Two cases of primary leiomyosarcoma of sigmoid colon treated with laparoscopic surgery: a case report and a review of literature

Ali-Mohammad Bananzadeh  
Shiraz University of Medical Sciences

Maral Mokhtari  
Shiraz University of Medical Sciences

Maryam Sohooli  
Shiraz University of Medical Sciences

Ramin Shekouhi  (shekouhi.ramin@gmail.com)  
Shiraz Medical School: Shiraz University of Medical Sciences

Research Article

Keywords: colon cancer, leiomyosarcoma, sigmoid colon

DOI: https://doi.org/10.21203/rs.3.rs-214702/v1

License: ☎️️ ️ This work is licensed under a Creative Commons Attribution 4.0 International License.  Read Full License
Abstract

Background

Leiomyosarcoma (LMS) of the colon is an unbelievably rare and highly invasive tumor arising from the muscularis propria of the gastrointestinal tract. After the introduction of the oncogenic role of KIT by immunohistochemistry (IHC), the reported cases of gastrointestinal leiomyosarcoma were limited. True LMS of the colon is such a rare disorder that there isn’t enough description of its nature. The classical colon LMS presents with a vast majority of non-specific symptoms including mild abdominal pain, fresh/obscure rectal bleeding, and weight loss. Case presentation: we experienced two extremely rare cases of colonic LMS. First patient was a 48-year-old man referred to our surgical outpatient clinic with mild intermittent abdominal pain and occasional rectal bleeding. After the initial investigation patient underwent colonoscopy that was suggestive of a large polypoid mass in 15 centimeters from the anal verge. Histopathology and Subsequent immunohistochemistry were in favor of LMS of sigmoid colon, and he underwent Laparoscopic anterior resection. The second patient was a 49-year-old man with 3-month history of fatigue, melena, and unintentional weight loss. Colonoscopy revealed a large circumferential mass in sigmoid colon 40 cm from the anal verge with the diagnosis of LMS. He underwent Laparoscopic left hemicolecctiony. Conclusion: Herein, we reported two rare cases of primary leiomyosarcoma of sigmoid colon treated with laparoscopic surgery. The tumors were surgically removed via laparoscopic approach. Overall, colonic LMS is a highly invasive neoplasm with poor oncologic outcome.

Background:

Leiomyosarcoma (LMS) of the colon is an unbelievably rare and highly invasive tumor arising from the muscularis propria of the gastrointestinal tract.[1] Before 1998, every neoplasm raised from mesenchymal cells was mistakenly classified as LMS; However, after the introduction of the oncogenic role of KIT by immunohistochemistry (IHC), only a very small number of true gastrointestinal leiomyosarcomas was reported[2]. Immunohistochemically, true LMS expresses actin (SMA) and desmin without the expression of GIST markers (CD117, CD34, and DOG1) and KIT mutations, which allows distinguishing LMS from other GI mesenchymal neoplasms[1, 3]. We herein describe two rare cases of Leiomyosarcoma of sigmoid colon that were treated with laparoscopic resection.

Case Presentation:

Case 1:

We reported a case of a 48-year-old man referred to our surgical outpatient clinic in December 2019. He presented with mild intermittent abdominal pain and occasional rectal bleeding for eight months without any history of weight loss, fatigue or night sweating. Furthermore, he had a blank family history of malignant neoplasia. General examination and vital signs were normal. Abdominal examinations revealed an ill-defined round mass at the left lower quadrant. Digital rectal examination was normal. Routine lab data were unremarkable, except mild microcytic anemia that was due to his thalassemia trait (Mentzer index=13.46). Carcinoembryonic antigen (CEA) test was normal. After the initial investigation patient underwent colonoscopy that was suggestive of a large polypoid mass with hard texture in 15 centimeters from the anal verge; rest of the colon were unremarkable.

