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Histotripsy for Neuroendocrine Tumors Liver Metastases: Safety and Clinical Outcomes in a Single-Institution Series

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BACKGROUND

Histotripsy is a novel, non-invasive, non-thermal ablative modality that employs focused ultrasound pulses to induce mechanical cavitation and precise tumor cell destruction. Preclinical and early clinical data suggest potential immune-stimulatory effects. While histotripsy has shown promise in hepatocellular carcinoma and colorectal liver metastases, data in neuroendocrine tumor (NET) liver metastases is limited. We report a single center review of using histotripsy for NET liver metastases.

METHODS

We performed a retrospective analysis of patients with pathologically confirmed NET and liver metastases evaluated for histotripsy at Cleveland Clinic from 2022–2025. Clinical data including demographics, primary site, grade, Ki-67, functional status, SSTR2 expression, prior therapies, histotripsy procedural details, adverse events (CTCAE v5.0), and outcomes were collected. Radiographic response was assessed using RECIST 1.1 criteria at 30, 90, and 180 days where available. Descriptive statistics were used.

RESULTS

Of the 66 patients evaluated, 13 patients were treated. Median age at time of histotripsy was 61 years [range 26–69] and 85% of patients were female and 85% white. Primary tumor sites were small bowel/midgut (n=7), pancreas (n=2), lung (n=2), and other (n=2). Tumors were well-differentiated, with median Ki-67 index of 8% (range 2–28%). Eleven patients (85%) had functional tumors, and all were SSTR2-positive. All patients had received prior systemic therapy (somatostatin analogs ± PRRT in 62%), 5 had prior resection and 2 had other locoregional liver therapy.

Histotripsy was delivered in a single session for 12 patients; one patient received two sessions. 53.8% of patients had 1 lesion treated (Range 1-5).

On radiographic assessment of the treated lesions at 30–180 days, 1 patient (8%) had complete response, 5 (38%) had a partial response, 4 (31%) had stable disease, and 3

patients had progression, yielding 77% local control. Necrosis within treated lesions was confirmed on follow-up imaging in 3/13 (23%) of patients. Six patients (55%) had clinical benefit with symptom improvement of carcinoid symptoms.

Most patients experienced minimal to no adverse events. Adverse events included grade 1 abdominal pain (n=3), grade 1 hematoma (n=1), grade 1 hemoptysis (n=1), grade 2 nausea (n=1), and grade 2 abdominal pain (n=1). There were no grade ≥3 adverse events, including prolonged hospitalizations, or treatment-related mortality.

CONCLUSIONS

In this single-institution series, histotripsy for NET liver metastases was safe and feasible, associated with local control rates, and improvement in carcinoid symptoms. Additional clinical data is needed to better define its optimal role in management.

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