Title: Mucous membrane pemphigoid-associated paronychia with onychomadesis.

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Author’s response to reviews:

Dear Dr. Guangde,

Thank you for considering our manuscript “Mucous membrane pemphigoid-associated paronychia with onychomadesis” to possibly be published in BMC journal as Case Report after addressing the interesting comments that you and the valuable reviewers have raised.

We took every single comment into consideration while making the revision and we did our best to modify the manuscript accordingly.

You kindly suggested to “reduce the overlap with published literatures in "Discussion and Conclusions" section”: Which we took into account in making this revision and all changes have been highlighted.

Dear Dr. Jacob Levitt (Reviewer1): Thank you for taking the time and putting in the effort to review our work.

1- “I would rename the title as MMP-associated Paronychia with Onychomadesis”: The title was renamed as suggested, thank you.

2- “it might be worthwhile to review briefly in a sentence or two (with references) in the discussion the diagnostic criteria for calling MMP.”: Thank you for pointing to this issue. We added a few sentences that were highlighted and referenced after going through the literature regarding the clinical, histological and immunological diagnosis of MMP:

Diagnosis of MMP can be done based on clinical picture, and histopathological, immunopathological (direct and indirect immunofluorescence) and immunochemical studies (including ELISA, immunoblotting and immunoprecipitation). Distinction from other subepidermal autoimmune bullous diseases could be difficult, and depends on clinical presentation with predominant mucosal involvement [7]. Both lesional skin and mucosal biopsies in our patient demonstrated subepithelial and subepidermal blister formation with
underlying mixed inflammatory cell infiltrate, which is consistent with pemphigoid disorders [7]. Direct immunofluorescence (DIF) testing was found to be unexpectedly negative. DIF test is considered to be the gold standard in the diagnosis of MMP [7]. However, many studies conducted on MMP patients reported DIF sensitivity rates of 70-80% [9,10,11]. In those studies the diagnosis of MMP for DIF-negative cases was established based on clinical and histopathological features.

Dear Reviewer 2: Thank you for taking the time and putting in the effort to review our paper.

1- “A brief discussion about DIF negativity or indeterminate cases should be made”: Thank you for the valuable suggestion which we took into consideration and added a short review of literature about DIF negativity and how to proceed in those cases: Diagnosis of MMP can be done based on clinical picture, and histopathological, immunopathological (direct and indirect immunofluorescence) and immunochemical studies (including ELISA, immunoblotting and immunoprecipitation). Distinction from other subepidermal autoimmune bullous diseases could be difficult, and depends on clinical presentation with predominant mucosal involvement [7]. Both lesional skin and mucosal biopsies in our patient demonstrated subepithelial and subepidermal blister formation with underlying mixed inflammatory cell infiltrate, which is consistent with pemphigoid disorders [7]. Direct immunofluorescence (DIF) testing was found to be unexpectedly negative. DIF test is considered to be the gold standard in the diagnosis of MMP [7]. However, many studies conducted on MMP patients reported DIF sensitivity rates of 70-80% [9,10,11]. In those studies the diagnosis of MMP for DIF-negative cases was established based on clinical and histopathological features.

2- "The paronychia described in our patient was believed to be a manifestation of MMP because it was chronologically associated with the disease activity and has cleared after controlling the symptoms." I'm not entirely satisfied with this rationale. Candida induced inflammation would improve with prednisone. Thus, I think it best to be slightly more speculative": The statement was changed to be more speculative as you kindly suggested: The paronychia described in our patient was chronologically associated with the disease activity and has cleared after controlling the symptoms, suggesting a possible association.