Neuroendocrine Proliferations in Inflammatory Bowel Disease

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Introduction:

- Patients with chronic inflammatory bowel disease (IBD) are at an increased risk of developing adenocarcinoma. However, whether IBD increases the risk of developing neuroendocrine tumors (NETs) is not clear.
- NETs are rare in IBD with only 83 cases reported in the literature, though one recent report suggests that NETs are 15 times more frequent in patients with Crohn’s disease.
- Small neuroendocrine cell clusters or micronests (NEMs) are sometimes observed in the lamina propria and muscularis mucosae of IBD patients.

Aims:

- To identify the incidence of NETs in IBD.
- To study the clinical and pathologic features of NETs and NEMs in IBD to understand their pathogenesis and biologic behavior.

Materials and Methods:

- Departmental surgical pathology archives were searched from 1994 to 2016 to identify cases of neuroendocrine cell proliferations (NEPs) arising in patients with IBD. Poorly differentiated neuroendocrine neoplasms were excluded.
- Hematoxylin and eosin-stained slides and immunohistochemical-stained slides were reviewed to investigate the pathologic features.
- NEPs were classified as NEMs (microscopic clusters of neuroendocrine cells in the lamina propria/muscularis mucosa, difficult to measure) and NETs (distinct mass-forming lesions).
- Mucosa adjacent to NEPs was evaluated for inflammation, glandular dysplasia and neuroendocrine cell hyperplasia.
- > 3.2 neuroendocrine cells per crypt (averaged over 10 crypts on each side of the lesion) was considered to represent neuroendocrine cell hyperplasia.
- Three random biopsies of normal colonic mucosa and three random cases of colonic NETs occurring in patients without IBD were also evaluated for the number of neuroendocrine cells per crypt to serve as controls.

Results:

- Twelve cases of NEPs (median age 32 years, range 18-62; M:F=7:5) were identified from a total of 21,206 IBD cases.
- All cases of NEPs in IBD were incidentally discovered.
- Four cases of NEM and 8 cases of NETs were identified.
- Active inflammation was identified in mucosa adjacent to 75% of NEMs, but only 37.5% of NETs were associated with adjacent active inflammation.
- Only one NEM and one NET exhibited neuroendocrine cell hyperplasia in the mucosa adjacent to these NEPs (4.4 and 4.0 neuroendocrine cells per crypt, respectively).
- All NETs were low-grade tumors. There was no progression of NEMs or NETs with follow-up years ranging from 1-7 years.

Conclusions:

- Compared to the incidence of gastrointestinal NETs in the SEER database (0.0025%). IBD patients in our institution were more likely to have NETs (0.038%).
- 75% of NCMs showed active inflammation in the adjacent mucosa, raising the possibility that inflammation may play a role in their development.
- NEPs in IBD are frequently not associated with either neuroendocrine cell hyperplasia or glandular dysplasia in the adjacent mucosa.
- NEPs occurring in IBD patients are generally small, incidental findings with indolent clinical behavior.