CDC/IDSA COVID-19 Clinician Call

CDC/IDSA COVID-19 Clinician Call: Multisystem Inflammatory Syndrome in Adults (MIS-A); Plus ACIP Meeting Update

April 24, 2021

Q&A

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1. **What was your cut off for "adult?" We have had 2 non-children with MIS, but they were under 22 years.**

   We have been using 21 and over for adult-- and certainly see a predominance of this presentation in relatively young adults. This is of course also potentially biased by the ease of diagnosis in patients with fewer comorbidities, generally younger adults.

   We are using >20-year-olds.

2. **Seems like MIS-C and MIS-A is the same disease with different spectrum across the age groups?**

   Certainly, more similar than distinct!

   Yes, they look like same disease with different spectrum.

3. **Vaccine question: Have any delayed reactions beyond 12-14 days been seen with vaccines? A patient in her 40s started developing some hives of her face exactly 2 weeks after her second Moderna shot. Her facial hives occur every afternoon, and resolve by morning, and she has it ongoing for about a week now. Any observation, insight, or info? Thanks a lot!**

   Any question that is not addressed in CDC guidance or the ACIP recommendations, can be submitted to CDC through CDC-Info. This is the link for CDC info: https://wwwn.cdc.gov/dcs/ContactUs/Form.

4. **My name in Mabel Aylwin, Infectious Disease MD from Chile. Was it difficult for you to convince adult physicians that this syndrome was not restricted to pediatric patients only? Was the diagnosis of MIS-A made later in adult patient units than in pediatric units?**

   It was first identified in children, and later reported in adults. There are a lot of publications describing MIS-A in adults.

5. **Threlkeld -did you look for anti-CXCL4 antibodies in the young doctor?**

   Good question, but unfortunately no.

6. **Do you have any updates on when Pfizer or Moderna will be approved/available for 12-15 y.o.?**

As of March 31, Pfizer and BioNTech were planning to submit their clinical trial data for persons age 12-15 to the Vaccine and Related Biologics Products Advisory Committee (VRBPAC: https://www.fda.gov/advisory-committees/blood-vaccines-and-other-biologics/vaccines-and-related-biological-products-advisory-committee), but I am not aware that a meeting of the VRBPAC has yet been scheduled to consider expanding the emergency use authorization to this age group. Watch their website (above) for updates. You can also find here all materials from prior meeting of the VRBPAC.

7. **Why not dexamethasone in the case presented?**

   It would certainly have been reasonable to give an alternative steroid at adjusted dose, I think, but many prior reports on MIS-C (and Kawasaki) had utilized methylprednisolone.

8. **If someone has a factor V Leiden disorder, or any clotting/ bleeding disorder, is it a not-good idea to take the J and J vaccine?**

   Specific patient-related questions can be challenging to respond to without more information. If any questions you have are not answered by the upcoming MMWR about the J&J vaccine or by existing CDC guidance, you can submit your question to CDC through this website: https://wwwn.cdc.gov/dcs/ContactUs/Form.

9. **Sad story for this young physician. Does he have any history for recent exposure to a confirmed COVID-19 case?**

   The patient did have IgG to nucleocapsid and retrospectively, family reported mild illness within the time frame of interest. Other family members were also antibody positive.

10. **Has tocilizumab been tried on MIS-A?**

    2 patients were treated with toci in the October MMWR report. I don't believe there are any meaningful data on comparison of therapies yet.

11. **Can one really be certain that the physician-patient really had SARS-CoV-2 associated MIS-A? Was his positive CoV-2 IgG antibody measured against the nucleocapsid protein? Were other infections with cardiac tropism or involvement excluded? Thank you!**

    Yes, the antibody was indeed an assay for nucleocapsid protein antibody, as many of the commercially available tests are. As expected, the spike protein Ab assay was positive as well.

12. **Is there any correlation with antibodies titer?**

    Not that we are aware of.

13. **How frequently has peripheral lymphadenopathy/lymphadenitis been seen among the 86 case patients?**

    I don’t have the exact number, but it has been reported in some patients. In fact, I remember a case with prominent lymphadenitis causing throat pain as a presenting symptom.

14. **Has there been any MIS-A in anyone who is elderly? How "old" is the oldest known victim of MIS-A?**

    I know of a suspected patient in the 60s.

15. **We had a similar case but procalcitonin was very high and we thought it might be a bacterial infection that failed to grow in cultures. Did you measure procalcitonin levels in these patients? How high were they?**

Unlike early covid 19 infection procalcitonin can be elevated in MIS-A.

16. **Did any of the adult cases have acute covid in the past? Is the adult presentation mostly GI symptoms? Do we have stool PCR findings in any of these adults?**

    All our cases had at least serologic evidence of prior covid 19. half had clinically apparent covid. GI symptoms of MIS-A are common, but the high fever is the most striking complaint in most. I'm not aware of stool PCR data.

17. **Does vaccine improve these MIS-A cases?**

    Not that has been noted.

18. **Why do adults have more acute COVID but less MIS-A compared to children?**

    Multiple hypotheses being discussed, possibly role of innate immunity? Some protection from more recent other coronavirus infections? We certainly are learning more and more.

