CASE REPORT | ENDOSCOPY

Novel Use of Endoscopic Clips as Fiducials for Radiotherapy in Small Bowel Lymphoma

Vanessa Mendez, MD1, Fernando J. Martinez, MD1, Frederick B. Soriano, RN2, Arnold M. Markoe, MD1, Izidore S. Lossos, MD1, Kunal Saigal, MD1, and Daniel A. Sussman, MD, MSPH1

1University of Miami Miller School of Medicine, Miami, FL
2University of Miami Hospital-Sylvester Comprehensive Cancer Center, Miami, FL

Abstract
A 31-year-old woman was diagnosed with duodenal grade 1 follicular lymphoma. The patient underwent radiotherapy and on surveillance enteroscopy, the lymphoma was persistently identified in the duodenum and jejunum. Endoscopic clips were used as fiducials to better localize the tumor during radiotherapy. Endoscopic clips are increasingly used as tumor localization tools because of their favorable risk-benefit ratio. In our case, endoscopic clipping was necessary to properly localize the tumor after prior treatment failure, and the patient now has no evidence of disease. Larger studies are needed to demonstrate the efficacy of clips in tumor localization and improved disease-related morbidity.

Introduction
Endoscopic clips are frequently used to effect hemostasis in the setting of gastrointestinal bleeding. Since inception, the indication for their use has been expanded to include demarcation of tumor boundaries to guide oncologic therapies. We describe the use endoscopic clips as fiducials to improve the radiotherapeutic treatment of small intestinal lymphoma.

Case Report
A 31-year-old woman raised near the Ukraine during the Chernobyl nuclear reactor disaster presented with non-bloody diarrhea, pyrosis, and abdominal pain. Esophagogastroduodenoscopy (EGD) displayed multiple sub-centimeter white nodules in the second portion of the duodenum. Biopsies revealed follicular lymphoma grade 1. Computed tomography (CT), positron emission tomography (PET) scan, and bone marrow biopsy confirmed that the disease was limited to the duodenum. Further staging with wireless capsule endoscopy revealed multiple nodular lesions localized to the fourth portion of the duodenum and proximal jejunum. Given the perceived superiority of direct endoscopic visualization and PET in tumor localization, and the predictable, fixed location of the duodenum, further marking to direct the radiation beam was not performed.

The patient underwent 20 fractions of radiotherapy to a total dose of 3,600 cGy. On surveillance push enteroscopy, the lymphoma was again identified in the fourth part of duodenum and proximal jejunum. Given the nearly universal responsiveness of this lymphoma to radiotherapy, the decision was made to use endoscopic clips as fiducials to better localize the tumor during subsequent therapy; a clip was placed proximal to the duodenal lesion, and 2 clips were placed distal to the jejunal lesions (Figure 1). After repeat radiation simulation, it was noted that a portion of the demarcated lymphomatous mucosa lay outside the previously irradiated field. A second...
course of 20 fractions of radiotherapy with a total dose of 3,600 cGy was administered with a 1-cm overlap with the first radiation treatment (Figure 2). This 1-cm overlap between the 2 radiation treatments would be the area at greatest risk for radiation-induced damage; however, there is little chance of dose-dependent radiation damage at 3,600 cGy. The patient achieved complete remission and currently has no evidence of disease on surveillance enteroscopy.

Discussion

Chernobyl nuclear disaster radiation exposure is associated with gastrointestinal malignancies, including gastric carcinoma, colon cancer, non-Hodgkin’s gastric lymphoma, sclerosing epitheloid fibrosarcoma of the cecum, and Krukenberg tumor arising from the gastroesophageal junction.\(^1\)\(^-\)\(^5\) A causal relationship has not been determined, as the comparative incidence for these tumors in relation to those not exposed to radiation is unknown.

As in other cancers, patients with primary follicular lymphoma of the gastrointestinal tract usually undergo imaging procedures to localize the tumor area in preparation for radiotherapy.\(^6\) However, localizing the diseased area can be complex, and inaccurate localization may result in radiation of normal tissue with complications such as fibrosis and damage to adjacent tissues.\(^7\)\(^-\)\(^8\) Poor tumor localization can also result in application of the radiotherapy beam outside tumor margins and inadequate treatment of disease.\(^9\) Endoscopic clips, originally developed for hemostasis of gastrointestinal bleeding, are being increasingly used for tumor localization, as advances in endoscopic devices have resulted in improved delivery of fiducial devices in a relatively inexpensive, easy, and safe manner.\(^8\)\(^,\)\(^10\)

Several articles were published over the last 2 decades describing endoscopic clipping as a tool for localization in preoperative and pre-radiotherapy planning in luminal tumors, including 3 esophageal and 1 gastric neoplasia,\(^6\)\(^-\)\(^9\) several reports with colorectal tumors,\(^11\)\(^-\)\(^13\) and, recently, a prospective study of 15 patients using endoscopically placed clips for tumor localization during CT gastroscopy and preoperative planning.\(^14\) Only 1 prior report describes duodenal follicular lymphoma tumor localization using endoscopic clips.\(^15\) At present, there are no randomized clinical trials demonstrating the efficacy of using fiducial markers in targeting radiotherapy for duodenal lymphomas. However, there are multiple trials for prostate cancer and anecdotal evidence for upper gastrointestinal tract malignancies that substantiate the use of fiducial markers for tumor localization, and their benefit for small bowel lymphomas merits further research.\(^16\)\(^-\)\(^18\) Larger studies should be done to demonstrate their efficacy in accurate approximation of tumor boundaries with associated decrease in treatment and disease-related morbidity.

Disclosures

Author contributions: Each author assisted in the writing and editing of this manuscript. FJ Martinez is the article guarantor.

Financial disclosure: The authors report no financial support or other conflicts of interest.

Informed consent was obtained for this case report.

Received: October 14, 2013; Accepted: May 28, 2014
References

1. Cardis E, Hatch M. The Chernobyl accident: An epidemiological perspective. Clin Oncol (R Coll Radiol). 2011;23(4):251–60.
2. Shchepotin IB, Valetsky VL, Chorny VA, et al. Carcinoma of the stomach following the Chernobyl nuclear accident. Eur J Cancer. 1997;33(9):1413–8.
3. Shchepotin IB, Evans SR, Shabahang M, et al. Primary non-Hodgkin's lymphoma of the stomach: Three radical modalities of treatment in 75 patients. Ann Surg Oncol. 1996;3(3):277–84.
4. Frattini JC, Sosa JA, Carmack S, Robert ME. Sclerosing epithelioid fibrosarcoma of the cecum: A radiation-associated tumor in a previously unreported site. Arch Pathol Lab Med. 2007;131(12):1825–8.
5. Matar HE, Elmetwally AS, Salu I, et al. Krukenberg tumour arising from adenocarcinoma of the gastro-oesophageal junction in a 28-year-old female presenting as lower abdominal swelling mimicking an inguinal hernia [published online March 29, 2011]. BMJ Case Rep. doi: 10.1136/bcr.12.2010.3597.
6. Isobe K, Uno T, Kawakami H, et al. A case of gastric lymphoma with marked interfractional gastric movement during radiation therapy. Int J Clin Oncol. 2006;11(2):159–61.
7. Weyman RL, Rao SS. A novel clinical application for endoscopic mucosal clipping. Gastrointest Endosc. 1999;49(4 pt 1):522–4.
8. Hui A, Abi-Hanna D, Rae R, Delaney G. Use of endoscopic mucosal clips in radiotherapy planning for oesophageal carcinoma: A series of three cases. Australas Radiol. 2002;46(1):111–4.
9. Pfau PR, Pham H, Ellis R, et al. A novel use of endoscopic clips in the treatment planning for radiation therapy (XRT) of esophageal cancer. J Clin Gastroenterol. 2005;39(5):372–5.
10. Lehman GA, Maveety PR, O’Connor KW. Mucosal clipping: Utility and safety testing in the colon. Gastrointest Endosc. 1985;31(4):273–6.
11. Ohdaira T, Konishi F, Nagai H, et al. Intraoperative localization of colorectal tumors in the early stages using a marking clip detector system. Dis Colon Rectum. 1999;42(10):1353–5.
12. Montorsi M, Opoche E, Santambrogio R, et al. Original technique for small colorectal tumor localization during laparoscopic surgery. Dis Colon Rectum. 1999;42(6):819–22.
13. Ohdaira T, Nagai H, Shoji M. Intraoperative localization of colorectal tumors in the early stages using a magnetic marking clip detector system (MMDCS). Surg Endosc. 2003;17(5):692–5.
14. Jeong SH, Bae K, Ha CY, et al. Effectiveness of endoscopic clipping and computed tomography gastroscopy for the preoperative localization of gastric cancer. Korean Surg Soc. 2013;84(2):80–7.
15. Franco P, Filippi AR, Ciammella P, et al. Primary duodenal follicular lymphoma: 6-years complete remission after combined radio-immunotherapy. Acta Gastroenterol Belg. 2011;74(2):337–42.
16. DiMaio CJ, Nagula S, Goodman KA, et al. EUS-guided fiducial placement for image-guided radiation therapy in GI malignancies by using a 22-gauge needle (with videos). Gastrointest Endosc. 2010;71(7):1204–10.
17. Sanders MK, Moser AJ, Khalid A, et al. EUS-guided fiducial placement for stereotactic body radiotherapy in locally advanced and recurrent pancreatic cancer. Gastrointest Endosc. 2010;71(7):1178–84.
18. Balter JM, Larm KL, Sandler HM, et al. Automated localization of the prostate at the time of treatment using implanted radiopaque markers: Technical feasibility. Int J Radiat Oncol Biol Phys. 1995;33(5):1281–6.