CIRUGÍA ESPAÑOLA

www.elsevier.es/cirugia

Original article

Primary small bowel adenocarcinoma

Jaime Ruiz-Tovar, Enrique Martínez-Molina, Vicente Morales, and Alfonso Sanjuanbenito*

Departamento de Cirugía General y del Aparato Digestivo, Hospital Universitario Ramón y Cajal, Madrid, Spain

ARTICLE INFORMATION

Article history:
Received October 2, 2008
Accepted December 28, 2008
Online April 2, 2009

Keywords:
Small bowel adenocarcinoma
Bowel resection
Retroperitoneal infiltration

A B S T R A C T

Introduction: Primary small bowel adenocarcinoma is an uncommon tumour, with non-specific symptoms that cause a delay in the diagnosis and consequently a worse outcome for the patient. We analyse our experience in the management of this disease.
Material and method: We performed a retrospective study of our experience with 17 patients diagnosed with primary small bowel adenocarcinoma, excluding all the cases suggesting secondary involvement of the small bowel from an adenocarcinoma in other locations.
Results: We analysed 9 females (53%) and 8 males (47%) with a mean age of 61.8 years. Tumour location was duodenum (8 cases), jejunum (5), and ileum (4). Those with duodenal tumours underwent 4 pancreaticoduodenectomies, 3 gastroenterostomies, and 1 diagnostic biopsy; 6 bowel resections with lymphadenectomy, 2 en-bloc resections, and 1 by-pass were performed on those with jejuno-ileal tumours. There were complications in 3 patients (18%). General survival was 18 months; in duodenal and jejunal tumours it was 15 months versus 58 in ileal ones (P=.048). Survival was 48 months in the absence of lymph node metastases versus 11 in those with (P=.067). In those tumours infiltrating the retroperitoneum, survival was 15 months compared to 23 when not affected (P=.09).
Conclusions: Curative treatment consists of small bowel resection. Retroperitoneal infiltration was a non-resectability criterion in our series. Ileal location is associated with a better outcome. Advanced stages, lymph node metastases, non-resected cases, and retroperitoneal infiltration tended to be associated with a poor prognosis in our group.

Adenocarcinoma primario de intestino delgado

Palabras clave:
Adenocarcinoma de intestino delgado
Resección intestinal
Infiltración retroperitoneal

R E S U M E N

Introducción: El adenocarcinoma primario de intestino delgado es un tumor poco frecuente, con síntomas inespecíficos, lo que condiciona un retraso en el diagnóstico que conlleva peor pronóstico. Evaluamos nuestra experiencia en el manejo de este trastorno.
Material y método: Realizamos un estudio retrospectivo de 17 pacientes diagnosticados de adenocarcinoma primario de intestino delgado, excluyendo los casos en que la afección de intestino delgado era secundaria a un adenocarcinoma de otra localización.

*Author for correspondence.
E-mail address: jruiztovar@gmail.com (J. Ruiz-Tovar).

Resultados: Estudiamos a 9 mujeres (53%) y 8 varones (47%) con una media de edad de 61,8 años. Los tumores se originaron en duodeno (8 casos), yeyuno (5) e íleon (4). En los tumores duodenales se realizaron 4 duodenopancreatectomías cefálicas, 3 gastroenteroanastomosis y 1 biopsia diagnóstica; en los tumores yeyunoileales se realizaron 6 resecciones intestinales, 2 resecciones multiorgánicas y una derivación digestiva. Aparecieron complicaciones postoperatorias en 3 pacientes (18%). La supervivencia total fue 18 meses; la de tumores duodenales y yeyunales, 15 meses, frente a 58 de los ileales (p = 0,048). En ausencia de metástasis ganglionares, la supervivencia fue 48 meses, frente a 11 con ganglios positivos (p = 0,067). En tumores que no infiltraban el retroperitoneo fue 23 meses, frente a 15 en los que sí (p = 0,09).

