One-year longitudinal study of antibody profiles in children : MIS-C versus children with uncomplicated COVID-19

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The Centers for Disease Control and Prevention recently reported an increase in pediatric streptococcal intracranial infections following the onset of the COVID-19 pandemic.[4] The SAG organisms have been increasingly reported in children with sinogenic and otogenic intracranial infections in recent years.[3] The reasons for this increase are unclear. The widespread use of pneumococcal conjugate vaccines has changed the microbial etiology of complicated sinusitis.[3] Additionally, the application of more modern microbiological techniques such as matrix-assisted laser desorption/ionization time-of-flight mass spectrometry or next-generation sequencing has increased the identification of SAG species. Lastly, the temporal association between COVID-19 pandemic and an increased number of complicated head and neck infections at our institution suggests that there may be a relationship. Speculative mechanisms of SARS-CoV-2 predisposing to complicated head and infections include (1) disruption of the respiratory microbiota and (2) alteration of the respiratory tract and oropharyngeal bacterial flora due to masking and social distancing. Prolonged use of face masks can lead to oral health problems, which are being termed "mask mouth syndrome," including bad breath, dry mouth, gingivitis, and eventually tooth decay.[5] In our case series, all 5 patients had poor oral hygiene and 2 patients had tooth decay. Since there is a known association between *S. constellatus* and dental plaque and periodontal diseases, this mechanism may be one of the reasons in our cases. Further studies are necessary to understand the reasons of the increased incidence or mechanisms of the *S. constellatus* infections.

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One-year Longitudinal Study of Antibody Profiles in Children

MIS-C Versus Children With Uncomplicated COVID-19

To the Editors:

In the spring of 2020, most children presented with an asymptomatic or paucisymptomatic infection to SARS-CoV-2,[1] while a subset of children developed a multisystem inflammatory syndrome (MIS-C). The physiopathology of MIS-C has been widely studied, but the exact cause leading to MIS-C development in some children is still unclear. We have shown previously that 1-month postinfection, the neutralizing activity of circulating antibodies and the level of serum IgA against SARS-CoV-2 were higher in MIS-C patients compared with children with uncomplicated COVID-19.[2] In contrast, no difference was observed in the levels of IgG and IgM antibodies. Here, we assessed whether the specific features of the antibody response of MIS-C children were sustained throughout a year after infection.

The MIS-C children had blood sampling at 1-month (first day of hospitalization), 6 months and 12 months postinfection (CCER 2020-00835). Control children with uncomplicated COVID-19 were drawn from the "understanding COVID" study (CCER 2020-00516)[3] for the baseline (T0), T6 and T12 examinations and from the SEROCOV-KIDS (CCER 2021-01973) for the T12 examination.[4] Importantly, both the MIS-C children and the controls had been infected during the same time-period, when the original strain and the antigenically similar alpha variant of SARS-CoV-2 circulated in Switzerland. Children who had been vaccinated during the study were excluded from the analysis. Methodological details were previously described.[2]

IgA antibodies levels underwent a rapid decrease at 6 months postinfection and remained stable at 12 months. There was no apparent difference in IgA antibodies levels and trajectories between the MIS-C children and children with uncomplicated COVID-19. At 6 months, MIS-C children reached neutralization titers like those of children with uncomplicated COVID-19 and the levels remained stable by 12 months postinfection. IgG antibody levels decreased slowly for most of the SARS-CoV-2 antigens at 6 months and 12 months in both groups. The level of S2-specific antibodies, however, remained higher than those of other IgGs (see Fig. 1).

