

THE UNKNOWN CONSEQUENCES OF COVID-19 IN PEOPLE WITH AUTISM SPECTRUM DISORDERS

CONSECUENCIAS DESCONOCIDAS DEL COVID-19 EN PERSONAS CON TRASTORNOS DEL ESPECTRO AUTISTA

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ABSTRACT

Alterations in the immune system are often found in children with Autism Spectrum Disorders [ASD], leading to an aberrant immune response which compromises host defense. Fewer regulatory T-cells, elevation in inflammatory cells and proinflammatory cytokines have been highly reported in this population and it has been recently seen as a chronic neuroinflammatory disorder. Cytokines are often dysregulated in ASD especially IL-6, which is one of the biggest concerns during the current COVID-19 pandemic, as well as other immune dysregulations. We strongly believe that this proinflammatory environment in ASD could increase the vulnerability of a poor clinical outcome for COVID-19 infection.

Keywords: ASD, COVID-19, immune system.

RESUMEN

Las alteraciones en el sistema inmunitario se encuentran a menudo en niños con trastornos del espectro autista [TEA], lo que conduce a una respuesta inmune aberrante que compromete la defensa del huésped. Menos células T reguladoras, elevación en las células inflamatorias y citoquinas proinflamatorias han sido muy reportados en esta población y se ha visto recientemente como un trastorno neuroinflamatorio crónico. Las citocinas a menudo están desreguladas en el TEA, especialmente la IL-6, que es una de las mayores preocupaciones durante la pandemia actual del COVID-19, así como otras desregulaciones inmunes. Creemos firmemente que este entorno proinflamatorio en TEA podría aumentar la vulnerabilidad de un resultado clínico pobre para la infección por COVID-19.

Palabras clave: TEA, COVID-19, sistema inmunitario.

INTRODUCTION

Up to now, scientists are uncertain about repercussions of the new coronavirus SARS-CoV-2 in populations with different immunological backgrounds. Alterations in the immune system are often found in children with Autism Spectrum Disorders [ASD], leading to an aberrant immune response which compromises host defense (Masi et al., 2017). In addition, sub-populations of ASD suffer from different autoimmune and metabolic disorders (Hughes et al., 2018; Mora et al., 2009); as a consequence, the outcome of COVID-19 patients with ASD as a concomitant, is so far, hard to predict.

COVID-19 infection and Autism Spectrum Disorders

Evidence has shown that the course of the COVID-19 can be influenced by existing comorbidities with an inflammatory component as seen in diabetes, obesity, and cardiovascular affected populations (Guo et al., 2020; Bravo-Acosta, 2020). Patients with severe COVID-19 have shown an influential decrease in CD8+ T-cells, NK cells (seen as exhaustion markers), and monocytes (Cao, 2020). On the other hand, Autism Spectrum Disorder has a multifactorial and heterogeneous etiology. Fewer regulatory T-cells, elevation in inflammatory cells, and proinflammatory cytokines have been highly reported (Hughes et al., 2018) and it has been recently seen as a chronic neuroinflammatory disorder (Kern et al., 2016). In addition, autoimmunity, immunodeficiency, and allergies have been observed in children with ASD (Enstrom et al., 2009; Heuer et al., 2008), and the latter has been recently linked with the central nervous system, suggesting a "brain allergy" phenomenon (Theoharides, 2013).



It is known that the viral-induced hyper inflammation expressed in COVID-19 patients can have severe outcomes leading to respiratory failure with multiple organ involvement (Huang et al., 2020). The innate response to environmentally relevant pathogens of the ASD population is described as dysfunctional, with elevated cytokine production in comparison with neurotypical individuals. Moreover, alterations in circulating monocytes, dendritic cells, and NK cells are frequently observed (Hughes et al., 2018; Bennabi et al., 2019). This immune dysfunction and dysregulation present in the vast majority of the ASD population is a worrying scenario for the current COVID-19 pandemic.

One of the cornerstones to understanding these severe consequences are the cytokines often dysregulated in ASD, especially IL-6, being one of the biggest concerns. Levels of IL-6 tend to be elevated in ASD individuals, as shown by Ashwood (2011) study where this cytokine was two-fold higher in plasma collected from ASD children than compared with neurotypical children. This cytokine has multiple functions including inflammation, autoimmunity, and acute phase response; simultaneously modulates the host immune response by enhancing monocytes differentiation into macrophages as well as other cell differentiation with further impairment of NK cell function (Wu et al., 2019). In fact, elevated levels of IL-6 have been reported to have a strong correlation with an upcoming respiratory failure for COVID-19 patients (Chen et al., 2020). In addition, elevated IL-6 has been discussed by different researchers to be a useful tool to predict the course of the infection or identify patients with a high risk of respiratory failure, therefore the possible need for mechanical ventilation (Herold et al., 2020).

Another concern that has arisen regarding this topic is the effect on the fetus of COVID-19 infected pregnant women (Steinman, 2020). This is based on the higher risk of postpartum autism after an infection accompanied by fever during the second trimester of pregnancy, related to the proinflammatory environment produced by the host in response to the infection (Croen et al., 2019). The combination of the immunological dysfunction and dysregulation could contribute to impair the virus clearance and exacerbate the severity of the clinical outcome by enhancing the proinflammatory “cytokine storm”. There is a reason to believe that this proinflammatory environment in ASD could increase the vulnerability of a poor clinical outcome for COVID-19 infection, but also expected to be highly variable within patients based on the heterogeneity of the disorder, mainly influenced by the type of existing immune or metabolic alteration.

CONCLUSIONS

The heterogenous immune background within ASD population is a grey area that leads to the remarked queries within this article regarding COVID-19 prognostics. Decrease in a subpopulation of immune cells, autoimmunity, immunodeficiencies, and cytokine dysregulation often present in this population could lead to an impairment of a proper immune response for viral clearance. However, we are in the need to clarify that these are assumptions based on what is known for ASD, thus COVID-19 research within ASD population must be performed to get trustworthy conclusions. We encourage the caretakers of people with ASD to take all possible and extra measures against COVID-19. The remaining question in the near future or soon is not only the consequences of the COVID-19 infection in people with ASD, but how effective immune response will be against the virus infection and if compensatory mechanisms of their dysregulated immune system are enough for viral clearance. For the time being, prevention is still the most important tool to avoid the severe consequences of the COVID-19 infection, and crucial for people with ASD.

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