CASE REPORT

TJG
The Turkish Journal of Gastroenterology

Small bowel leiomyosarcoma: A case report and literature review

Rob ARTS[1], Koop BOSSCHA[1], Erik RANSCHAERT[2], JEROEN VOGELAAR[1]

Departments of [1]Surgery and [2]Radiology, Jeroen Bosch Hospital, 's-Hertogenbosch, Netherlands

Small bowel neoplasms are very uncommon, especially leiomyosarcoma of the small bowel. Therefore, there is often a delay before small bowel leiomyosarcoma is diagnosed and treatment is started. A 60-year-old Caucasian male was admitted to our hospital with progressive melena. Gastroscopy and colonoscopy did not reveal the cause of the melena, but magnetic resonance imaging showed a jejunal tumor. After laparoscopic resection, the tumor appeared to be a grade 2 leiomyosarcoma. Small bowel neoplasms can be accurately detected by magnetic resonance enterography or wireless capsule endoscopy. Treatment almost always consists of resection of the primary tumor and its metastases. The role of chemo- and radiotherapy is not yet clear and prognosis remains very poor, with low five-year survival rates.

Key words: Leiomyosarcoma, small intestine neoplasms, small bowel tumors, jejunal neoplasms, jejunal tumors

İnce barsak leiyomiyosarkomu: Vaka bildirimi ve literatürün gözden geçirilmesi

İnce barsak neoplazileri, özellikle de leiyomiyosarkomu çok nadirdir. Bu nedenle ince barsak leiyomiyosarkom tanı ve tedavisinde gecikme olmaktadır. 60 yaşında beyaz bir erkek hastanemize devam eden melena şikayetiyle başvurdu. Gastroskopi ve kolonoskopide melenanın nedeni aydınlatılamayınca çekilen manyetik rezonans görüntülemede, jejunal bir tümör görüldü. Laparoskopik rezeksiyonla tümörün evre 2 leiyomiyosarkomu olduğu belirlendi. İnce barsak neoplazileri, manyetik rezonans enterografi veya kablosuz kapsül endoskopi ile doğru şekilde tanınabilir. Tedavi her zaman primer tümör ve metastazlarının rezeksiyonudur. Kemo- ve radyoterapinin tedavideki rolü henüz açık değildir. Prognoz çok kötü ve 5 yıllık sağ-kalım oranı düşüktür.

Anahtar kelimeler: Leiyomiyosarkom, ince barsak neoplazileri, ince barsak tümörleri, jejunal neoplaziler, jejunal tümörler

INTRODUCTION

Malignant tumors in the small intestine are very rare, with an annual incidence of 22.7 per million (1). Less than 5% of all malignancies in the gastrointestinal (GI) tract originate from the small bowel (2). Sarcomas rank fifth (~1.2%) among all malignant small bowel tumors, after carcinoids (~44.3%), adenocarcinomas (~32.6%), lymphomas (~14.7%), and gastrointestinal stromal tumors (GISTs) (~7.2%). Leiomyosarcoma (LMS) is the most common sarcoma that can develop in the small intestine (1). It originates from smooth muscle cells within the muscularis mucosa or muscularis propria. It occurs most frequently in the jejunum, ileum, and duodenum, respectively (3). The highest incidence of LMS is found in the 6th decade, with a small preponderance in males (4). If LMSs elicit symptoms, these are most likely ferriprive anemia and/or recurrent melena. Since small tumors are not likely to cause symptoms, a prolonged period can elapse before these slow-growing tumors are revealed (5). Moreover, as small bowel tumors are not very common, there is often

Address for correspondence: Rob ARTS
Department of Surgery, Jeroen Bosch Hospital,
's-Hertogenbosch, Netherlands
Phone: 00 316 103 85 264
E-mail: rjw.arts@gmail.com

Manuscript received: 04.07.2011 **Accepted:** 08.10.2011

Turk J Gastroenterol 2012; 23 (4): 381-384
doi: 10.4318/tjg.2012.0406

a delay in the diagnosis (6). Therefore, at time of diagnosis, these tumors are mostly far-advanced and are frequently accompanied by complications, which deteriorate the prognosis (7). In this article, we present a patient with an intestinal LMS, and we give an overview of the diagnosis, treatment and prognosis of small bowel LMSs.

