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The Natural History of Small Bowel Neuroendocrine Tumor (SBNET) Metastases

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BACKGROUND

Small bowel neuroendocrine tumors (SBNETs) have a strong propensity to metastasize, with stage IV (M1) disease present in >50% of cases at diagnosis. Most patients develop liver metastases, but the frequency of metastases to other sites is less well documented. We set out to define these sites, identify risk factors and outcomes associated with metastases, and determine how many patients presenting with M0 disease developed metastases in follow-up.

METHODS

Review of a single institution database identified patients from 2005-2024 with a histopathologic diagnosis of SBNET who underwent surgical intervention (primary/nodal resections with/without metastatic cytoreduction). Demographics, disease characteristics, treatments, and outcomes were abstracted. Overall survival (OS) was estimated by Kaplan-Meier Method and compared by Log Rank Test. Multivariate regression (MR) was utilized to identify variables associated with metastatic disease at presentation.

RESULTS

396 SBNET patients were included in the study and rate of metastatic disease (over their entire disease course) was 77%, with the most common sites being liver (74.5%), peritoneum (30.1%) and bone (20.2%; Table). 288 (72.7%) presented with metastatic disease. The frequency of preoperative functional imaging (DOTA-PET, Octreoscan) was 66.9% (83.2% in past 5 years). Patients presenting as M1 had higher T stage, grade, and neuroendocrine biomarker levels; on MR, higher grade, T stage and elevation of neuroendocrine markers were independently associated with increased risk of presenting with metastatic disease. 20/108 (18.5%) patients presenting with M0 disease developed metastases (at median of 59 months) with the most common sites being liver (95%) and peritoneum (25%). There was no difference in OS between long-term M0 patients (median 169 months) vs. M0 patients who later developed metastases (median not reached; $p=0.60$) and both groups had better OS than patients presenting as M1 (median 119 months; $p<0.01$). Patients who progressed to M1 disease underwent more additional treatments than long-term M0 patients, with 35% undergoing reoperation.

Sites of Metastases	Overall n = 396 (%)

CONCLUSIONS

Most patients with SBNETs at our institution presented with metastatic disease, predominantly in the liver, peritoneum, and bone. One-fifth of M0 patients developed metastases at a median of 59 months after resection. Despite this, most patients with metastatic SBNETs have extended survival with surgical and medical therapy, and these results highlight the importance of long-term follow-up in SBNET patients.

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