Conclusiones: El tratamiento curativo consiste en la resección del segmento intestinal. La infiltración retroperitoneal fue un criterio de irresecabilidad en nuestros pacientes. La localización en ileon es un factor de buen pronóstico. Los estadios avanzados, las metástasis ganglionares, los casos no resecados y la infiltración del retroperitoneo tienden a asociarse a peor pronóstico en nuestro estudio

Introduction

Primary adenocarcinoma of the small intestine is an infrequent tumour, representing less than 1% of all digestive tract neoplasias. More common in the small intestine are metastases of adenocarcinomas from other locations, which are both digestive and non-digestive (lung, cervix, melanoma, etc). Because of its low frequency and the unspecific symptoms produced, primary adenocarcinomas of the small intestine do not initially cause suspicion, and this causes a delay in diagnosis which leads to a worse prognosis for the patient.[1,2]

Material and method

Retrospective study of all patients diagnosed and operated on for primary adenocarcinoma of the small intestine between 1984 and 2007 in the Hospital Universitario Ramón y Cajal (Madrid, Spain).

All patients with primary adenocarcinomas of the duodenum, jejunum, and ileum were included in the study, and patients with coexisting adenocarcinomas in other locations and those with histological characteristics which did not indicate the small intestine as the primary origin were excluded.

Variables analyzed in the study were age, gender, personal antecedents of interest, clinical manifestations, diagnostic methods used, preoperative diagnosis, intraoperative findings, location, surgical technique implemented, postoperative complications, adjuvant treatment, and survival.

Diagnostic profitability was defined as the test indicating the diagnosis with certainty. The follow-up protocol consisted of quarterly reviews during the first year, half-yearly in the second, and annual reviews subsequent to this. Protocol included physical examination, abdominal computerized tomography (CT), thoracic x-ray, and analysis.

Statistical analysis was done with help from the computer program SPSS 12.0 for Windows. Quantitative variables which followed a normal distribution were defined by average and interval of values. For quantitative variables which did not follow a gaussian distribution, median was used instead of average as the central measurement. Qualitative variables were defined by number and percentage of cases. Survival was analyzed by the Kaplan-Meier method. The values $P<.05$ were considered statistically significant.

Results

We analyzed a total of 17 patients, 9 women (53%) and 8 men (47%) with an average age of 61.8 (interval, 40–80) years. Noteworthy personal antecedents of interest were: Crohn's disease in 1 patient and in another carcinoma of the colon (T2 N0 M0) resected 8 years previously without signs of recurrence. The tumours originated in the duodenum in 8 cases (47%), in the jejunum 5 (29%), and in the ileum 4 (24%).

The most frequent clinical manifestations were vomiting in 10 (59%) patients, abdominal pain in 8 (47%), subocclusive episodes in 5 (29%), and weight loss in another 5. Vomiting was more frequent in duodenal tumours; and abdominal pain and subocclusive episodes, in distal tumours (jejunum

Table 1 – Diagnostic tests carried out and profitability

	Test, No. (%)		Profitability, %
Duodenal tumours (8 patients)	Endoscopy	6 (75)	67
	Barium study	3 (37)	0
Jejunoileal tumours (9 patients)	Abdominal CT	8 (89)	0
	Barium study	7 (78)	0

and ileum). Diagnostic tests used and their profitability are described in Table 1. Preoperative diagnosis for duodenal tumours was certain in 4 (50%) patients, and this was based on findings from upper digestive endoscopy with biopsies and histological confirmation. In other 4 patients, the preoperative diagnosis was unspecific duodenal stenosis based on findings from barium studies and 2 non-conclusive oral endoscopy cases. The preoperative diagnosis in distal tumours was a mass in the small intestine in 7 (78%) cases and intestinal obstruction of unknown origin in 2 (22%); both the CT and barium studies could not offer a certain diagnosis of neoplasia in the small intestine because of the lack of histological confirmation.