Histopathology revealed a neoplasm consists of spindle cells with hyperchromatic nuclei and mild pleomorphism. Subsequent immunohistochemistry showed immunoreactivity for smooth muscle actin and desmin but the tumor cells were negative for S100, CD34, C-KIT and DOG-1. The Ki-67 index was 15-20%. KIT mutation study also showed no mutation in exon 9, 11, 13 and 17. Therefore, the diagnosis of leiomyosarcoma was made.

Treatment:
Before the operation, patient was scheduled for a routine metastatic workup with Contrast-enhanced computed tomography (CT) of thoracic and abdomen and pelvis, and liver function test (LFT). The abdominal CT showed diffuse wall thickening of the sigmoid colon and distal part of the left colon associated with enhancing soft tissue mass measuring about 72×40 mm in sigmoid colon that was suggestive of a malignant process. Also, evidence of multiple regional lymph nodes was seen adjacent to the sigmoid colon. Chest CT and Liver function test (LFT) were unremarkable. The surgery was conducted under general anesthesia with the purpose of complete resection of the tumor and involved lymph nodes. Laparoscopic anterior resection was performed with resection of sigmoid colon and upper part of rectum. Colorectal anastomosis was performed with no diverting ileostomy. Tumor dimensions were 8×6×4.5 cm with a smooth surface and the cross-section showed homogenous white appearance. The specimen was sent for IHC profiling and histologic evaluation.

Outcome and Follow-up:

The post-operative course was uneventful without any signs of short-term complications. The patient discharged four days after surgery. The patient was scheduled for Contrast-enhanced computed tomography (CT) of thoracic and abdomino-pelvic every 6 months, and colonoscopy every 12 months. Patient has no signs of local recurrence or distant metastasis. We will follow the patient for at least 5 years of close surveillance.

Case 2:

On April 29th 2020, a 49-year-old man came to Shiraz Colorectal Clinic with 3-month history of fatigue, melena, and unintentional weight loss. Family history was negative for any previous disease. General examination showed temporal wasting and cachexia. Vital signs and abdominal examinations were unremarkable. Digital rectal examination showed grade-II internal hemorrhoids. Lab data was in favor of microcytic-hypochromic anemia (HB=11.7). Carcinoembryonic antigen (CEA) test was normal. Colonoscopy revealed a large 3×4×3.5 cm circumferential mass with deep central ulceration in sigmoid colon 40 cm from anal verge.

Prior to surgery, Abdomino-perineal CT showed circumferential wall thickening of distal descending colon in Lt. lower quadrant with maximum wall thickness of 24 mm and length of involvement about 43 mm. Also, thickening of adjacent peritoneum was demonstrated. Pre-op chest CT was normal.

Treatment:

Laparoscopic left hemicolectomy was conducted under general anesthesia with the purpose of complete resection of the tumor and involved lymph nodes. The specimen was extracted via a mid-midline incision and extra-corporal anastomosis was done. The specimen was sent for IHC profiling and histologic evaluation.

Outcome and Follow-up:

Surgery was successfully performed without any short-time complications and patient was discharged 4 days after surgery. Histology of tumor was suggestive of spindle cells with hyperchromatic nuclei with moderate pleomorphism (mitotic activity> 5 / 50 HPF). IHC results were positive for desmin and SMA. Ki-67 was positive in 15-20% of neoplastic cells. C-KIT, CD34, DOG1, and S100 were negative. Furthermore, histologic evaluations revealed peritoneal and abdominal wall involvement by high grade sarcoma. He was referred to an oncologist for chemotherapy initiation with Adriamycin, and Ifosfamide. The patient was scheduled for Contrast-enhanced computed tomography (CT) of Thoracic and Abdomino-pelvis every 6 months, and colonoscopy every 12 months. Follow-up CT scan revealed multiple small nodules in both lungs with the largest being 4-mm in lateral segment of right lower lobe in favor of metastatic lesions. Abdominal CT showed multiple malignant-looking lesion in peritoneal cavity with the largest being 38×39 mm. Patient is alive and is under close follow up by an oncologist.

