

## Multisystem inflammatory syndrome in adult COVID-19 patients

As we pass the peak of the COVID-19 epidemic in South Africa (SA), we want to remind healthcare workers to have heightened vigilance of a multisystem inflammatory syndrome reported in children and adolescents (MIS-c).<sup>[1-3]</sup> In Europe and North America (where this syndrome was initially reported), it is common practice for adolescents to be admitted to paediatric wards,<sup>[4-6]</sup> but in SA, those >13 years of age are conventionally admitted to adult wards. Since this life-threatening syndrome is mainly described in children, we are concerned that this seemingly rare condition may be missed by clinicians who treat adolescents and adults.

At Tygerberg Hospital, Cape Town, South Africa, the first paediatric patient was diagnosed with MIS-c on 4 July 2020, and a number of cases followed thereafter.<sup>[7]</sup> The first three patients in the adult service were diagnosed between 13 and 20 August 2020, and aged 15, 22 and 27 years (all presenting within a single week), respectively. All three met the World Health Organization (WHO)<sup>[8]</sup> and Centers for Disease Control and Prevention (CDC) criteria<sup>[9]</sup> for MIS-c, although prior COVID-19 infection could not be proven due to unavailability of the antibody tests. They presented with mucocutaneous involvement resembling a viral exanthem, cracked lips, sore throat, non-exudative conjunctivitis, oedema, abdominal pain, severe myocardial dysfunction resulting in shock, confusion, meningism and acute kidney injury. Despite having markedly raised inflammatory markers, no definite source of sepsis was found. They were treated with intravenous immunoglobulin (IVIG) and corticosteroids, with remarkable clinical, biochemical and echographic improvements.

MIS-c cases are described to occur after the peak of the epidemic, and resemble both Kawasaki disease (familiar to paediatricians) and toxic shock, but are a distinct entity.<sup>[1,5]</sup> The condition is characterised by shock and/or other features of severe organ dysfunction with inflammation including severe abdominal pain, conjunctival injection, rash and notably renal and cardiac dysfunction. Laboratory features include raised inflammatory markers, abnormal coagulation profiles and markers of organ dysfunction.<sup>[2-6]</sup> The diagnosis is by exclusion of sepsis, toxic shock and autoimmune diseases.<sup>[7-9]</sup> The patients must have compatible clinical features, laboratory markers and evidence of prior COVID-19 diagnosis (as manifested by a current/prior positive SARS-CoV-2 diagnosis by polymerase chain reaction, or contact with a person who has COVID-19, or a positive antibody test). This currently poses a challenge in Africa as access to the COVID-19 antibody test is limited.<sup>[10]</sup> The WHO<sup>[8]</sup> definition includes patients up to 19 years of age and the CDC<sup>[9]</sup> includes patients up to 21 years of age. However, there have been reports of patients beyond their 20s who develop this syndrome,<sup>[11,12]</sup> and it may be more appropriate to use the term MIS after COVID-19 (MIS-C).

Management is supportive and includes intensive care if required. Specific treatment is yet to be determined but the current protocol includes IVIG, corticosteroids and the use of biological agents such as tocilizumab, anakinra or infliximab. Typically, patients respond rapidly to the treatment (within a matter of days).<sup>[13]</sup> Failure to administer treatment is associated with mortality.<sup>[14]</sup>

In conclusion, clinicians should have an increased index of suspicion and be familiar with the proposed case definitions to identify this syndrome early and be aware of its variable manifestations. Although antibody tests are not yet widely available, the diagnosis can be made in low-resource and highly endemic settings by careful and systematic analysis of clinical clues. Prompt recognition and collaboration from various medical and paediatric disciplines may be the key to optimal patient care, as in our case.

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1. Dufort EM, Koumans EH, Chow EJ, et al. Multisystem inflammatory syndrome in children in New York State. *New Engl J Med* 2020;383(4):347-358. <https://doi.org/10.1056/NEJMoa2021756>

2. Jiang L, Tang K, Levin M, et al. COVID-19 and multisystem inflammatory syndrome in children and adolescents. *Lancet Infect Dis* 2020 (epub 17 August 2020). [https://doi.org/10.1016/S1473-3099\(20\)30651-4](https://doi.org/10.1016/S1473-3099(20)30651-4)
3. Feldstein LR, Rose EB, Horwitz SM, et al. Multisystem inflammatory syndrome in US children and adolescents. *N Eng J Med* 2020;383:334-346. <https://doi.org/10.1056/NEJMoa2021680>
4. Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. *Lancet* 2020;395(10237):1607-1608. [https://doi.org/10.1016/S0140-6736\(20\)31094-1](https://doi.org/10.1016/S0140-6736(20)31094-1)
5. Verdoni L, Mazza A, Gervasoni A, et al. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: An observational cohort study. *Lancet* 2020;395(10239):1771-1778. [https://doi.org/10.1016/S0140-6736\(20\)31103-X](https://doi.org/10.1016/S0140-6736(20)31103-X)
6. Riollano-Cruz M, Akkoyun E, Briceno-Brito E, et al. Multisystem inflammatory syndrome in children (MIS-C) related to COVID-19: A New York City experience. *J Med Virol* 2020 (epub 25 June 2020). <https://doi.org/10.1002/jmv.26224>
7. Webb K, Abraham DR, Faleye A, McCulloch M, Rabie H, Scott C. Multisystem inflammatory syndrome in children in South Africa. *Lancet Child Adolescent Health* 2020 (epub 21 August 2020). [https://doi.org/10.1016/S2352-4642\(20\)30272-8](https://doi.org/10.1016/S2352-4642(20)30272-8)
8. World Health Organization. Multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19. Geneva: WHO, 2020. <https://www.who.int/news-room/commentaries/detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19> (accessed 15 August 2020).
9. Centers for Disease Control and Prevention (CDC). Multisystem inflammatory syndrome in children (MIS-C) associated with coronavirus disease 2019 (COVID-19). Atlanta: CDC, 2020.
10. Gray CM, Peter J, Mendelson M, Mahdi S, Blackburn JM. COVID-19 antibody testing: From hype to immunological reality. *S Afr Med J* 2020;110(9):(epub ahead of print). <https://doi.org/10.7196/SAMJ.2020.v110i9.15155>
11. Shaigany S, Gnirke M, Guttman A, et al. An adult with Kawasaki-like multisystem inflammatory syndrome associated with COVID-19. *Lancet* 2020;396(10246):e8-10. [https://doi.org/10.1016/S0140-6736\(20\)31526-9](https://doi.org/10.1016/S0140-6736(20)31526-9)
12. Sokolovsky S, Soni P, Hoffman T, Kahn P, Scheers-Masters J. COVID-19 associated Kawasaki-like multisystem inflammatory disease in an adult. *Am J Emerg Med* 2020;S0735-6757(20):30542-30548. <https://doi.org/10.1016/j.ajem.2020.06.053>
13. Most ZM, Hendren N, Drazner MH, Perl TM. The striking similarities of multisystem inflammatory syndrome in children and a myocarditis-like syndrome in adults: Overlapping manifestations of COVID-19. *Circulation* 2020 (epub 13 August 2020). <https://doi.org/10.1161/CIRCULATIONAHA.120.050166>
14. Abrams JY, Godfred-Cato SE, Oster ME, et al. Multisystem inflammatory syndrome in children (MIS-C) associated with SARS-CoV-2: A systematic review. *J Peds* 2020 (epub 5 August 2020). <https://doi.org/10.1016/j.peds.2020.08.03>

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