Elective surgery was carried out on 15 (88%) patients and emergency surgery on the 2 diagnosed with intestinal obstruction. In intraoperative findings, infiltration of the retroperitoneum was confirmed in 5 (29%) patients (4 duodenal tumours and 1 jejunal), infiltration of the transverse colon in 1 jejunal tumour (5%) and infiltration of the bladder in 1 of ileal location. Surgical techniques carried out are summarized in Table 2. A jejunal tumour with retroperitoneal infiltration was considered unresectable and a jejunojejunal bypass was undertaken. In the jejunal tumour which infiltrated the transverse colon, an en bloc resection was carried out, including the transverse colon with colocolic and jejunojejunal anastomosis, and in the ileal tumour infiltrating the bladder, partial extirpation of the affected vesical wall was carried out (multi-organ resections). In a duodenal tumour with retroperitoneal infiltration and hepatic metastasis, only a diagnostic biopsy was carried out, and a bypass surgery was rejected, as the patient did not have obstructive symptoms. Postoperative complications appeared in 3 (18%) patients: 1 hemoperitoneum which required reintervention, 1 intraabdominal collection drained percutaneously, and 1 low debit pancreatic fistula, managed conservatively after a cephalic duodenopancreatectomy. There was no postoperative mortality.

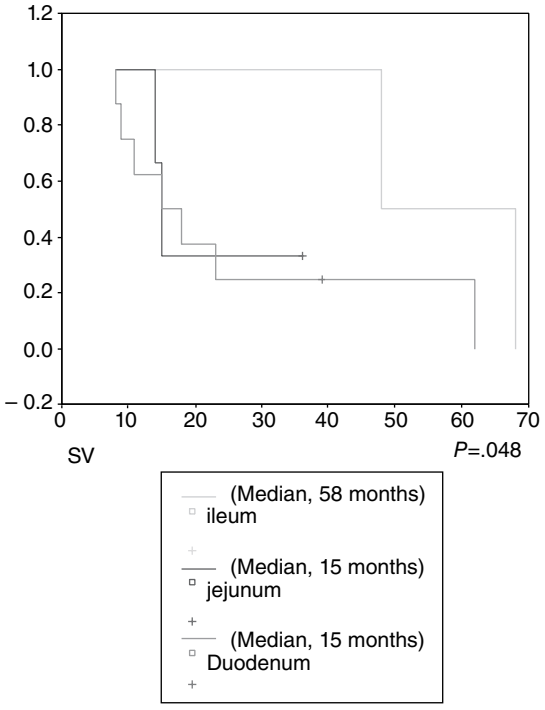

Figure 2 – Survival according to location.

Table 2 – Surgical technique

	No. (%)
Jejunoileal tumours (9 patients)	
Resection DI+lymphadenectomy	6 (67)
Multi-organ resection	2 (22)
Digestive bypass	1 (11)
Duodenal tumours (8 patients)	
Whipple	4 (50)
Gastroenteroanastomosis	3 (37)
Diagnostic biopsy	1 (13

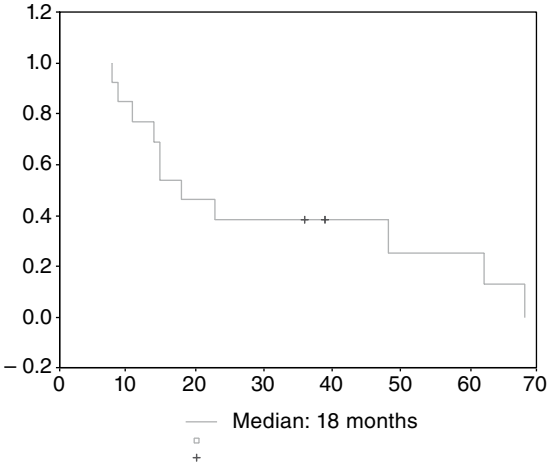

Figure 1 – Total survival.

TNM[14] staging was 4 (24%) patients in stage I; 3 (18%) in stage II; 9 (53%) in stage III; and 1 (5%) in stage IV. Five (29%) patients received adjuvant chemotherapy: four with FOLFOX-4 protocol (all with T4 jejunal and ileal tumours) and 1 with 5-fluorouracil (T3 duodenal tumour).

Overall survival was a median (interval) of 18 (8–68) months; 2 patients are currently still alive (Figure 1). Median survival of those with duodenal and jejunal tumours was 15 months, while survival of ileal cases was 58 (Figure 2); the difference of survival between ileal tumours and the rest is statistically significant. A greater tendency for survival was observed with a lower stage tumour, and this did not reach statistical significance (Figure 3). Median survival of patients without lymph node metastasis was 48 months, versus 11 in those with positive lymph node metastasis (*P*=.067); in patients with distant metastasis, survival was 14 months, versus 23 for those who did not present with this. In tumours which did not infiltrate the retroperitoneum, median survival was 23 months, versus 15 for those with this infiltration (*P*=.09) (Figure 4).

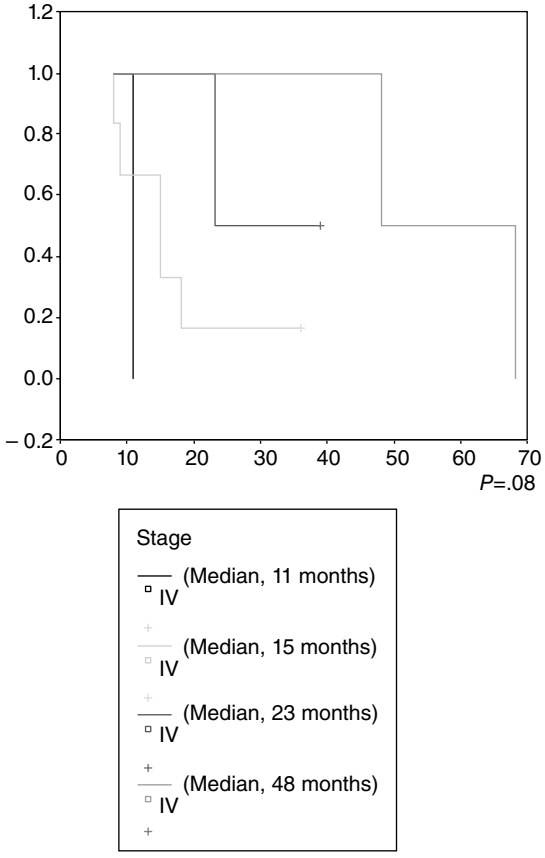

Figure 3 – Survival according to stage.

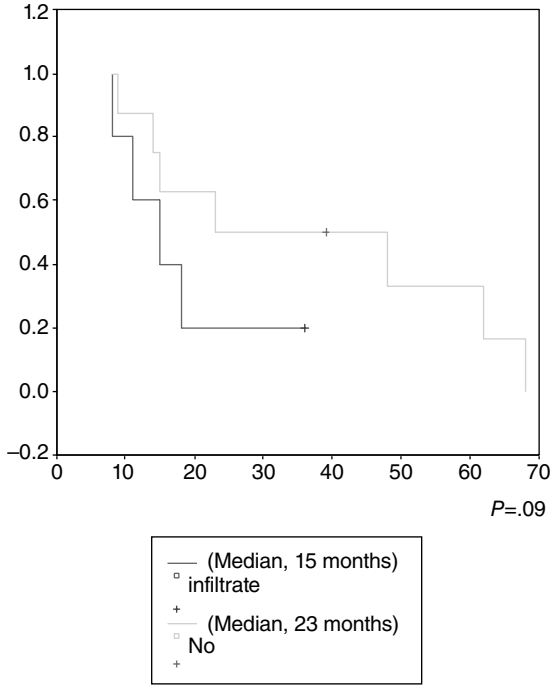

Figure 4 – Survival according to retroperitoneal infiltration and surgical resectability.

Discussion

Primary adenocarcinoma of the small intestine is 40-60 times less frequent than that of the colon. It appears at adult ages, normally between 50 and 70 years, with no gender preference, such as demonstrated by our study. It may develop in any location, but it is more frequent in proximal segments, and duodenal tumours are 40%-50% of all cases,[3] coinciding with our data.