Discussion:
GISTs are the most common mesenchymal GI malignancies with the incidence of 1–3 % of all GI malignancies. Moreover, LMS is an extremely rare cancer representing 3–6% of all GI mesenchymal tumors. They arise from muscularis mucosae or propria occurring mostly in middle-aged males[3, 4]. In the pre-KIT area, most of the GI mesenchymal malignancies were wrongfully diagnosed as leiomyoma, LMS, or leiomyoblastomas. However, their incidence declined after the diagnosis of KIT mutations and the immunohistochemical differences between LMS and other GI mesenchymal tumors, particularly GISTs[5].

In 1998, Hirota et al identified the presence of activating KIT-mutations in 94% of GISTs[6]. Kit gene, a tyrosine kinase receptor proto-oncogene, causes increased cellular proliferation. Subsequently, this mutation can lead to cellular atypia and neoplasia. Later studies confirmed that 95% of GISTs expressed CD34, CD137, and DOG1.1 [7]. On the contrary, the LMS is negative for kit-mutations and mostly positive for desmin, SMA, h-caldesmon, and vimentin[8].

Differentiation between LMS and GISTs is paramount importance since they have very similar clinical presentations but require radically different courses of treatment. The cellular origin of GISTs, the interstitial cells of Cajal, was first introduced in mid-1990s. however, LMS originates from muscle fibers of the muscularis mucosae and muscularis propria [9]. Most of the colon LMS are polypoid, while esophageal LMS is mainly intramural[10].

The most common location of GI involvement in GISTS is in the stomach (55%), small intestine (29%), colon (2.9%), and rectum (2.7%) [11]. Furthermore, GI LMS mainly involves stomach followed by small intestines, rarely colon and rectum[12]. True LMS of the colon is such a rare disorder that there isn't enough description of its nature. The classical colon LMS presents with a vast majority of non-specific symptoms including mild abdominal pain, fresh/obscure rectal bleeding, intra-abdominal hemorrhage, weight loss, changes in bowel habits, bowel obstruction, and tenesmus. [13] Diagnosis is based on colonoscopy and histologic evaluation and IHC profiling.

Based on our survey, there are only thirty-four previous cases of published colonic LMS after the pre-kit era that was confirmed with immunohistochemistry (Table 1). The most common location for colonic LMS is the sigmoid colon, followed by the ascending colon. The prognostic factors for the disease outcome have not been established properly. The most important prognostic factor for survival and recurrence seemed to be age, tumor grade, disseminated disease and tumor size[14]. Yamamoto et al, concluded that the only negative predictive factor for survival is tumor size of more than 5 centimeters[15]. However, based on previous case studies local and distal recurrence occurred even with favorable tumor features[13]. Compared with adults, infantile LMS has a better prognosis even with poor histologic features[16].
All cases of published colonic LMS after the pre-kit era.