19. **In the MIS-A cases you have reviewed, have you seen coronary artery abnormalities more commonly in the cases with predominant rash/mucocutaneous findings (e.g., more Kawasaki-like)? Thank you all for a great presentation!**

    Hey Dr. Lim! We have not seen coronary artery abnormal in the adults -- I think a minority but a substantial minority in children, but not really seen in adults. More hypokinesis, myocarditis, troponin leak implying myocardial tissue stress of some sort, but not via artery dilatation and in the early patients who were catheterized, no evidence of thrombosis.

20. **Should we test to SARS-CoV-2 prior to COVID vaccine?**

    This is not recommended. As previously mentioned by others on the call, many persons who have been vaccinated have had a history of COVID-19 infection.

21. **Re: MIS-A post-vaccination. If they've been vaccinated, are you doing N Ab and S Ab to differentiate infection vs. vaccination?**

    For any cases of MIS-A reported to CDC, history of COVID-19 vaccination AND history of previous SARS-CoV-2 infection is being discerned. If history of SARS-CoV-2 is not elicited through history, it is assessed through nucleocapsid antibody. Only 4 cases that met the CDC working case definition for MIS-A involved persons vaccinated for COVID-19; all of those were in persons with a history of SARS-CoV-2 infection and / or positive nucleocapsid antibody test results. No case of MIS has been reported to CDC involving vaccination alone.

22. **If a patient developed MIS towards one platform but did not finish the series, do you offer the other platform in this case J and J to complete series?**

    Specific cases like the one you described, can be submitted to CDC through CDC-info: https://wwwn.cdc.gov/dcs/ContactUs/Form. These are typically best addressed on a case-by-case basis after more discussion with the treating physician. CDC guidance in the end is simply intended to assist and is not prescriptive.

23. **Any increased incidence of MISC-A in those who received monoclonals?**

    Not that we know of.

24. **What could be the role of plasmapheresis in most severe cases of MISC A?**

Unclear at this time, but the role of plasmapheresis in the treatment of COVID-19 has not been shown to be beneficial. I believe NIH guidelines still state that there is no evidence to support use of plasmapheresis, and currently not recommended for treatment of MIS.

25. **Any other case reported MISC-A in a vaccinated outside of USA?**

    Yes-- MIS-A cases have been reported after vaccination outside of the US. Only a few cases that we are aware of at this time. We do not know timing and do not know if those patients had SARS-CoV-2 infection.

26. **If MIS is present in children and none of them are vaccinated, it seems less possible that there is an exacerbation mediated by the vaccine?**

    It would certainly seem that we would see more than literally less than a handful of cases in vaccinated individuals given that there must be many millions who have received the vaccine after natural infection by now.

27. **Seems the spectrum of this illness overlaps with the late critical illness with cardiac dysfunction and multiorgan failure with elevated inflammatory markers (3-4 weeks into prolonged Covid pneumonia with prolonged ventilator support) but without rash (maybe suppressed/prevented by ongoing steroids already) seen in some covid patients. Is severe covid pneumonia preventive of progression to MIS-A vs. we exclude subsequent MIS-A from diagnostic consideration in cases of severe covid pneumonia with later inflammatory deterioration? Is anyone assessing immunologic genetic subtypes/markers common to MIS-A and MIS-C and late inflammatory deterioration in severe Covid pneumonia cases?**

    Dr. Gluckstein -- thank you. I don't know that anyone is necessarily, although I know that research is ongoing at NIH, more focused on MIS-C, but I think this is exactly on point, and what we have been thinking.

28. **So, what will we look forward to vaccinating kids? It's more common and we don't have enough time to get study info out, but we don't want to trigger more MISC?**

    We are working very closely with vaccine safety to watch the trials and note any occurrence of MIS-C among kids who are vaccinated in trials and are primed to monitor for this.

29. **Hello, will this syndrome have its own ICD-10 code in the future?**

    Already has ICD-10 code. Find details at https://www.cdc.gov/mis-c/hcp/.

30. **What is the race distribution amongst TTS women? What % whites vs nonwhites compared with what % of the J&J vaccine taken by white vs. non-white women in US?**

    Dr. Ravishankar, I will ask Dr. Brooks to confirm, but I believe all the cases presented in the US, were white women. I do not know the distribution of those that have received the vaccine (7-8 million).

    That's an excellent question and the data were not presented. Others noted the absence like you and these data are being pulled and will be part of a larger publication shortly about the US cases.

31. **Are there any risk factors identified in cases of MIS-A? Race? family history of autoimmune conditions? Patients with MIS-C are typically older than 7 years of African or Hispanic origin and show greater elevation of inflammatory markers. https://www.thelancet.com/pdfs/journals/laninf/PIIS1473-3099(20)30651-4.pdf.**

Not clear in MIS-A as it is in MIS-C. In children, non-Hispanic blacks seem to have an appreciably higher risk of MIS-C that cannot be explained by a higher risk of COVID-19 in that population.

32. Will J&J vaccine rollout resume in the US this week?

States will be making those decisions -- many are moving forward to do so after the ACIP recommendation.

33. Would you advise a family member who has access to J&J to get it?

I would and have! But again, I think it is important to know what to watch for.