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Pathologic Features of Small Pancreatic Neuroendocrine Tumors with Liver Metastasis

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BACKGROUND: Management of pancreatic neuroendocrine tumors (PanNETs) ≤3cm is controversial as many remain localized, but metastasis can occur. We sought to identify pathologic features associated with metastatic disease in small PanNETs (≤3cm).

METHODS: Institutional approval was obtained for this HIPAA-compliant study. Surgical Pathology archives were searched for PanNET resections (pancreatectomy/enucleation) between 01/01/2005 to 12/30/2019. Ninety-three cases with tumor size ≤3.0 cm, slides available to review and follow-up data were included in the study. Hematoxylin and Eosin (H&E) slides were reviewed for various pathologic features. Pathology reports and electronic medical records were also reviewed.

RESULTS: Liver metastasis was discovered at initial presentation in 3 and developed during follow-up in 5 of 93 patients. No liver metastases were identified in the 17 cases with a tumor size up to 1 cm, whereas 4 of 48 (8%) patients with a tumor size >1 cm to 2 cm and 4 of 28 (12%) with a tumor size >2 cm to 3 cm presented with synchronous or metachronous liver metastasis. None of 8 insulinoma cases developed liver metastasis. One of 2 gastrinomas (2.4 cm) presented with liver metastasis at initial diagnosis. Four of 8 cases with liver metastasis showed prominent stromal fibrosis (sclerosing variant), despite the 3 of the four having a tumor size ≤2 cm. Seven cases with liver metastasis showed venous invasion, demonstrated by tumor nodules surrounded by thickened fibrotic septa on H&E stain. All cases with liver metastasis displayed at least focal infiltrating growth pattern. Ki67 index was available in 6 metastatic cases, ranging from 4-27%, with three of them having a Ki67 index >20%.

CONCLUSION: Sclerosing morphology, infiltrating growth pattern and venous

invasion may be associated with liver metastasis in small PanNETs. Further studies are needed to identify biomarkers associated with distant metastasis in these small tumors.

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