Overall, IgG, IgA and neutralizing antibodies against SARS-CoV-2 remain high up to 1-year postinfection, irrespective of whether children had developed MIS-C. The fact that the initially strongest IgA and neutralizing antibody response was lost at 6 months postinfection, suggests that those previous observations probably reflect the consequences of the gastrointestinal inflammation, which is a prominent feature of MIS-C children.[5]

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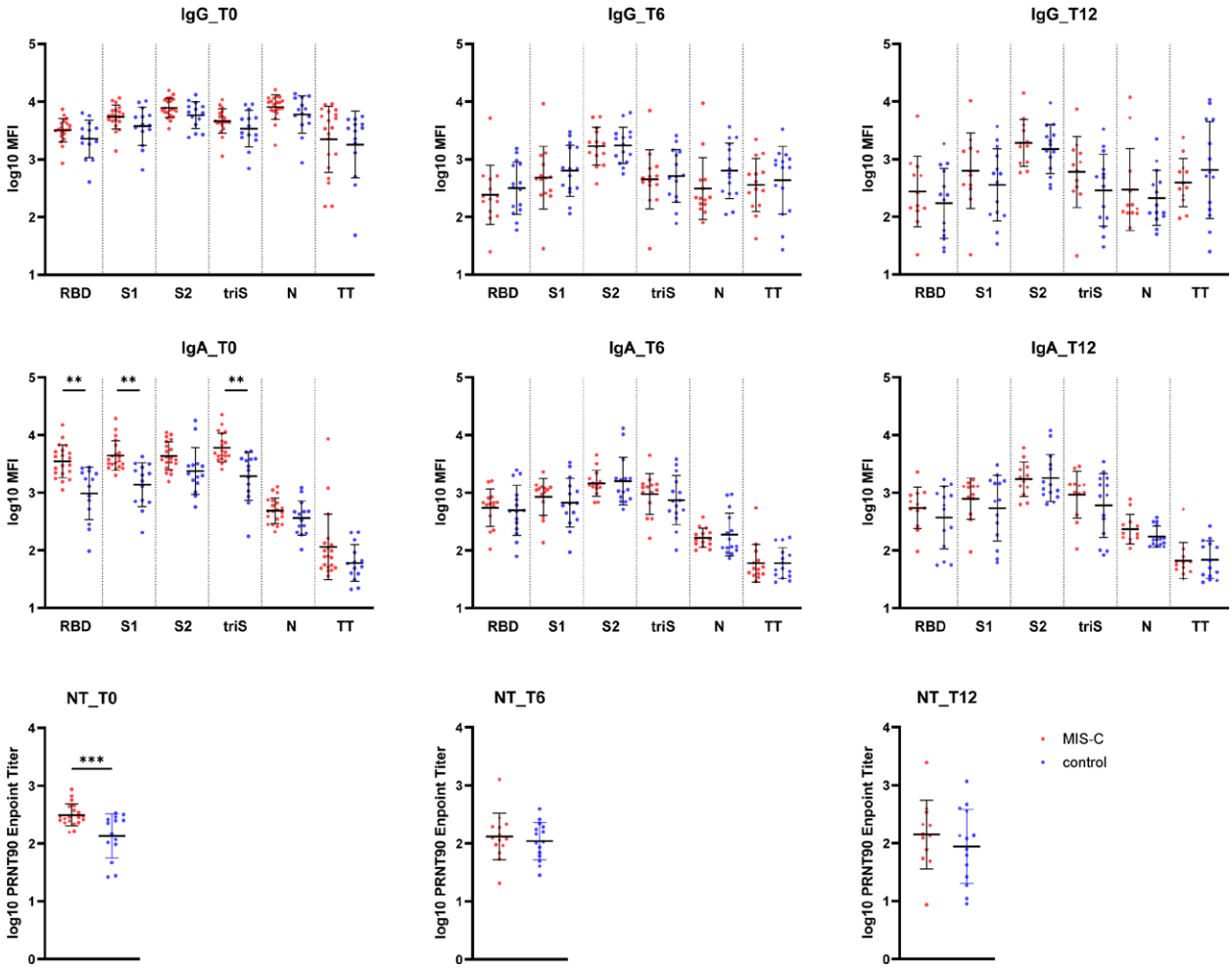

FIGURE 1. Antibody response against SARS-CoV-2 in MIS-C and control children. IgG (upper line) and IgA (middle line) antibody levels against SARS-CoV-2 receptor binding domain (RBD), S1 and S2 domain of the spike protein, trimerized full-length spike (triS) and nucleocapsid protein (N) as well as a tetanus toxoid (TT) in MIS-C (red dots) and control children (blue dots) at 1-month postinfection and then at 6 months and 12 months. SARS-CoV-2 specific neutralizing antibodies determined by plaque reduction neutralization assay in MIS-C and control children (lower line).

