Questions remain regarding the presence of fungal species biofilm in women with vulvovaginal candidiasis

Check for updates

TO THE EDITORS: In the insightful publication by Swidsinski et al,[1] the authors address important questions regarding the presence of vaginal biofilm in cases of vulvovaginal candidiasis (VVC). They conclude following evaluation of vaginal biopsies that lesions are primarily polymicrobial and do not contain biofilm.

In a related study by our group, demonstrating that *Candida albicans* actively forms biofilm on the vaginal mucosa in the mouse model of VVC,[2] similar questions regarding clinical VVC were raised. While we applaud the authors for designing a clinical study that addressed the issue through vaginal biopsies, we believe it important to point out some limitations to the study that stress caution in the interpretation of the results.

First, because the biopsies were all taken from the middle side wall, and without colposcopy, areas of discontinuous biofilm formation might not have been sampled. Second, although infected areas did appear to be sampled based on the level of invasion and presence of mycelium/hyphae, surface biofilm could have been disrupted or dislodged with biopsy removal and sample preparation. Third, the biopsy sections were not evaluated for fungal extracellular matrix, the hallmark of *Candida* biofilm formation, or assessed by confocal microscopy for high-resolution serial sectioning that provides 3-dimensional reconstruction of thick microbial biofilm structures.[2]

As an alternative argument in agreement of the interpretations/conclusions made, there is evidence for less frequent antifungal resistance in recurrent VVC (RVVC) than in other forms of recurrent candidiasis.[3] Less antifungal resistance may reflect reduced biofilm presence. In addition, erythema (redness) is a common documented sign of VVC/RVVC.[4] This sign of infection is synonymous to the erythematous form of oral candidiasis and not the pseudomembranous form that presents as white plaques that visually reflect the presence of biofilm.[4]

Conversely, another common sign of VVC/RVVC is a cottage cheese–like discharge that is considered a mix of *Candida*, dead epithelial cells/leukocytes, and vaginal secretions.[4] As such, parts of the discharge could represent biofilm sloughed from the vaginal wall. Swidsinski et al[1] did not evaluate discharge in their study.

In conclusion, while the interpretations made by the authors regarding the histopathology of VVC were correct based on the study design and results obtained, the limitations of the study and inability of the methods to specifically detect biofilm elements, stress caution relative to data overinterpretation. Hence, important questions remain regarding the presence of biofilm or role of biofilm formation in VVC. ■

Mairi C. Noverr, PhD
Paul L. Fidel Jr, PhD
Department of Oral and Craniofacial Biology
Center of Excellence in Oral and Craniofacial Biology
School of Dentistry
Louisiana State University Health Sciences Center
1100 Florida Avenue
New Orleans, LA 70119
pfidel@lsuhsc.edu

The authors report no conflict of interest.

REFERENCES

1. Swidsinski A, Guschin A, Tang Q, et al. Vulvovaginal candidiasis: histologic lesions are primarily polymicrobial and invasive and do not contain biofilms. Am J Obstet Gynecol 2019;220:91.e1–8.
2. Harriott MM, Lilly EA, Rodriguez TE, et al. *Candida albicans* forms biofilms on the vaginal mucosa: implications for the pathogenesis of vaginal candidiasis. Microbiology 2010;156:3635–44.
3. Lynch ME, Sobel JD, Fidel PL Jr. The role of antifungal drug resistance in the pathogenesis of recurrent vulvovaginal candidiasis. J Med Vet Mycol 1996;34:337–9.
4. Fidel PL Jr. *Candida albicans*: from commensal to pathogen. In: Tannock G, ed. Medical importance of the normal microflora. London: Kluwer Academic Publishers; 1999; p 441–476.80.

 https://doi.org/10.1016/j.ajog.2019.04.017

REPLY

Check for updates

We appreciate the thoughtful comments of Noverr and Fidel as to the findings in our recent publication evaluating the presence of *Candida*-associated biofilm in women with acute vulvovaginal candidiasis (VVC).[1] The study produced 2 conclusions: (1) the extensive and previously unreported human vaginal mucosal invasion and infiltration by *Candida* microorganisms as well as the clinical consequences of tissue invasion; and (2) failure to document using a well-described and widely used technique of fluorescent in situ hybridization with ribosomal gene-based probes, the presence of microscopic biofilm, containing *Candida* species microorganisms.

The latter finding is also of clinical significance in that no justification was forthcoming for utilizing biofilm busters as