Concomitant Carcinoid, Gastrointestinal Stromal Tumor and Ganglioneuroma in a male with abdominal pain

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Background
Concomitant presentation of Carcinoid, Gastrointestinal Stromal Tumor (GIST) and Ganglioneuroma (GN) has not yet been reported. Due to its rarity, screening, management, and prognosis of tri-concomitant malignancies involving carcinoid tumor is unknown. Although various case reports of concomitant carcinoid tumors have been documented (1, 2).

Case Report
We describe a 51-year-old male with no pertinent past medical history who presented to the primary care physician with intermittent diffuse abdominal pain. Colonoscopy revealed an invaginated ileocecal valve with superficial lobular changes at the proximal colon. Immunohistochemistry of biopsied specimen was positive for chromogranin and synaptophysin establishing the diagnosis of carcinoid tumor. CT for staging identified two hepatic lesions that also happened to be positive post octrode scan, indicative of metastatic disease.

Exploratory laparotomy revealed extensive disease resulting in resection of the small bowel and jejunal tumors, right hemicolectomy, and partial liver wedge resection. Pathologic findings on resected specimen revealed three distinct malignancies: [1] low risk GIST measuring 0.4cm within the small bowel (fig. 1A and B); [2] a solitary 0.6cm GN within the right colon (fig. 2A and B); and [3] low grade carcinoid tumor within the right colon and distal ileum with separate smaller foci involving the ileocecal valve and appendix (fig. 3A and B, and data not shown). Furthermore, lymph node and hepatic pathology was consistent with metastatic carcinoid disease (fig. 3C, D, and E).

GIST diagnosis was further supported by positive immunohistochemical staining with c-Kit and CD34, while negatively staining for S100 (fig. 1C and data not shown). Conversely, solitary ganglioneuroma identified within the colon stained positively with S100 and CD34, while appropriately failed to stain with GFAP, NF, and c-Kit (fig. 2C and data not shown).

Patients’ post-op course was complicated by right perihapatic fluid collection which was successfully drained. Approximately one year post resection, patient remains asymptomatic and with no evidence of recurrent local or metastatic disease as suggested by serial CT and PET scans.

Discussion
Although not frequently diagnosed, carcinoid tumors are the most common gastrointestinal (GI) neuroendocrine tumors with an overall incidence of 2.9 per 100,000 in the United States (1). Over one half of the carcinoid tumors are found within the GI tract while nearly a quarter reside within the bronchopulmonary system (2). Vast majority of GI carcinoids are located within the small intestine (45%), rectum (20%), or the appendix (16%). However, colon (11%) and stomach (7%) may also be involved (3). The underlying mechanism of carcinoid oncogenesis remains to be determined.

GIST is the most common mesenchymal tumor of the GI tract with an incidence of 7-20 per million in the United States, and constitute only one percent of primary GI cancers (4). Though most GIST are located in the stomach and small bowel (85%) and 25%, respectively, the involvement of the colon has also been observed (10%). A majority of GIST possess activating mutations in either KIT (75-80%) or platelet-derived growth factor receptor alpha (5-10%) which render them resistant to standard chemotherapeutics (5).

GN is an uncommon tumor of the autonomic nervous system with involvement of the colon being extremely rare. They commonly arise from the sympathetic ganglia and adrenal glands, however other locations have been infrequently reported (6). Although associations between GN and other GI syndromes such as MEN, tuberous sclerosis, Von Recklinghausen’s, and Cowden’s disease have been reported, the precise mechanism linking these diseases are only speculative (7).

Various studies have documented an increased incidence of secondary malignancies in patients diagnosed with a carcinoid tumor. An NCI study evaluating over 13,000 patients with primary carcinoid tumors found twenty two percent with secondary malignancies. A majority of these synchronous neoplasias involved the GI tract (8). In another study of 112 patients with carcinoid tumor, twenty five percent had synchronous secondary malignancies. Consistent with the findings of the NCI study, a majority of the synchronous cancers involved the GI tract (33%) with adenocarcinoma of the colon accounting for almost half (25%) (9). Though the mechanism linking these associations remains uncertain, a putative secretory entity from the carcinoid tumor possessing mitogenic potential has been proposed (6).

Conclusion
To our knowledge, synchronous presentation of Carcinoid, GIST and Ganglioneuroma has not yet been reported, and a thorough literature search failed to find such cases. Pathogenesis of concomitant presentation within this patient remains unclear. One could speculate that the occurrence of these neoplasms may involve common oncogenic pathways that are yet to be discovered, or alternatively carcinoid tumor render other cell types susceptible to malignancy. The reported increased incidence of other malignancies in carcinoid patients begs the question whether a thorough screening protocol should be instituted at time of carcinoid diagnosis. Furthermore, does synchronous presentation affect prognosis that may perhaps influence management?

References
6) Demetri GD., et al. Epidemiology, classification, clinical presentation, and diagnostic work-up of gastrointestinal neuroendocrine neoplasms including GIST. In: UpToDate, Tanabe KK (Ed), UpToDate, Waltham, MA, 2009.