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Letter to Editor

Human Papillomavirus-Associated Oral Epithelial Dysplasia: A Practical Approach to Make the Diagnosis: Letter to Editor

Dear Editor

In a recently published article (IJMS issue: Volume 49, number 3, March 2024), Parchami and colleagues investigated various Human Papillomavirus (HPV) detection methods in HPV-associated oral epithelial dysplasia (HAOED) cases.[1] We commend the authors for providing a practical, step-by-step combinational approach to differentiate HAOED from common oral epithelial dysplasia (OED) cases.

One of the significant findings of this study that attracted our attention was the histopathological presence of koilocytes and the HPV status of the OED cases. Our previous analysis of the literature highlighted koilocytes as a viable marker for HPV diagnosis due to their correlation and association with molecular confirmation from next-generation sequencing (NGS), droplet digital polymerase chain reaction (ddPCR), and quantitative real-time PCR tests.[2] However, Parchami and colleagues found no statistically significant results (P=0.62) when comparing koilocyte status with the HPV status in OED cases.[1] To address this discrepancy, a more in-depth discussion is required.

Firstly, four cases were HPV-positive. However, they showed no evidence of koilocytic features. This phenomenon might suggest that HPV was not transcriptionally active enough to manifest histopathologically as koilocytes. This might also imply that HPV residing inside the epithelial cells was in a latent stage and had less potential for malignant transformation. Supporting this notion, latent infections are more common in low-risk HPV types than in high-risk HPV types.[3] This hypothetical proposition can be investigated in the future by prospectively assessing cases for malignant transformation and comparing HPV-positive but koilocyte-negative cases with those showing koilocytic features. Nonetheless, it is possible that latent HPV activation may occur over time and lead to the development of koilocytic symptoms. Contrary to the above notion of latent infection, Okodo and colleagues reported that HPV genotypes with higher oncogenic potential had no relationship with the koilocytic changes.[4]

Secondly, eleven cases were koilocyte-positive but HPV-negative. This implied that koilocytic changes, observed in epithelial cells, characterized by pyknosis and transparent perinuclear halos, typically occupy more space than the cytoplasm, and might reflect some other phenomenon. These features could also be attributed to histotechnique artifacts, such as drying and fixation artifacts. Consequently, such cases require further examination to rule out any processing artifacts.

When it comes to low and middle-income countries, the primary hurdle is the feasibility factor, owing to the infrastructure and expenses associated with NGS, droplet digital PCR, and quantitative real-time PCR experiments. In this context, the most practical option is to identify HPV infection through histopathology by observing koilocytic features. By comparing koilocytes with molecular expression, the authors made a substantial contribution to the advancement of science in this area. To obtain a better understanding of the complexities related to HPV-positivity and koilocytic manifestations, further studies, involving malignant transformation, are required in the future.

Authors' Contribution

SS and GS contributed equally to the conceptualization, writing, editing, and final draft review of the manuscript. Both authors have read and approved the final manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Conflict of Interest: None declared.

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