

**Small Intestine Neuroendocrine Tumors:
Frequently of Unrecognized Primary Site and Multifocal**

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Background: Because small intestine neuroendocrine tumors (SI-NETs) are typically small, arise from the submucosa, and grow outwardly into the mesentery, they are frequently not identified despite extensive preoperative evaluation in patients with biopsy-proven neuroendocrine liver or lymph node metastases. In such cases, the primary site is considered unknown. However, evidence is accumulating that most NETs of unknown primary can be found by surgical exploration. Moreover, there is conflicting data on the incidence of multifocal primary tumors, which should be identified and removed at the time of surgery.

Methods: We conducted a retrospective cohort analysis of patients who underwent resection of SI-NETs from 2005 to 2014 at an academic medical center where surgical exploration and careful palpation of the small intestine is done to identify unknown primary tumors and multifocal primaries.

Results: Fifty-nine patients underwent resection of SI-NETs. Preoperatively, nearly two-thirds of patients (37/59; 62.7%) had an unknown primary tumor, and all primary tumors were found by surgical exploration (34 in the ileum, 3 in the duodenum). Almost half of patients (26/59; 44.1%) had multifocal tumors. Patients with multifocal tumors were older (mean age = 65 yo vs. 57 yo). The size of the largest tumor in patients with multifocal tumors (mean = 2.2 cm; median = 2 cm) did not differ from that of unifocal tumors (mean = 2.2 cm; median = 2 cm). Most patients had lymph node metastases; however, no lymph node metastases were detected in one patient (3.8%) with multifocal tumors and two patients (6.1%) with unifocal tumors.

Conclusion: At an academic medical center, most patients who underwent surgery for SI-NETs had an unknown primary tumor. Surgical exploration successfully identified all primary tumors in this series despite a negative preoperative workup. The ileum is the most common site from which SI-NETs arise. When careful palpation of the small intestine is routinely done, multifocal primary tumors were identified in nearly half of patients who underwent SI-NET resection. For patients with a NET of unknown primary, the primary site is really not unknown; rather, it is unrecognized. For carefully selected patients, surgical exploration will effectively identify the primary site, which is typically in the ileum. The small intestine should be palpated routinely to identify multifocal primary tumors, so they can be resected.