| Case  | Year | Age | Sex | site  | Size (CM) | Local recurrence | Metastasis | survival | α- kit | α- SMA | Desmin | CD-34 |
|-------|------|-----|-----|-------|-----------|------------------|------------|----------|--------|--------|--------|-------|
| 1     | 2000 | 54  | M   | D     | 3.2       | U                | U          | Dead     | Neg    | Pos+   | Pos+   | Neg   |
| 2     | 2000 | 61  | M   | A     | 4.2       | None            | None       | Alive    | Neg    | Pos+   | U      | Neg   |
| 3     | 2000 | 75  | M   | A     | 6.5       | U                | U          | Dead     | Neg    | Pos+   | U      | Neg   |
| 4     | 2000 | 76  | F   | C     | 7.8       | U                | U          | Dead     | Neg    | Pos+   | U      | Neg   |
| 5     | 2000 | 36  | F   | S     | 6.5       | None            | Lung       | Dead     | Neg    | Pos+   | Pos+   | Neg   |
| 6     | 2000 | 66  | M   | A     | U         | None            | Liver      | Dead     | Neg    | Pos+   | U      | Neg   |
| 7     | 2000 | 41  | M   | C     | 7.5       | None            | Humerus    | Alive    | Neg    | Pos+   | Pos+   | Neg   |
| 8     | 2004 | 65  | M   | D     | 10        | None            | Positive(U)| Dead     | Neg    | Pos+   | Pos+   | Neg   |
| 9     | 2004 | 67  | F   | T     | 5.7       | None            | None       | Alive    | Neg    | Pos+   | U      | Neg   |
| 10    | 2007 | 77  | F   | S     | U         | Positive        | None       | U        | Neg    | Pos+   | Pos+   | Neg   |
| 11    | 2007 | 52  | M   | S     | U         | None            | Liver      | U        | Neg    | Pos+   | Pos+   | Neg   |
| 12    | 2009 | 74  | F   | A     | 6         | None            | Lung       | Dead     | Neg    | Pos+   | U      | U     |
| 13    | 2011 | 70  | F   | S     | 3.7       | None            | None       | Dead     | Neg    | Pos+   | Pos+   | Neg   |
| 14    | 2011 | 56  | M   | C     | U         | None            | Liver      | Alive    | Neg    | Pos+   | Pos+   | Neg   |
| 15    | 2012 | 66  | F   | S     | 3         | None            | Liver      | Dead     | Neg    | Pos+   | Pos+   | Neg   |
| 16    | 2013 | 94  | F   | D     | 25        | None            | Liver      | Dead     | Neg    | Pos+   | U      | Neg   |
| 17    | 2013 | 56  | M   | S     | 1         | None            | LN         | Alive    | Neg    | Pos+   | U      | Neg   |
| 18    | 2013 | 78  | F   | S     | 8.5       | None            | Lung       | Dead     | Neg    | Pos+   | U      | Neg   |
| 19    | 2013 | 87  | M   | T     | 11        | None            | None       | Dead     | Neg    | Pos+   | U      | Neg   |
| 20    | 2013 | 65  | M   | S     | U         | None            | None       | Alive    | Neg    | Pos+   | U      | U     |
| 21    | 2014 | 66  | F   | T     | 4         | None            | None       | Alive    | Neg    | Pos+   | U      | Neg   |
| 22    | 2014 | 65  | M   | S     | U         | None            | None       | Alive    | Neg    | Pos+   | U      | U     |
| 23    | 2015 | 46  | M   | T     | 11.8      | Positive        | None       | Alive    | Neg    | Pos+   | U      | Neg   |
| 24    | 2015 | 89  | F   | A     | 4.5       | None            | Liver      | U        | Neg    | Pos+   | U      | U     |
| 25    | 2015 | 54  | M   | A     | 13        | Positive        | None       | Alive    | Neg    | Pos+   | Pos+   | Neg   |
| 26    | 2015 | 59  | M   | A     | 10        | None            | None       | Alive    | Neg    | Pos+   | Pos+   | Neg   |
| 27    | 2016 | 89  | M   | C     | 2.2       | None            | None       | Alive    | Neg    | Pos+   | Pos+   | U     |
| 28    | 2016 | 51  | F   | D     | 4         | None            | None       | Alive    | Neg    | Pos+   | Pos+   | Neg   |
| 29    | 2016 | 44  | M   | SF    | 8.5       | None            | None       | Alive    | Neg    | Pos+   | Pos+   | Neg   |
| 30    | 2017 | 55  | F   | A     | 8         | None            | None       | Alive    | Neg    | Pos+   | Pos+   | Neg   |
| 31    | 2018 | 57  | F   | S     | U         | U               | U          | Alive    | Neg    | Pos+   | U      | Neg   |
According to the recent survey by Faraj et al., lymph node involvement is very unlikely and distant metastasis is mostly by hematogenous spread\[17\]. Liver is the most common site of secondary tumor metastasis followed by lungs and peritoneum. Due to the paucity of data, there is not enough evidence to establish reliable mortality estimates. However, based on a study by Aggarwal et al. in 2012 only 2 of 11 cases of colon LMS survived in 5-year surveillance\[1\]. The main cause of death was spreading of the primary tumor and multiple organ failure\[1\].

