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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 has 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,may be thatis why the symptomsdescribed in children were generally milder in children compared toadults, but some children do require hospitalization and intensive care [3], and now in Europe and USA there has been described a new syndrome that appears till 4 weeks after infection with SARSCoV-2-The Pediatric Multisystem Inflammatory Syndrome. This Syndrome has features from both Kawasaki (Kawasaki disease shock syndrome (KDSS) and toxic shock syndrome (TSS) [4].

Kawasaki disease KD), or acute febrile mucocutaneous lymph node syndrome, is a pediatric pathology with acute systemic inflammatory vasculites and coronary artery damage, with 25% of untreated patients developing lifelong coronary artery lesions(Diagnostic criteria for classic Kawasaki disease.). The diagnosis may vary from incomplete or atypical and others more uncommon,may present with hypotension or shock [5]. The presenting clinical features of TSS include fever, a rash, hypotension and multisystem involvement, usually associated with bacteremia/sepsis [4]. TSS requires appropriate antimicrobial therapy in addition to fluid resuscitation and vasopressors in contrast, for patients with KDSS, antibiotics are not necessary, but intravenous gamma globulin 2g/kg for four days (IVGG) therapy, acetylsalicylic acid (ASA) at a doseof 30–50mg/kg/day every 6h, orally and then 3–5mg/kg/day and follow-up echocardiography .

According to the Scientific brief of WHO this Pediatric Multisystem Inflammatory Syndrome aplies 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 muco-cutaneous 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 lately 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 puting the edotelial cells and imune complexes(ICs) at the core of the disease. he 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 COVID19we have alsoIgG andIgMdetectableas soonas 4 the day and IgG persistence til 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 (FcRs). 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(celular 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 imune complexes and complemente activationa nd other pro-inflammatory pathways [7,8]. In antibody-dependent enhancement of infection, low quality, low quantity, non-neutralizing antibodies (mainly IgG1 andIgG3) 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 complemente activation and pro-inflamatory citokynes leading to vasculites 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 imune response to SARS-CoV-2 [9].

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