CASE REPORT

A 60-year-old Caucasian male with diabetes type 2 was admitted to the Department of Internal Medicine with progressive melena. Routine laboratory examination showed only a ferriprive anemia, i.e. hemoglobin 5.7 mmol/L (8.5-11), mean corpuscular volume (MCV) 78 fl (80-100) and erythrocytes 3.87 x 10^{12}/L (4.5-5.5). No abnormalities were observed in leukocytes, thrombocytes, haptoglobin, liver enzymes, kidney function, and electrolytes. As a bleeding in the upper GI tract was presumed, a gastroscopy was preformed, revealing a flat ulcer in the distal part of the esophagus and a grade IV reflux esophagitis. Because this was presumed to be the cause of the melena and anemia, esomeprazole was started. However, after two months of treatment, the melena persisted, and the anemia worsened, i.e. hemoglobin was decreased to 4.8 mmol/L. Because a second gastroscopy revealed a healed ulcer, a colonoscopy was performed, which did not show any abnormalities. A magnetic resonance (MR) enterography was performed with administration of intravenous contrast. This showed a homogeneously enhancing solid tumor of 4.7 x 3.2 cm in the distal part of the jejunum with malignant morphological characteristics (Figure 1). Further staging procedures showed no local or distant metastases. A radical resection was preformed via a laparoscopic procedure, showing a mobile tumor without any other intra-abdominal abnormalities. Histological analysis revealed a 7 x 7.5 cm tumor, which was positive for vimentin, smooth muscle actin (SMA) and desmin, but negative for CD34, CD117, S-100, HMB-45, and melan-a. Hence, a grade 2 LMS of the jejunum was diagnosed. At the follow-up, the patient was asymptomatic and the anemia had resolved. No further treatment was given.

REVIEW

Small Bowel Evaluation

Preoperative diagnosis of small intestine tumors remains very difficult, especially differentiating between benign and malignant tumors (8). Several radiological methods have been proposed in imaging tumors of the small intestine. For LMS, computed tomography (CT)- and MRI-enterography and enteroclysis have been described (9-11). In a recent review about small bowel imaging (12), it appears that CT- and MR enterography or MR enteroclysis are good options. Which of these three methods is the best remains under debate. As MRI acquires better soft tissue contrast and is therefore more sensitive in detecting (small) mucosal lesions, it has the advantage of differentiating between different tumors based on the T1 and T2 characteristics, and there is no need for ionizing radiation. However, CT is faster and provides a better resolution (12,13). MR enteroclysis is supposed to gain a better distention of small bowel loops than MR enterography, as contrast is administered through a nasojejunal tube (14).

Furthermore, positron emission tomography (PET) imaging has been proven to be contributive, as the level of tumor metabolism correlates with tumor grade, and metastases can be evaluated (15).

Because MRI and CT are not very accurate in detecting smaller superficial lesions, wireless capsule endoscopy (WCE) can be useful. A capsule that acquires images to evaluate the small bowel muco-

