Letters to the Editor

Equine gamma herpesvirus presence and viral load are not associated with equine glandular gastric disease

With great interest I read the recent paper in *AJVR* by Thompson et al[1] on the detection and quantification of equine gamma herpesvirus in gastric lesions in a total of 33 horses. They could not prove their initial hypothesis of a potential link between gamma herpesviruses and a certain subform of the equine gastric ulcer syndrome, equine glandular gastric disease. This is remarkable, as conceded by the authors themselves, since it is in contrast to other studies, namely a recent study[2] in straight equine gastric ulcers. As I wrote in a comment on their work,[3] referring to our original study[4] of human gastric ulcers, it is not only about the mere presence of herpesvirus as such in ulcerative lesions. It is the location relative to the ulcerative lesion and, more importantly, what cell type is harboring the virus. We could demonstrate human herpesvirus (HSV-1) at the margin of gastric ulcers, residing in enterochromaffin (ie, neuroendocrine cells). Recent evidence from rodents suggests that herpesvirus travels along the vagus nerve toward the stomach.[5]

Looking carefully at the provided histology, the herpesvirus-positive cells seem to be located at the margin of the ulcerative lesions; however, it is difficult to determine the exact cell type at the magnification provided. Trying to link the herpesvirus-positive cells to a certain cell type (eg, neuroendocrine cells) may provide a basis to explain the disparity of the findings in the recent paper. The absolute number, reported to be higher in the nonaffected specimens may not be the relevant figure but the exact location of the virus in relation to the ulcerative lesion.

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The authors respond:

Dr. Löhr's thoughtful letter in response to our recent paper raises the question of whether the location and cell type infected might indicate a potential pathologic connection between gamma herpesvirus infection and glandular gastric disease in horses, despite there being no association between viral load and disease. In human herpesvirus (HSV-1) gastric infections, the virus is reported to infect the neuroendocrine cells,[1] which is typical of many alpha herpesviruses.[2] High-magnification review of our samples confirms that infected cells were primarily epithelial cells throughout the mucosa and mucosal glands, as well as some smooth muscle cells in the lamina muscularis mucosa. Epithelial tropism has been described for many gamma herpesviruses in humans and horses.[3–5] Especially given the samples in which nearly every epithelial cell in the mucosa showed hybridization, we cannot attribute infection to only neuroendocrine-origin cells. Additionally, widespread hybridization was observed in ulcer beds, at the margin of ulcer beds, in inflammatory gastritis lesions, and in normal glandular mucosa. While these findings cannot rule out an influence of equine gamma herpesviruses on glandular ulcer disease, it will be exceeding difficult to tease out a possible connection given the ubiquitous nature of infection.

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