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Patterns of Metastases and Outcomes in Patients with Pancreatic Neuroendocrine Tumors

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BACKGROUND

Half of patients with pancreatic neuroendocrine tumors (PNETs) present with distant metastases, with a median overall survival (OS) of 25 months. Some patients will also develop metastases after surgical resection. This study seeks to evaluate the anatomic distribution of metastases in PNET patients having operations at a tertiary center, determine how many patients develop metastases in follow-up, and to compare OS between patients with no metastases (M0), those presenting with metastases (M1 initial), and for those developing metastases later (M1 late).

METHODS

Patients with PNETs who underwent surgical intervention (primary/nodal resections with/without metastatic cytoreduction) between 2000-2023 were identified from a single-institutional prospective database. Demographics, disease characteristics, treatments, and outcomes were abstracted. Primary endpoints were the rate of M0 to M1 progression and risk factors for progression. Secondary endpoint was OS (assessed from first surgery) which was estimated by Kaplan-Meier Method and compared by Log Rank Test.

RESULTS

208 patients met inclusion criteria. 85 (40.9%) patients presented with metastases (M1 Initial), most commonly in the liver (95.3%), bone (25.9%), and retroperitoneal nodes (23.5%). Presence of nodal metastases and elevated preoperative pancreastatin were associated with increased odds of M1 at presentation on multivariable analysis. 24/123 (19.5%) of patients presenting with M0 disease developed metastases at a median of 40 months (M1 Late; 95% CI: 25 – 77 mos.). The most common sites of metastases in the M1 Late group were the liver (91.7%), retroperitoneal nodes (37.5%) and bone (16.7%). About 30% of both M1 Initial and M1 Late patients had extra-abdominal sites of metastases. Nodal metastases and Grade 3 disease were associated with increased odds of progressing from M0 to M1 on multivariable analysis. Patients with M0 disease had better

OS than both M1 Initial (not reached vs 103 mos., p<0.01) and M1 Late (150 mos., p=0.02). M1 Late had better OS than M1 Initial patients (p=0.05).

CONCLUSIONS

Metastases were seen in 41% of PNET patients at presentation, and another 20% developed metastases at a median of 40 months. OS was highest in patients with M0 disease, and those presenting later with metastases had significantly improved OS relative to those presenting initially with metastases. Improved outcomes in M1 Late vs M1 Initial patients may be due to earlier detection of metastases, lower disease burdens, and use of additional therapies. These results demonstrate the patterns and prognosis of metastases in surgically managed patients with PNETs and highlight the importance of long-term surveillance.

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