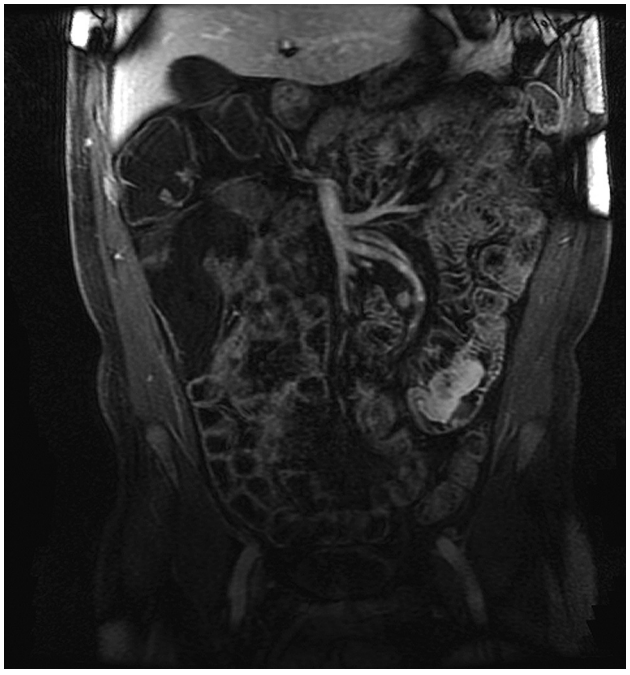

Figure 1. A coronal T1 3D fat suppression MRE in the venous phase with gadolinium-DTPA intravenous contrast, showing a homogeneously enhancing solid tumor of 4.7 x 3.2 cm in the distal part of the jejunum, with malignant morphological characteristics.

sa is swallowed. It appears that the likelihood of detecting small lesions is far higher (up to 80% better) than with conventional methods (16). Another diagnostic tool is enteroscopy, an extended version of gastro- or colonoscopy, also having the advantage of a biopsy. However, it is a difficult examination to perform, requiring substantial experience. Moreover, the detection rates of the different forms of enteroscopy appear to be slightly smaller than with WCE (17). Furthermore, with WCE or enteroscopy, only the lumen can be evaluated; extraluminal growth and metastases cannot be visualized, which is therefore the major disadvantage of these two methods.

Concluding, in our opinion, MRE should be accomplished first, and in symptomatic patients with a negative MRE, WCE should be applied afterwards, as recommended by others (13,14). However, further research is needed to determine the best method to detect small bowel neoplasms.

Histology

Histologically, LMS often has a similar morphologic appearance as gastrointestinal stromal tumor (GIST), so immunohistochemical methods should be applied to differentiate. In the last 10 years, these methods have been developed thoroughly, identifying more GISTs than LMSs. The main antibodies to detect GISTs are aimed at CD117 (KIT) and CD34, which were positive in 76-100% and 60-70% of the GISTs, respectively, and were negative in all studied cases of LMS. To detect LMS, antibodies against desmin and smooth muscle actin (SMA) are required, as most LMSs are positive for these antibodies, while GISTs are positive in only <5% and 20-30%, respectively (18,19).

To stage small bowel LMSs routinely, the Tumor-Node-Metastasis (TNM) classification for soft tissue sarcomas is used (20). Another applied, but more archaic method, is to count mitotic activity. High-grade tumors have 10 or more mitoses per 50 high-power fields (HPF) (21).

Metastases

In a review of 321 cases of LMS, it appeared that 36% had metastases. The location of the tumor, duration of symptoms, and age of the patient were not predictors for metastasis, but metastasis was more likely with a tumor size larger than 5 cm (8). LMS appeared to metastasize hematogenously, especially to the liver (65% of metastases), other GI locations (15%), and the lungs (4%). Moreover, more than with other sarcomas, it does spread lymphogenously (13%) or via peritoneal route (18%) (22).

Treatment

Surgical treatment remains the only effective treatment for small intestine LMS. The primary tumor should be excised radically, including a wide mesenteric resection. No data are available about the effect of radiotherapy in small bowel LMS. Furthermore, LMSs have a very low response rate to chemotherapy (23,24). Therefore, metastasectomy, if possible, should be considered (5,8,25). In the case of hepatic LMS metastases, primary and repeated metastasectomy combined with the resection of extrahepatic metastases showed better survival than chemotherapy (26). Moreover, in the case of unresectable pulmonary metastases, radiofrequency ablation has been shown to be effective on survival (27).

Large phase II and III studies combining docetaxel and gemcitabine yielded impressive response rates in LMSs (mostly of uterine origin) (28,29). However, others were not able to confirm the efficacy of this combination (30). Recently, trabectedin showed response rates up to 56% in LMSs (31), and it appeared to be especially useful in far-advanced and metastatic LMSs after failure of the combination of anthracyclines and ifosfamide (32), which is presently the best standard chemotherapy available in soft tissue sarcomas (33,34). Nonetheless, all effects are only small, and none of these treatments has been proven effective in small bowel LMS.

