics of novel coronavirus disease 2019 (COVID-19) in newborns, infants and children. *Pediatr Neonatol* 2020;**61**:131—2.
2. Qin C, Zhou L, Hu Z, Zhang S, Yang S, Tao Y, et al. Dysregulation of immune response in patients with COVID-19 in Wuhan, China. *Clin Infect Dis* 2020. https://doi.org/10.1093/cid/ciaa248.
3. Pangrazzi L, Weinberger B. T cells, aging and senescence. *Exp Gerontol* 2020;**134**:110887.
4. Thapa P, Farber DL. The role of the thymus in the immune response. *Thorac Surg Clin* 2019;**29**:123—31.

https://doi.org/10.1016/j.pedneo.2020.04.001

5. Rea IM, Gibson DS, McGilligan V, McNerlan SE, Alexander HD, Ross OA. Age and age-related diseases: role of inflammation triggers and cytokines. *Front Immunol* 2018;**9**:586.

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