It has been associated with different intestinal diseases such as familial adenomatous polyposis, Lynch syndrome type II, cystic fibrosis, peptic ulcer, or celiac sprue. However, Crohn's disease is the most important risk factor, which increases the risk of suffering from this neoplasia 10 years after diagnosis, and it seems to be related to the chronic inflammation process occurring in the intestine. A greater frequency has also been described in patients who are carriers of oesofagojejunostomies in Roux en Y and ileostomies. This has been related to the continuous contact of the intestinal mucosa with biliopancreatic juice, which could act as a carcinogenic agent.[4-6] A patient from our study had an antecedent of colon cancer; the patient could therefore be treated for Lynch syndrome. Patients with Lynch syndrome have a risk of adenocarcinoma of the small intestine of 4% (100 times greater than in the general population). Tumour screening of the small intestine of these patients is currently being discussed.[5]

As demonstrated in our study, clinical manifestations are unspecific and do not lead toward diagnosis. Normally, these symptoms are unspecific abdominal pain, vomiting, mainly in duodenal tumours when these are obstructive, subocclusive episodes in neoplasias distal to the Treitz angle, palpation of abdominal masses, weight loss, or even acute abdominal symptoms due to perforation.[7]

The most profitable diagnostic tests are upper digestive endoscopy for duodenal tumours, where a sensitivity of 90% is reached, according to a few studies, and this allows for biopsies of suspicious lesions to be taken.[8] In our experience, diagnostic profitability from the upper digestive endoscopy was 50%, and even with this, it is the only test that has been capable of giving a certain diagnosis based on endoscopic findings and confirmed by histological study of the biopsy. The literature estimates that the gastrointestinal transit has a higher number of distal tumours. In our study, this test showed an obstruction or decrease of intestinal lumen in localization of the tumour in 89% of cases. CT provides useful information in studying the tumour's extension, but its output is limited regarding local assessment of the tumour.[1] Capsule endoscopy is described as a very promising technique for diagnosing jejunoileal tumours, because it provides images of all the small intestine; but it does not allow for biopsies to be obtained. The simple image of the mucosa may reveal neoplasia at that level.[8]

Surgical treatment will depend on location and extension of the tumour. At the time of diagnosis, the majority of tumours are invasive and show lymph node or distant metastasis, therefore attributing to a delay in diagnosis. This makes it where the surgery may often not be curative and on occasions, with unresectable tumours, only palliative actions may be taken, as occurring in 5 of our patients. Curative

surgery in distal, jejunal and ileal duodenal tumours consists of segmental intestinal resection and lymphadenectomy; in tumours localized in the second duodenal portion, a cephalic duodenopancreatectomy should be carried out. In the case of infiltration of potentially resectable adjacent viscera, an en bloc extirpation is recommended, just as we did in 2 patients of our study. In our group of patients, retroperitoneal infiltration was the only criterion of unresectability, because of the impossibility of resecting vital structures in that location and therefore not allowing for a curative surgery without leaving a residual tumour. The literature recommends en bloc extirpation of all the tumoural tissue when possible, but in unresectable tumours, bypass surgery is recommended.[5,9] In one of our patients with an unresectable tumour, no bypass was carried out, because the patient no longer presented with obstructive symptoms; in the patient's case, with retroperitoneal infiltration and multiple hepatic metastasis, the vital prognosis seemed to be limited, and therefore the possibility of this leading to intestinal obstruction was small, as what was confirmed in the patient's evolution.

Because of its rare frequency, the role of adjuvant or palliative chemotherapy in locally advanced or metastatic tumours is not clearly defined, and experience is based on descriptions of isolated clinical cases. The majority of cases described refer to locally advanced or metastatic tumours, where a decrease of tumoural size and even complete remissions have been described, and unresectable tumours have become resectable ones. The most frequently used agents were 5-fluorouracil, leucovorin, irinotecan and gemcitabine.[10,11] There is no experience in the use of adjuvant treatment for tumours with lymph node metastasis, but based on promising isolated results, its administration would possibly be suggested for patients with lymph node metastasis.

Prognosis of primary adenocarcinoma of the small intestine is poor, with a general survival rate of 5 years of 20%–30%, as occurring with our patients. The literature describes the following as factors for poor prognosis: advanced age, localization of the tumour in the duodenum, advanced tumoural stage, incomplete tumoural respectability, and the presence of lymph node metastasis.[5,12] The small sampling size of our study does not allow for statistical significance to be reached in many parameters, but it does allow for significant tendencies to be shown. Ileal tumours show a significantly better survival rate than tumours in other locations; however, jejunal tumours show survival similar to duodenal tumours. Nevertheless, the literature estimates that jejunal tumours have a better prognosis than duodenal ones, and there are authors who defend that neoplasias of the small intestine have a better prognosis the more distal they are.[13]

Also and logically, as occurs in our study, the tumoural stage shows a statistically significant tendency (P=.08); the lesser the stage, the greater survival.

