Reviewer’s report

Title: Measles Infection Causing Bacillus Calmette-Guérin Reactivation: A Case Report

Version: 0 Date: 21 Jun 2019

Reviewer: Frederick Schaltz-Buchholzer

Reviewer's report:

Thank you for an interesting manuscript that provides a new case-report of a seemingly novel discovery - that measles infection can lead to "reactivation" of BCG.

I have some major and minor comments/edits to suggest.

First, I believe that it would be better for the overall readability and comprehensibility of the manuscript if the photo of the BCG reaction is displayed earlier. Also, I would prefer if the authors could describe in closer detail how the reaction actually looked. The pictures I received were in a low resolution, but to me it seemed that the BCG reaction had not transformed into a BCG scar yet before the measles infection. This is, however, just guessing on my side, but upon interview with the parents it should be possible to retrieve detailed information to confirm whether the reaction was, in fact, a pustule before the infant was infected with measles.

The standard BCG reaction route is:

No reaction for 2-4 weeks -> Papule for 1-2 months -> Pustule during 3-6 months -> Scar

I interpret having a BCG pustule as having live-attenuated bacteria still present at the site of vaccination with the pus discharge thus being a mixture of dead mycobacteria and neutrophils.
If the infant had a BCG pustule at the time it was infected with measles, then what the authors are presenting is in fact a reactivation of BCG, given that the immunocompromised status of the infant allowed BCG to start replicating to larger numbers and thus produce the induration, redness and probably pain at the site of original inoculation. If the infant had completed the normal course of BCG reactions by 7 months of age and thus had a scar, then it is less likely that viable mycobacteria were still present at the site of the inoculation, and the BCG "reactivation" (induration and redness seen) would be more likely to be a non-specific activation of immune cells located at the inoculation site with an absence of mycobacteria. It would thus technically not be a reactivation. Since that measles disease diminishes the immune response, I believe it is most likely that the infant had a pustule or a semi-healed BCG scar than a completely sealed BCG scar and I would appreciate the author's considerations on this point in the article. An explanation of the normal sequence of BCG reactions in the beginning of the manuscript would also ease the understanding of this. I would appreciate considerations from the authors as to whether they believe that BCG "reactivation" represents reactivation of BCG mycobacteria which most thus still be present at the inoculation site or a non-specific stimulus of the immune system due to induction of cytokines and inflammatory responses caused by measles.

If possible, it would be appreciated to include which strain of BCG that the infant had received and whether the infant was vaccinated at a health center or a major hospital. BCG strains are known to contain different colony-forming units (CFUs). A major determinant for the development of BCG pustules and BCG scar reaction rates is the strain of BCG administered. Also, the size of the post-vaccination wheal is important. It is thus probable that infants that received a vaccine containing more CFUs and a high vaccine dose (as measured by the post-vaccination wheal) are more likely to have a BCG pustule (containing live-attenuated BCG) for a longer time. If possible to retrieve these data from the child's vaccination card or national data concerning the BCG strains used in the country, it would be a good addition to the article. Infants vaccinated at major health centers are more likely to have been vaccinated by an experienced vaccinator.

The discussion features a rather long description of standardized diagnostic procedures in measles infections. This section does not fit well in the discussion section.
There is some mentioning of the possibility that this infant could have suffered other viral infections as well, aside from measles infection, and that any such infection could be responsibility of the induration at the inoculation site, rather than measles. This is a good point and also a weakness of the study since the infant was not tested broadly and it should be stated clearer that it is unknown whether the "reactivation" occurred due to the measles infection or due to another infection. Theoretically, for example, the infant could have suffered from acute-HIV+measles and thus was immunocompromised which gave the still-live mycobacteria at the inoculation site the possibility to replicate.

I request also further details on the diagnostic workup of coronary artery disease in Kawasaki's disease so that it is clear whether the two echocardiographic examinations performed are sufficient to rule out any heart conditions in this infant.

Finally, it should be stated which databases were sought to identify other cases of "BCG reactivation" during acute measles infection. It was both unclear which databases had been sought and which search words or MeSH terms that the authors applied. "To our knowledge" is insufficient.

I attach a PDF with some minor edits and suggestions to the manuscript, which I would be happy to review again after the above input has been processed.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?
If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal