

CASE REPORT

“Stereotactic Ablative Radiation Therapy (SABR) as a potential curative treatment in duodenal adenocarcinoma: a case report in an old male.”

**F.M. Aquilanti , M.C. Barba , F. Bianciardi , B. Nardiello , G. Raza , R. El Gawhary ,
C. D'Ambrosio and P. Gentile .**

Corresponding author: F.M. Aquilanti

Abstract

Small bowel cancer is one of the most rare cancers of the gastrointestinal tract. Because of this rarity, there is limited experience regarding its biological behavior and decisions for treatment. The diagnosis is usually late and most patients present with an advanced disease. (1)

Stereotactic Ablative Radiation Therapy (SABR) augmented by image guided radiation therapy (IGRT) is becoming a treatment option in many tumors not only with palliative intent but also with curative intent, especially when surgery cannot be performed due to comorbidities. This therapy revealed a good toxicity profile with excellent tumor control rate thanks to its specific schedule: high radiotherapy dose on a limited, well defined area. (2-10)

This is a report of a 83-year-old male affected by arterial hypertension and congestive cardiomyopathy, who was admitted to our unit with six months history of upper abdominal pain, weight loss over 10 kg and a progressive severe fatigue. Blood tests revealed normochromic anemia (HB 7 g/dl) that required multiple transfusions. The patient underwent endoscopy that showed a large mass partially obstructing the second part of the duodenum; a lesion biopsy revealed the presence of a moderately-differentiated adenocarcinoma and associated duodenitis. A staging CT scan confirmed a localized disease. Due to age and comorbidities, a Stereotactic Ablative Radiation -SABR- was proposed, by a multidisciplinary team, as the preferred mode of treatment. Endoscopic clips were placed as fiducials to better localize the tumor during radiotherapy (11). The patient received 25 Gy in 5 fractions on alternate days, with resolution of duodenal obstruction and bleeding that lasted for 14 months, when the patient died of a myocardial infarction.

Conclusions: Our experience with this case suggests that SABR could have a role in the palliative treatment of small bowel cancers, with good tolerance, particularly in patients for whom surgical treatment is not a viable option.

Introduction

Small intestine is approximately 75% of the length and 90% of the mucosal surface of the gastrointestinal tract. Its neoplastic lesions represent only 2% to 5% of all primary gastrointestinal tumors. Malignant diseases in the small intestine are about 13 to 18 times less common than colon cancer (12-13). Histologically, there are four subtypes of malignant tumors of the small intestine: adenocarcinomas (around 40%), neuroendocrine tumors (35% to 40%), lymphomas (15%) and sarcomas (11% to 13%) (14-15). Adenocarcinomas are more common in the duodenum and proximal jejunum, neuroendocrine tumors and lymphomas are more common in the distal portions, while sarcomas

have diffuse distribution (16). Duodenal adenocarcinoma represents approximately 0.5% of all malignant gastrointestinal tumors and the most studied are those located in the first and second (mainly periampullary) portions (17-18). In this paper, we present the case report of an adenocarcinoma of the second portion of duodenum in a patient for whom surgery was deemed as too poor risk and, therefore, underwent SABR.

Case report

The patient was a 83 years old, non-smoker male with arterial hypertension, congestive cardiomyopathy, who was admitted to our unit with six months history of upper abdominal pain, dyspepsia, weight loss over 10 kg and severe, progressive fatigue. Blood tests demonstrated normochromic anemia (HB 7 g/dl) requiring multiple transfusions. Upper GI endoscopy was performed revealing a large necrotic, substenotic mass in the second duodenal portion (Fig. 1)



Fig.1: Upper Gastro-intestinal endoscopy of the second duodenal portion revealing the large necrotic tumor mass.

Biopsy specimens showed a moderately-differentiated adenocarcinoma and associated duodenitis. The patient subsequently underwent a CT scan showing a mass of about 5,2 cm, with no loco-regional nodal involvement and no distant metastasis. Due to comorbidities, a surgical approach was excluded and Stereotactic Ablative Radiation Therapy (SABR) was proposed by a multidisciplinary team, as the preferred mode of treatment.

As in other cancers, patients with adenocarcinoma of the gastrointestinal tract usually undergo imaging procedures to localize the tumor area as preparation for radiotherapy. However, localizing the disease area can often be difficult and an inaccurate localization may result both in target missing with a subsequent low disease control and in excessive normal tissue irradiation. Therefore, the team decided to use the endoscopic clips as markers to better localize the tumor during subsequent therapy: one clip was placed proximal to the duodenal neoplasm and a second one was placed distal to the lesion. The patient also underwent upper abdominal contrast enhanced MRI for better target definition; an image-fusion between the planning CT scan and staging MRI was used to contour the gross tumor volume. A 3 mm margin was added to CTV for PTV (Clinical Target Volume for Planning Target Volume): a dynamic arc therapy was employed.

The patient received 25 Gy in 5 fractions on alternate days. Before each radiotherapy session, an Exactrac control using fiducials and a Cone Beam CT scan were performed as imaging control. The patient completed the treatment without interruption and any evidence of acute toxicity.

At follow-up, nine months later, he was eating regularly and recovered weight: an endoscopy control revealed the disappearance of the granular lesions and lack of cancer cells in biopsy specimens. Multiple biopsies of the duodenal mucosa during repeated endoscopies failed to demonstrate the presence of neoplasm. The patient showed no sign of pain or bleeding for 14 months, and then died of myocardial infarction .

Discussion

Primary small bowel adenocarcinoma (SBA) is a rare malignancy. Compared to colorectal cancer, there is a small knowledge regarding the pathogenesis of SBA. SBA is associated with familial adenomatous polyposis, Lynch syndrome, Peutz-Jeghers syndrome, celiac sprue, and Crohn Disease. It can be difficult to detect SBA owing to its rarity and nonspecific symptoms. However, 43% to 66% of patients with SBA have abdominal pain at the time of diagnosis, and they are often diagnosed during emergencies involving occlusion or bleeding.

Treatment of primary duodenal adenocarcinoma depends on the location and staging: if feasible, the preferred treatment is a curative surgical removal. There is no established protocol for small bowel adenocarcinomas, due to the lack of randomized trials (19) and the few data from retrospective studies have shown no significant benefit in overall survival (20).

In some cases, a locally-advanced disease or coexisting comorbidities could compromise the principal treatment. Like in other conditions, i.e.. in Stage I lung cancer, Stereotactic Ablative Radiation Therapy (SABR) is becoming a possible treatment option with excellent disease control rate and good tolerance thanks to its particular schedule: high radiotherapy dose on a limited, well defined area. Many recent experiences are also testing SBRT in abdominal lesions, as treatment of localized oligo metastatic disease, revealing an optimal tumor control without severe toxicities.

To treat the large duodenal adenocarcinoma that affected our patient the surgical options would have been to remove the tumor via a cefaloduodeno-pancreasectomy or by-pass it with a gastroenterostomy. The first option was deemed too high risk, because of the severe co-morbidities, and the second would have relieved the duodenal sub-occlusion but not the bleeding.

The stereotactic treatment that was used relieved occlusion and bleeding caused by the tumor with no side effect and allowing the patient several months of improved quality of life.

We suggest that, with proper imaging localization of the tumor IGRT based-SABR is a valid therapeutic option in duodenal adenocarcinomas not amenable of surgical therapy in poor-risk patients.

References:

1. Overman MJ. Recent advances in the management of adenocarcinoma of the small intestine. *Gastrointest Cancer Res* 2009;33:90-6.
2. Hadziahmetovic M, Loo BW, Timmerman RD, Mayr NA, Wang JZ, Huang Z, et al. Stereotactic body radiation therapy (stereotactic ablative radiotherapy) for stage I non-small cell lung cancer—updates of radiobiology, techniques, and clinical outcomes. *Discov Med* 2010;9:411–17.
3. Martin A, Gaya A. Stereotactic body radiotherapy: a review. *Clin Oncol* 2010;22: 157–72.
4. Onishi H, Araki T, Shirato H, Nagata Y, Hiraoka M, Gomi K, et al. Stereotactic hypofractionated high-dose irradiation for stage I non-small cell lung carcinoma: clinical outcomes in 245 subjects in a Japanese multiinstitutional study. *Cancer* 2004;101: 162331.
5. Lax I, Panettieri V, Wennberg B, Amor Duch M, Naslund I, Baumann P, et al. Dose distributions in SBRT of lung tumors: comparison between two different treatment planning algorithms and Monte-Carlo simulation including breathing motions. *Acta Oncol* 2006;45:978–88.
6. Timmerman R, Heinzerling J, Abdulrahman R, Choy H, Meyer JL. Stereotactic body radiation therapy for thoracic cancers: recommendations for patient selection, setup and therapy. *Front Radiat Ther Oncol* 2011; 43:395–411.
7. Lagerwaard FJ, Haasbeek CJ, Smit EF, Slotman BJ, Senan S. Outcomes of riskadapted fractionated stereotactic radiotherapy for stage I non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys* 2008;70:685–92.
8. Nagata Y, Takayama K, Matsuo Y, Norihisa Y, Mizowaki T, Sakamoto T, et al. Clinical outcomes of a phase I/II study of 48Gy of stereotactic body radiotherapy in 4 fractions for primary lung cancer using a stereotactic body frame. *Int J Radiat Oncol Biol Phys* 2005;63:1427.

9. Timmerman R, Papiez L, McGarry R, Likes L, DesRosiers C, Frost S, et al. Extracranial stereotactic radioablation: results of a phase I study in medically inoperable stage I nonsmall cell lung cancer. *Chest* 2003;124:1946.
10. Haasbeek CJ, Senan S, Smit EF, Paul MA, Slotman BJ, Lagerwaard FJ. Critical review of nonsurgical treatment options for stage I nonsmall cell lung cancer. *Oncologist* 2008;13: 309–19.
11. Vanessa Mendez, MD, Fernando J. Martinez, MD, Frederick B. Soriano, RN, Arnold M. Markoe, MD, Izidore S. Lossos, MD, Kunal Saigal, MD, and Daniel A. Sussman, MD, MSPH. Novel Use of Endoscopic Clips as Fiducials for Radiotherapy in Small Bowel Lymphoma. *ACG Case Rep J*. 2014 Jul; 1(4): 184–186.
12. Aparicio T, Zaanen A, Svrcek M, Laurent-Puig P, Carrere N, Manfredi S, Locher C, Afchain P. Small bowel adenocarcinoma: epidemiology, risk factors, diagnosis and treatment. *Dig Liver Dis*. 2014;46:97–104.
13. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. *CA Cancer J Clin*. 2012;62:10–29.
14. Dabaja BS, Suki D, Pro B, Bonnen M, Ajani J. Adenocarcinoma of the small bowel: presentation, prognostic factors, and outcome of 217 patients. *Cancer*. 2004;101:518–526.
15. Bilimoria KY, Bentrem DJ, Wayne JD, Ko CY, Bennett CL, Talamonti MS. Small bowel cancer in the United States: changes in epidemiology, treatment, and survival over the last 20 years. *Ann Surg*. 2009;249:63–71.
16. Pan SY, Morrison H. Epidemiology of cancer of the small intestine. *World J Gastrointest Oncol*. 2011;3:33–42.
17. Ryder NM, Ko CY, Hines OJ, Gloor B, Reber HA. Primary duodenal adenocarcinoma: a 40-year experience. *Arch Surg*. 2000;135:1070–1074; discussion 1074–1075.
18. Solej M, D'Amico S, Brondino G, Ferronato M, Nano M. Primary duodenal adenocarcinoma. *Tumori*. 2008;94:779–786.
19. Singhal N, Singhal D. Adjuvant chemotherapy for small intestine adenocarcinoma. *Cochrane Database Syst Rev* 2007; (3): CD005202
20. Overman MJ, Kopetz S, Lin E, Abbruzzese JL, Wolff RA. Is there a role for adjuvant therapy in resected adenocarcinoma of the small intestine. *Acta Oncol* 2010; 49: 474-479