Medical therapy is the main course of treatment in mesenchymal GI malignancies, particularly GISTs. However, Due to absence of KIT-mutations in LMS, tyrosine kinase inhibitors (TKI) are not effective in tumor treatment. Therefore, Surgery is considered as the gold standard treatment for LMS\[18\]. Since, there are only a few numbers of true LMS cases reported, no standard therapeutic strategy has been established. Radical excision is the most reasonable option since even with low-grade tumors recurrences occurred\[19\]. According to YTNM Lee et al., all cases of smooth muscle sarcomas, should undergo wide excisional surgery with 4 cm tumor margin involving mesentery\[20\].

Although lymph node involvement is very uncommon in LMS, lymph node dissection is recommended due to its highly invasive nature\[3, 15\]. Anthracyclines, first-line conventional chemotherapy regimen for soft tissue sarcomas, have minimal to no effect on LMS. A multi-drug regimen of Doxorubicin plus dacarbazine may have some clinical response in treatment. In conclusion, Adjuvant chemotherapy is unnecessary when tumors are completely resected. \[18\]. However, neoadjuvant chemotherapy may decrease the risk of local recurrence in some cases of rectal sarcomas\[21\]. Furthermore, radiotherapy is completely unbeneicial since LMS is highly radio-resistant\[22\].

**Conclusion:**

Herein, we described two rare cases of colon LMS which was confirmed with IHC. The tumors were surgically removed via laparoscopic approach, with wide, tumor-free margins. Due to the rarity of disease, there is not enough information about tumor characteristics. Overall, colonic LMS is a highly invasive neoplasm with poor oncologic outcome.

**Declarations**

**Availability of data and materials:**
All data generated or analyzed during this study are included in this published article.

**Acknowledgements:**
Not applicable.

**Funding:**
No funding was obtained for this study.

**Compliance with ethical standards:**

**Conflict of interest:** The authors declare that they have no competing interests.
**Ethics Approval and consent to participate:** The purpose of this research was completely explained to the patient, and was assured that their information will be kept confidential by the researchers. The present study was approved by the medical ethics committee of the academy.

**Consent for publication:**

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

**Authors' contributions:**

AB – drafted the manuscript and provided images. MS- helped with the draft and reviewed the literature. MM- provided histologic evaluations. RS- Supervisor, provided initial feedback and reviewed the final manuscript (corresponding author). The authors read and approved the final manuscript.

