Pediatric Multisystem Inflammatory Syndrome Physiopathology and Covid-19

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Introduction
There are now more than 4 million confirmed cases of COVID-19, and more 285,000 deaths. The risk of severe disease and death has been highest in older people, and associated with age and one or more of the risk factors such as noncommunicable diseases (NCDs): hypertension, cardiovascular diseases, chronic lung diseases, kidney chronic disease, cancer and immunocompromised patients, or those exposed to high viral loads [1,2]. Children have more ACE2/ACE 2 receptors in mouth and nose and the elderly in the lungs, but there are also receptors in the kidney, endothelial cells and epithelial cells in the gastrointestinal tract. Maybe this is why the symptoms described in children were generally milder in children compared to adults, but some children do require hospitalization and intensive care [3], and now in Europe and USA there has been a new syndrome that appears till 4 weeks after infection with SARS-CoV-2-The Pediatric Multisystem Inflammatory Syndrome. This Syndrome has features from both Kawasaki disease shock syndrome (KDSS) and toxic shock syndrome (TSS) [4].

According to the Scientific brief of WHO this Pediatric Multisystem Inflammatory Syndrome applies to: Children and adolescents 0–19 years of age with fever > 3 days AND two of the following: a) Rash or bilateral non-purulent conjunctivitis or mucocutaneous inflammation signs (oral, hands or feet). b) Hypotension or shock. c) Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP). d) Evidence of coagulopathy (by PT, PTT, elevated d-Dimers). e) Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain). AND Elevated markers of inflammation such as ESR, C-reactive protein, or procalcitonin. 2- AND No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes. AND Evidence of COVID-19 (RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19 [5].

Physiopathology
This Pediatric Multisystem Inflammatory Syndrome that appears as latest as 4 weeks after tracing the SARSCoV2 might be looked as KD as a generalized vasculitis that involves medium-sized arteries. Vascular inflammation is important in the coronary vessels, but vasculitis can also occur in other vessels and larger arteries putting the endothelial cells and immune complexes (ICs) at the core of the disease. The immune response in the acute phase of patients with KD and in COVID 19 in general involves activation of many different components of the innate and adaptive immune systems. In COVID19 we have also IgG and IgM detectable as soon as 4 days, IgG persistence till 7 weeks. ICs are formed during many infectious, and play an important role in immunopathogenesis of infectious and inflammatory processes such as COVID19 and Pediatric Multisystem Inflammatory Syndrome. They are bind to inflammatory cells through the heavy chain constant region to immunoglobulin Fc receptors (FcR). Binding of immunoglobulin to some classes of FcRs may lead to activation of inflammatory cells while binding to FcγRIIB result in suppression of inflammation.
ICs may bind to FcRs and activate a range of cells including monocytes, basophils, eosinophils, lymphocytes and neutrophils [6].

The appearance of neutralizing antibodies (NAb) [7]. These responses are mainly driven by replication, viral-mediated ACE2 down regulation and shedding, and host anti-viral responses( cellular and humoral). Secondary inflammatory responses begin with the generation of adaptive immunity and NAb. The virus-NAb complex can also trigger FcR-mediated inflammatory responses and acute vessel injury through immune complexes and complement activation and other pro-inflammatory pathways [7,8]. In antibody-dependent enhancement of infection, low quality, low quantity, non-neutralizing antibodies (mainly IgG1 and IgG3) bind to virus particles through the Fab domains. Fc receptors (FcRs) expressed on monocytes or macrophages bind to Fc domains of antibodies and facilitate viral entry and infection and complement activation and pro-inflammatory cytokines leading to vasculitis and organ damage that we see in Pediatric Multisystem Inflammatory Syndrome. Potential therapeutics based on targeting the (FcRs) to block SARS-CoV-2-induced inflammatory responses. FcR can be blocked using anti-Fc specific antibodies, small molecules, or intravenous immunoglobulin (IVIG) [7].

**Conclusion**

This manifestation in children has in the underlying physiopathology the landscape of the immune response to SARS-CoV-2 [9].

**References**