Prognosis

The prognosis of patients with a small intestine LMS is very poor. In a review of 22 series with 705 patients in total, the five-year survival was 27.8% (range, 10 to 48%), but it has to be mentioned that in this analysis, tumor grade and number of metastases were not taken into account (8). In low-grade disease, the five-year survival rate was 55%, in contrast to 5-20% in high-grade disease, which is most common (20,35). No specific data are available about metastatic small bowel LMS.

In conclusion, small bowel LMS is a very rare diagnosis. In this case report, we showed that in case of melena, the diagnosis of a small bowel tumor should always be considered. MRI and WCE are good methods to detect small bowel tumors. The prognosis of small bowel LMS remains very poor. Resection of the primary tumor is nearly always indicated and should in specific cases be combined with metastasectomy. The real value of chemotherapy remains to be assessed.

REFERENCES

1. Bilimoria KY, Bentrem DJ, Wayne JD, et al. Small bowel cancer in the United States. Ann Surg 2009; 249: 63-71.
2. Jemal A, Siegel R, Ward E, et al. Cancer statistics, 2008. CA Cancer J Clin 2008; 58: 71–96.
3. Akwari OE, Dozois RR, Weiland LH, Beahrs OH. Leiomyosarcoma of the small and large bowel. Cancer 1978; 42: 1375-84.
4. Evans HL. Smooth muscle tumors of the gastrointestinal tract: a study of 56 cases followed for a minimum of 10 years. Cancer 1985; 56: 2242-50.
5. Gill SS, Heuman DM, Mihas AA. Small intestinal neoplasms. J Clin Gastroenterol 2001; 33: 267-82.
6. Catena F, Ansaloni L, Gazzotti F, et al. Small bowel tumours in emergency surgery: specificity of clinical presentation. ANZ J Surg 2005; 75: 997-9.
7. North JH, Pack MS. Malignant tumors of the small intestine: a review of 144 cases. Am Surg 2000; 66: 46-51.
8. Blanchard DK, Budde JM, Hatch GF 3rd, et al. Tumors of the small intestine. World J Surg 2000; 24: 421-9.
9. Maglinte DDT, Kelvin FM, O'Connor K, et al. Current status of small bowel radiography. Abdom Imag 1996; 21: 247-57.
10. Megibow AJ, Balthazar EJ, Hulnick DH, et al. CT evaluation of gastrointestinal leiomyomas and leiomyosarcomas. Am J Roentgenol 1985; 144: 727-31.
11. Ohinishi T, Yoshioka H, Ishida O. MR imaging of gastrointestinal leiomyosarcoma. Radiat Med 1991; 9: 114-7.
12. Jarman BT. Small bowel imaging. Surg Clin N Am 2011; 91: 109-25.
13. Fidler JF, Guimaraes L, Einstein DM. MR imaging of the small bowel. RadioGraphics 2009; 29: 1811-25.
14. Masselli G, Gualdi G. Evaluation of small bowel tumors: MR enteroclysis. Abdom Imaging 2010; 35: 23-30.
15. Punt S, Eary JF, O'Sullivan J, Conrad EU. Fluorodeoxyglucose positron emission tomography in leiomyosarcoma: imaging characteristics. Nucl Med Commun 2009; 30: 546-9.
16. Triester SL, Leighton JA, Leontiadis GI, et al. A meta-analysis of the yield of capsule endoscopy compared to other diagnostic modalities in patients with obscure gastrointestinal bleeding. Am J Gastroenterol 2005; 100: 2407-18.
17. Rockey DC. Occult and obscure gastrointestinal bleeding: causes and clinical management. Nat Rev Gastroenterol Hepatol 2010; 7: 265-79.
18. Miettinen M, Kopczynski J, Makhlouf HR, et al. Gastrointestinal stromal tumors, intramural leiomyomas, and leiomyosarcomas in the duodenum: a clinicopathologic, immunohistochemical, and molecular genetic study of 167 cases. Am J Surg Pathol 2003; 27: 625-41.
