ランチョンセミナー L4

[日時] 1 月 23 日（金） 12:20 ～ 13:10
[会場] 11 階 中会議室 1101

[タイトル] Proposal for classification of histologic inflammatory lesions and mucosal epithelial changes in the stomach of cynomolgus macaques (*Macaca fascicularis*)

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co-sponsored by
AnaPath Services GmbH, Switzerland https://anapath.ch/
AnaPath Research S.A.U., Spain https://www.anapathresearch.com/

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Abstract

Evaluation of the stomach in non-human primates (NHP) is conducted to demonstrate the potential local and systemic toxic effects of administered compounds in non-clinical safety studies. Adequate examination of the stomach requires accurate recognition of mucosal changes to avoid misinterpretations. To date, there are no extended published data describing gastric mucosal inflammatory and epithelial lesions in NHP, and the nomenclature proposed in toxicologic pathology guidelines remains limited. Therefore, we aimed to histologically evaluate the stomach of control cynomolgus macaques (*Macaca fascicularis*) adopting a practical pattern-based approach which is defined by the extent and predominant type of inflammatory cell infiltrate and other unique features.
The categories of morphological patterns were then subcategorized to be associated with specific differential diagnoses/etiologies. Two broad categories are herewith proposed: 1) Prominent lamina propria inflammation, and 2) Limited lamina propria inflammation.
Subcategories in cases of prominent lamina propria inflammation include a) lymphoplasmacytic gastritis without increased intraepithelial lymphocytes (IELs), b) lymphoplasmacytic gastritis with increased IELs, c) eosinophilic-predominant, d) neutrophilic-predominant, and e) granulomatous/ histiocytic-predominant.
For limited lamina propria inflammation, subcategories are a) epithelial/glandular damage only, b) foveolar hyperplasia and mucin depletion, and c) increased epithelial apoptosis, mitotic figures and/or nuclear atypia.
Parameters evaluated in order to categorize and subcategorize the proposed morphologic patters were: lamina propria inflammation (lymphoplasmacytic superficial, lymphoplasmacytic diffuse, eosinophilic, neutrophilic, histiocytic), degenerative changes in superficial epithelium (loss of apical mucin, epithelial denudation, erosion, ulceration), glandular epithelium (degeneration, necrosis, loss of glands), intraepithelial lymphocytes (superficial and glandular epithelium), fibrosis, mucosal atrophy, foveolar hyperplasia, simple regeneration, atypical regeneration, metaplasia, presence/absence of lymphoid follicles, presence/absence of Helicobacter species.
From all examined control cynomolgus macaque (n=137), three animals (2.1%) had normal gastric histologic appearance. One hundred twenty-one (88.3%) animals had prominent lamina propria inflammation. From these, sixty animals (49.5%) were subcategorized into lymphoplasmacytic gastritis with increased IELs, sixty-one animals (50.4%) into lymphoplasmacytic gastritis without increased IELs. Predominant eosinophilic, neutrophilic and/or granulomatous/histiocytic gastritis were not observed. Thirteen animals (9.4%) showed limited lamina propria inflammation and all belonged to epithelial/glandular damage only subcategory. There was no influence of sex, age, origin (Vietnam and Mauritian), and administration route (intravenous, subcutaneous, intravitreal and oral gavage) on the category or subcategory groups distribution.