Immune response of condyloma acuminatum after 5-aminolevulinicacid-photodynamic therapy treatment

Yiu-Tai Li[a], Wen-Ling Lee[b,c], Peng-Hui Wang[d,e,f,g,*]

[a]Department of Obstetrics and Gynecology, Kuo General Hospital, Tainan, Taiwan, ROC; [b]Department of Medicine, Cheng-Hsin General Hospital, Taipei, Taiwan, ROC; [c]Department of Nursing, Oriental Institute of Technology, New Taipei City, Taiwan, ROC; [d]Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [e]Department of Obstetrics and Gynecology, National Yang-Ming University, Taipei, Taiwan, ROC; [f]Institute of Clinical Medicine, National Yang-Ming University, Taipei, Taiwan, ROC; [g]Department of Medical Research, China Medical University Hospital, Taichung, Taiwan, ROC

DEAR EDITOR,

We read with much interest for the article entitled "Macrophages participate in the immunosuppression of condyloma acuminatum through the PD-1/PD-L1 signaling pathway," which has been published in the May issue of the *Journal of the Chinese Medical Association (JCMA)*.[1] The authors found that more M2-like macrophages than M1-type macrophages were present on wart lesion.[1] It is not surprising to see this report, because M1 macrophages, which are activated by proinflammatory mediators interferon-gamma (INF-γ), tumor necrosis factor (TNF), and damage-associated pattern molecules, have a known scavenger function, and these classically activated M1 macrophages prolifically produce purulent amount of proinflammatory cytokines, such as TNF and interleukin-6 (IL-6), and other mediators, enabling them to phagocytose cells that have undergone apoptosis and remove any pathogens or debris in the inflammatory, damage or cancer tissues.[2–4] M2 macrophages are typically anti-inflammatory and often considered as immunosuppression or immune tolerance.[2,3] If a shift from M1 to M2 subtypes of macrophage occurs, there is no doubt that the "pathogen" or "disease" might be escaped from the "clearance" by body. As predicted, patients with condyloma acuminatum have a lot of both M1 and M2 macrophages in their lesion; however, it is relatively interesting that 5-aminolevulinicacid-photodynamic therapy (ALA-PDT) results in dampening purulent inflammation, decreasing macrophage numbers (both M1 and M2 macrophages) in the condyloma acuminatum lesion. Although the authors have already calculated the ratio of M1/M2 in the three groups, such as normal controls, condyloma acuminatum before and after ALA-PDT treatment, we are wondering why the absolute number of M1 or M2 macrophages is decreased after ALA-PDT treatment. We totally agree that "as similar to the concept of tumor infiltrating immune cells, the immune cells might be ineffective in the clearance of "abnormal" and/or "disease" status. However, after treatment, the dysfunction of the immune systems cannot be restarted to the "functional" ability, the therapeutic effect might be in vain. That is why we applaud the success of Dr. Liao's excellent works to highlight the importance of the immune check points PD-1/PD-L1 (programmed death-1/programmed death ligand 1) signaling pathway.[1] A recent study showed that the timing of evaluation might be important. Xie and colleagues found that at 4 hours after ALA-PDA treatment, CD4+ (one subtype of T lymphocytes) increased, accompanied by increased levels of mRNA expression of INF-γ, and paradoxically, CD4+ and mRNA expression levels of INF-γ were decreased at 24 hours after ALA-PDA treatment,[5] hinting that the evaluation of the inflammatory markers and/or immune responses should consider the "time course" after treatment. We hope to see the positive response by the authors.

Address correspondence: Dr. Peng-Hui Wang, Department of Obstetrics and Gynecology, Taipei Veterans General Hospital, 201, Section 2, Shi-Pai Road, Taipei 112, Taiwan, ROC. E-mail addresses: phwang@vghtpe.gov.tw; pongpongwang@gmail.com; or phwang@ym.edu.tw (P.-H. Wang).

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