Gastroduodenal Ulceration Associated with Radioembolization for the Treatment of Liver Malignancies; a Newly Observed Complication

Institutional Experience and Review of the Literature

Steven Naymagon MD, Richard R.P. Warner MD, Kalpesh Patel MD, Josef Machac MD, Joshua L. Weintraub MD, Michelle K. Kim MD,MSc

Departments of Medicine and Radiology, Mount Sinai School of Medicine, New York, NY

Background

• Microsphere radioembolization is a method of delivering radiation therapy directly to tumors thereby minimizing toxicity to adjacent structures.
• Despite the relatively high precision of this modality numerous adverse effects have been recognized. One particularly untoward complication is the development of severe gastroduodenal ulceration.
• We analyzed our institutional experience of gastroduodenal ulceration in patients treated with radioembolization and reviewed the current literature on the subject.
• Our aim was to characterize the incidence, clinical presentation, endoscopic findings, diagnosis and treatment of this emerging entity.

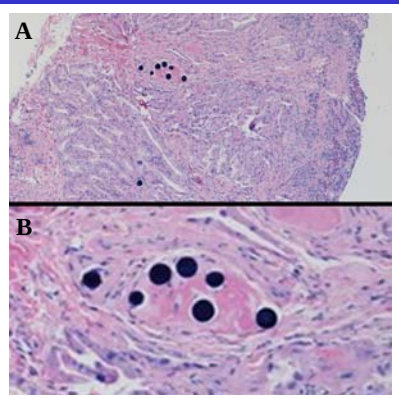
Five Cases of Radioembolization-associated Gastroduodenal Ulceration at Mount Sinai Hospital

Case History	Ulcer Presentation	Treatment & Outcome
62M w/ small-bowel carcinoid metastatic to liver	- epigastric pain 3 months post radioembolization - 1.5 cm stellate antral ulcer	- esomeprazole 40mg BID w/ resolution of symptoms - no recurrence at 3 months f/u
69F w/ carcinoid tumor (unknown primary) metastatic to liver	- dyspepsia 9 months post radioembolization - 0.5 cm pre-pyloric ulcer	- esomeprazole 40mg BID w/ mild symptomatic relief - persistent ulcer several years later
55M w/ small-bowel carcinoid metastatic to liver	- epigastric & RUQ pain 2 months post radioembolization - 2 cm antral ulcer	- esomeprazole 40mg BID w/o response - gastrectomy & cholecystectomy w/ resolution of symptoms
67F w/ bronchial carcinoid metastatic to liver	- epigastric & R-sided abdominal pain, nausea, weight loss 5 months post radioembolization - ulcer in pylorus	- lansoprazole 60mg BID w/ minimal response - persistent symptoms & ulcer on EGD at 3 months f/u
66M w/ HBV & HCC s/p resection & TACE w/ recurrence	- dyspepsia, weight loss 1 month post radioembolization - pyloric ulcer & 2 duodenal ulcers, CMV inclusion bodies in ulcer specimen	- esomeprazole 40mg BID w/ resolution of symptoms - no recurrence at 16 months f/u

Figure 1: Endoscopy

Endoscopic appearance of radioembolization-associated gastroduodenal ulcers in four patients.

Figure 2: Pathology



Ulcer specimens revealing micropsheres in mucosa at (A) high & (B) low magnification.

Results & Discussion

• *Etiology:* Current evidence suggests that radioembolization-associated gastroduodenal ulceration results from the inadvertent delivery of microspheres to the microvasculature of the gastrointestinal tract leading to direct radiation toxicity.
• *Incidence:* Based on the existing literature the incidence of this entity ranges between 3.1% and 4.6%.
• *Clinical:* Our experience, as well as the current literature, shows that most patients with this complication present with abdominal pain often associated with nausea, vomiting, and anorexia (***Table***). Symptoms can arise from hours to months after the radioembolization treatment.
• *Endoscopy:* Radioembolization-associated gastroduodenal ulcers lack a distinct appearance or location that may enable endoscopic differentiation from ulcers of other etiologies. The degree of disease can be severe (***Figure 1***).
• *Diagnosis:* Definitive diagnosis is made via endoscopic biopsy and histopathologic evaluation of the ulcer specimen which reveals microspheres in the mucosa or submucosa (***Figure 2***).
• *Treatment:* Radiatioembolization-associated ulcers have proven to be extremely difficult to treat. In our experience, therapy based on acid suppression has had limited success (***Table***). Other centers have had similar results. There is promise in the use of antioxidants and anti-inflammatory agents but the evidence is still sparse. Early surgical consultation is warranted in non-responders with severe disease.

Conclusions

• The increasing utilization of radioembolization will inevitably lead to adverse events including gastroduodenal ulceration.
• This entity is not uncommon and must be considered in any patient treated with radioactive microspheres presenting with symptoms of dyspepsia.
• Accurate diagnosis and aggressive treatment are necessary to improved patient's outcomes.