Further studies are still required to elucidate the pathophysiology of MIS-C and the factors predisposing individuals to develop MIS-C. We show that humoral immunity is maintained similarly in MIS-C and uncomplicated COVID-19 children, suggesting that both groups remain protected from an episode of MIS-C since fewer cases were reported upon immunization in children. In addition, almost no MIS-C cases were reported with the last circulating strains.

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Mycoplasma pneumoniae and Viral Pneumonia Coinfection

Something NOT to be Overlooked

To the Editors:

We have read with great interest the recent publication by Guo et al,[1] which analyzed the differences in clinical characteristics between *Mycoplasma pneumoniae* pneumonia (MPP) and viral pneumonia. The authors included 210 pediatric patients with community-acquired pneumonia (CAP) and reported significant differences in symptomatology (fever and vomiting) and investigation results between the MPP and viral pneumonia groups. The MPP group also had a higher disease burden and required more intensive monitoring.

It is noteworthy that patients with coinfections were excluded in this study. Coinfections with more than one causative pathogen in pediatric CAP were not uncommon. Jiang et al[2] reported that coinfection was identified in more than one-third of patients with CAP, and the majority had a combination of viral and bacterial infections.

In a 2-year analysis in our center, we managed 142 pediatric patients diagnosed with *Mycoplasma pneumoniae* infections. Of these, 123 of them had CAP, while the remaining had other diagnoses including upper respiratory tract infections and encephalopathies. The mean (standard deviation) age of the CAP cohort was 6.8 ± 3.8 years old. Nasopharyngeal swabs were obtained for respiratory viral panels in all patients, which revealed coexisting viral infections in 16 (13%) of them. These included enterovirus/rhinovirus (n = 9), adenovirus (n = 3), respiratory syncytial virus (n = 2), influenza B (n = 1) and parainfluenza (n = 1) infections. In comparison to those without respiratory coinfection, our cohort showed a higher prevalence of rhinorrhea in the coinfection group (75% vs. 41%, P = 0.015). However, there were no significant differences in other symptoms such as fever, cough, sputum production, sore throat, vomiting, diarrhea and dermatological manifestations. Furthermore, patients with viral coinfection had worse outcomes, as indicated by a higher likelihood of pediatric intensive care unit admission (19% vs. 3%, P = 0.029), oxygen therapy requirement (56% vs. 25%, P = 0.017), mechanical ventilation (13% vs. 1%, P = 0.044) and a longer hospital stay [median 4 (interquartile range, 3–11) vs. 3 (interquartile range, 2–5) days, P = 0.022].

The incidence of MPP had drastically decreased during the COVID-19 pandemic, likely attributed to the widespread implementation of nonpharmaceutical interventions during the years.[3] However, in recent months, there has been a notable upsurge of MPP cases across different regions.[4] In addition, owing to the reduced global population exposure to *Mycoplasma* in the preceding years, the resurgence of MPP may also be associated with increased extrapulmonary manifestations with a more severe disease spectrum.[3] Given the possible detrimental effects of coinfections, early detection of coexisting viral infections and high vigilance for atypical extrapulmonary manifestations become crucial for effective risk stratification and timely interventions to improve clinical outcomes in these patients.

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A Recombinant CVA6 Infection Aggravates Left Ventricular Dysfunction and Myocardial Injury in a Child With Cardiomyopathy

To the Editors:

The patients diagnosed with cardiomyopathy have a higher risk of ventricular arrhythmias earlier in life, and often develop atrial fibrillation and heart failure in adulthood. The development of left ventricular

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Y.J. and F.W.: conceptualization, methodology and supervision. Y.C.: software, formal analysis and writing—original draft. S.C.: investigation and data curation. G.D.: supervision. W.J.: software and validation. Y.Z. and X.Z.: investigation and data curation. Y.J.: writing—review and editing, project administration and project administration. All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.
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This study received ethical approval from the Committee for Ethical Review of Zhengzhou University (ZZUIRB2023-152) and written informed consent was obtained from all participants' parents.
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