In analyzing surgical radicality, we observed a tendency for greater survival for patients whose tumours were resected (P=.09); this was also referred to in the literature. All patients in our study without tumoural resection presented with retroperitoneal infiltration, which was the only criterion for unresectability which we found, and it is therefore also a factor for poor prognosis.

Conclusions

Primary adenocarcinomas of the small intestine are infrequent neoplasias, which are not usually included in differential diagnosis of abdominal symptoms. Curative treatment consists of resection of the intestinal segment. Retroperitoneal infiltration was an unresectability criterion in our patients. Ileal location is a factor for good prognosis. Advanced stages, lymph node metastasis, non-resected cases, and retroperitoneal infiltration tend to be associated with a poor prognosis in our study.

REFERENCES

1. Bruna M, Galindo P, Roig JV, Salvador A, Ismael A, García Fadrique A. Adenocarcinoma primitivo de intestino delgado con presentación de novo. Rev Esp Enferm Dig. 2006;98: 789–90.
2. Kam MH, Barben CP, Eu KW, Seow-Choen F. Small bowel malignancies: A review of 29 patients at a single centre. Colorectal Dis. 2004;6:195–7.
3. Lien GS, Mori M, Enjoji M. Primary carcinoma of the small intestine. A clinicopathological and immunohistochemical study. Cancer. 1988;61:316–23.
4. Palascak-Juif V, Bouvier AM, Cosnes J, Flourié B, Bouché O, Cadiot G, et al. Small bowel adenocarcinoma in patients with Crohn's disease compared with small bowel adenocarcinoma de novo. Inflamm Bowel Dis. 2005;11:828–32.
5. Chaiyasate K, Jain AK, Cheung LY, Jacobs MJ, Mittal VK. Prognostic factors in primary adenocarcinoma of the small intestine: 13-year single institution experience. World J Surg Oncol. 2008;6:1–6.
6. Guadagni S, Catarci M, Ventura T, Leocata P, Carboni M. Primary adenocarcinoma arising in the jejunal limb of a Roux en Y esophagojejunostomy. A case report. Jpn J Clin Oncol. 1993;23:59–63.
7. Rosai J. Adenocarcinoma of the small bowel. In: Ackerman's surgical pathology, Vol. 1. St Louis: Mosby; 1996. p. 686–7.
8. Friedrich-Rust M, Ell C. early stage small bowel adenocarcinoma: review of local endoscopic therapy. Endoscopy. 2005;37:755–9.
9. de Castro SM, van Heek NT, Kuhlmann KF, Busch OR, Offerhaus GJ, van Gulik TM, et al. Surgical management of neoplasms of the ampolla of vater: local resection or pancreatoduodenenctomy and prognostic factors for survival. Surgery. 2004;136:994–1002.
10. Bruckner HW, Hrehorovich VR, Sawhney HS, Meeus SI, Coopeman AM. Chemotherapeutic management of small bowel adenocarcinoma associated with Crohn's disease. J Chemother. 2006;18:545–8.
11. Polyzos A, Kouraklis G, Giannopoulos A, Bramis J, Delladetsima JK, Sfikakis PP. Irinotecan as salvage chemotherapy for advanced small bowel adenocarcinoma: a series of three patients. J Chemother. 2003;15:503–6.
12. Dabaja B, Suki D, Pro B, Bonnen M, Ajani J. Adenocarcinoma of the small bowel. Cancer. 2004;101:518–26.
13. Howe JR, Karnell LH, Menck HR, Scott-Conner C. The American College of Surgeons Commission on cancer and

the merican Cancer Society. Adenocarcinoma of the small bowel: review of the National Cancer Data Base, 1985–1995. Cancer. 1999;86:2693–706.

14. Small intestine. In: American Joint Committee on Cancer: AJCC Cancer Staging Manual. 5th ed. Philadelphia: Lippincott- Raven; 1997. p. 77–81.