Is There a Role for Radiation in Neuroendocrine Neoplasms with Hepatic Metastases?

ABSTRACT

Background: The liver is the most common metastatic site for neuroendocrine neoplasms (NEN). Its presence is a major prognostic factor. While stereotactic body radiotherapy (SBRT) has been successful in treating non–neuroendocrine hepatic metastases, it has not been incorporated into NEN hepatic metastases management. This study investigates radiation’s potential role in treating NEN hepatic metastases.

Methods: Four patients with hepatic metastases from advanced gastrointestinal NEN were prospectively identified and treated with SBRT. Radiation treatment method consisted of respiratory-gated simulation and treatment, individualized dosing with radiobiological calculation of normal tissue complication probability.

Results: One patient with hepatic metastases from a gallbladder primary was only able to receive low-dose radiation (3000 cGy/10). She died of in-field recurrence 5 months post-SBRT. Two patients, one with hepatic metastases from a functional, well-differentiated, 5-HIAA positive, neuroendocrine small bowel carcinoma, and another with hepatic metastases from a well-differentiated, non-functional, pancreatic neuroendocrine carcinoma achieved progression-free, stable disease after being treated with 4200 cGy/6, and 5574 cGy/6 of SBRT, respectively. Both remain alive 3.5 years post-SBRT. The fourth patient was treated with SBRT for hepatic metastases from esophageal NEN without major toxicity, and remains alive more than 2 years post-SBRT. However, status of his disease and local control are unknown, as he has declined imaging follow-up. No NCIC CTC grade ≥2 toxicities were observed.

Conclusion: External beam radiation for NEN liver metastases appears to be well tolerated, and may achieve disease stability for a substantial period of time. While it is a small case series with a heterogeneous patient group, this represents the first case series of SBRT for NEN hepatic metastases, and the results are encouraging. The effectiveness of SBRT appears to have a good side-effect profile for NEN patients. There was no evidence of RILD, deterioration in liver function or elevation in liver enzymes. Three patients experienced transient fatigue or abdominal discomfort.

METHODS

• Four patients with liver metastases from advanced gastrointestinal NEN were prospectively assessed.

• The radiation treatment method involved respiratory-gated simulation and treatment, individualized dosing with radiobiological calculation of normal tissue complication probability described separately.

• Imaging follow-up was performed at 1-, 3-, 6-, 12-, 18- and 24–months post-SBRT. RECIST criteria were used to assess tumor response.

DISCUSSION

• This study suggests a minimum dose threshold that is beyond 30 Gy to achieve tumor control.

• SBRT appears to have a good side-effect profile for NEN patients. There was no evidence of RILD, deterioration in liver function or elevation in liver enzymes.

• A literature review found no studies on radiation for NEN hepatic metastases. Two studies suggest that pancreatic NEN may be radiosensitive. A 36 patient series found a 90% symptomatic palliation clinical response rate with external beam radiotherapy of unresectable pancreatic NEN primary tumors.

• May consider applying non–NEN liver metastases SBRT guidelines for NEN: 3 or fewer lesions (≤ 6 cm), at a distance >1.5 cm from any luminal GI organ, with minimal prior systemic therapy, in the absence of extra-hepatic disease.

• Limitations: this is a small case series with a heterogeneous patient population who had undergone various treatments previously.

REFERENCES