19. Miettinen M, Sarlomo-Rikala M, Sobin LH, Lasota J. Gastrointestinal stromal tumors and leiomyosarcomas in the colon : a clinicopathologic, immunohistochemical, and molecular genetic study of 44 cases. Am J Surg Pathol 2000; 24: 1339-52.
20. Edge SB, Byrd DR, Compton CC, et al. AJCC (American Joint Committee on Cancer) Cancer Staging Manual. 7th ed. New York: Springer, 2010; 285.
21. Dougherty MJ, Compton C, Talbert M, Wood WC. Sarcomas of the gastrointestinal tract. Separation into favorable and unfavorable prognostic groups by mitotic count. Ann Surg 1991; 214: 569–74.
22. Skandalakis JE, Gray SW, Skandalakis LJ. Metastasis of malignant smooth muscle tumors of the gastrointestinal tract: pattern and process. J Med Assoc Ga 1991; 80: 701-9.
23. Lindberg RD, Martin RG, Romsdahl MM, Barkley HT Jr. Conservative surgery and postoperative radiotherapy in 300 adults with soft-tissue sarcomas. Cancer 1981; 47: 2391-7.
24. Fernandez-Trigo V, Sugarbaker PH. Sarcomas involving the abdominal and pelvic cavity. Tumori 1993; 79: 77-91.
25. Donohue JH. Malignant tumours of the small bowel. Surg Oncol 1994; 3: 61-8.
26. Lang H, Nussbaum KT, Kaudel P, et al. Hepatic metastases from leiomyosarcoma: a single-center experience with 34 liver resections during a 15-year period. Ann Surg 2000; 231: 500-5.
27. Ding JH, Chua TC, Glenn D, Morris DL. Feasibility of ablation as an alternative to surgical metastasectomy in patients with unresectable sarcoma pulmonary metastases. Interact Cardiovasc Thorac Surg 2009; 9: 1051-3.
28. Hensley ML, Maki R, Venkatraman E, et al. Gemcitabine and docetaxel in patients with unresectable leiomyosarcoma: results of a phase II trial. J Clin Oncol 2002; 20: 2824-31.
29. Maki RG, Wathen JK, Patel SR, et al. Randomized phase II study of gemcitabine and docetaxel versus gemcitabine alone in patients with metastatic soft tissue sarcomas: results of sarcoma alliance for research through collaboration study 002. J Clin Oncol 2007; 25: 2755–63.
30. Duffaud F, Bui BN, Penel N, et al. A FNCLCC French Sarcoma Group–GETO multicenter randomized phase II study of gemcitabine versus gemcitabine and docetaxel in patients with metastatic or relapsed leiomyosarcoma. J Clin Oncol 2008; 26: abstr 10511.
31. Le Cesne A, Judson I, Crowther D, et al. Randomized phase III study comparing conventional-dose doxorubicin plus ifosfamide versus high-dose doxorubicin plus ifosfamide plus recombinant human granulocyte macrophage colony-stimulating factor in advanced soft tissue sarcomas: a trial of the European Organisation for Research and Treatment of Cancer/Soft Tissue and Bone Sarcoma Group. J Clin Oncol 2000; 18: 2676-84.
32. Demetri GD, Chawla SP, von Mehren M, et al. Efficacy and safety of trabectedin in patients with advanced or metastatic liposarcoma or leiomyosarcoma after failure of prior anthracyclines and ifosfamide: results of a randomized phase II study of two different schedules. J Clin Oncol 2009; 27: 4188-96.
33. Bramwell VH, Anderson D, Charette ML. Doxorubicin-based chemotherapy for the palliative treatment of adult patients with locally advanced or metastatic soft tissue sarcoma. Cochrane Database Syst Rev 2003; (3): CD003293.
34. Le Cesne A, Blay JY, Judson I, et al. Phase II study of ET-743 in advanced soft tissue sarcomas: a European Organisation for the Research and Treatment of Cancer (EORTC) soft tissue and bone sarcoma group trial. J Clin Oncol 2005; 23: 576-84.
35. Licht JD, Weissmann LB, Antman K. Gastrointestinal sarcomas. Semin Oncol 1988; 15: 181-8.