**References**

1. Aggarwal G, et al. Primary leiomyosarcomas of the gastrointestinal tract in the post–gastrointestinal stromal tumor era. Annals of diagnostic pathology. 2012;16(6):532–40.
2. Katz SC, DeMatteo RP. Gastrointestinal stromal tumors and leiomyosarcomas. Journal of surgical oncology. 2008;97(4):350–9.
3. Yahagi M, et al. Laparoscopic surgery to treat leiomyosarcomas of the sigmoid colon: a case report and literature review. Surgical Case Reports. 2019;5(1):20.
4. Kiran P, et al. Diagnosis of leiomyosarcoma of colon. J Cancer Res Ther. 2015;11(4):1035.
5. Kono M, et al. Primary leiomyosarcoma of the colon. Clinical journal of gastroenterology. 2015;8(4):217–22.
6. Hirota S, et al. Gain-of-function mutations of c-kit in human gastrointestinal stromal tumors. Science. 1998;279(5350):577–80.
7. Liegl B, et al. Monoclonal antibody DOG1. 1 shows higher sensitivity than KIT in the diagnosis of gastrointestinal stromal tumors, including unusual subtypes. Am J Surg Pathol. 2009;33(3):437–46.
8. Yang J. Primary leiomyosarcoma in the colon: A case report. Medicine, 2018. 97(7).
9. Miettinen M, Lasota J. Gastrointestinal stromal tumors: review on morphology, molecular pathology, prognosis, and differential diagnosis. Arch Pathol Lab Med. 2006;130(10):1466–78.
10. Agaimy A, Wünsch PH. True smooth muscle neoplasms of the gastrointestinal tract: morphological spectrum and classification in a series of 85 cases from a single institute. Langenbeck's archives of surgery. 2007;392(1):75–81.
11. Ma GL, et al. Epidemiology of gastrointestinal stromal tumors in the era of histology codes: results of a population-based study. Cancer Epidemiology Prevention Biomarkers. 2015;24(1):298–302.
12. Singh P, et al. Rectal leiomyosarcoma in association with ulcerative colitis: a rare condition with an unusual presentation. Int J Colorectal Dis. 2014;29(7):887–8.
13. Crystal JS, et al., Primary leiomyosarcoma of the colon: a report of two cases, review of the literature, and association with immunosuppression for IBD and rheumatoid arthritis. Case reports in surgery, 2018. 2018.
14. Gladdy RA, et al. Predictors of survival and recurrence in primary leiomyosarcoma. Ann Surg Oncol. 2013;20(6):1851–7.
15. Yamamoto H, et al. Clinicopathological features of primary leiomyosarcoma of the gastrointestinal tract following recognition of gastrointestinal stromal tumours. Histopathology. 2013;63(2):194–207.
16. Yamamoto H, et al. Infantile intestinal leiomyosarcoma is prognostically favorable despite histologic aggressiveness: case report and literature review. Journal of pediatric surgery. 2004;39(8):1257–60.
17. Faraj W, et al. Liver resection for metastatic colorectal leiomyosarcoma: a single center experience. Journal of gastrointestinal oncology. 2015;6(5):E70.
18. Group EESNW. Soft tissue and visceral sarcomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2014;25(suppl_3):iii102–12.

19. Ng E. N, Pollock RE, Munsell MF, Atkinson EN, Romsdahl MM. 1992 Prognostic factors influencing survival in gastrointestinal leiomyosarcoma: implications for surgical management and staging. Ann Surg. 215: p. 68–77.

20. Lee Y-TNM. Leiomyosarcoma of the gastro-intestinal tract: general pattern of metastasis and recurrence. Cancer treatment reviews. 1983;10(2):91–101.

21. Luna-Pérez P, et al. Colorectal sarcoma: analysis of failure patterns. Journal of surgical oncology. 1998;69(1):36–40.

22. Koczkowska M, et al. Primary leiomyosarcoma of the mesentery in two sisters: clinical and molecular characteristics. Pol J Pathol. 2013;64(1):59–63.

23. Miettinen M, et al. Gastrointestinal stromal tumors and leiomyosarcomas in the colon: a clinicopathologic, immunohistochemical, and molecular genetic study of 44 cases. Am J Surg Pathol. 2000;24(10):1339–52.

24. Insabato L, et al. Malignant gastrointestinal leiomyosarcoma and gastrointestinal stromal tumor with prominent osteoclast-like giant cells. Arch Pathol Lab Med. 2004;128(4):440–3.

25. Michalopoulos A, et al. Colorectal gastrointestinal mesenchymal tumours. Report of a stromal case of the rectum (GIST) and a leiomyosarcoma of the transverse colon. Tech Coloproctol. 2004;8(1):s155–7.

26. Alvite CM, et al., Leiomyosarcoma of the colon with lung metastases as the first manifestation. Revista espanola de enfermedades digestivas: organo oficial de la Sociedad Espanola de Patologia Digestiva, 2009. 101(2): p. 145.

27. Resch T, et al. Leiomyosarcoma of the colon: unresolved issues of a rare but highly aggressive malignancy. Am Surg. 2011;77(4):E62.

28. Hamai Y, et al. Leiomyosarcoma of the sigmoid colon with multiple liver metastases and gastric cancer: a case report. BMC Gastroenterol. 2012;12(1):98.

29. Samie AA, et al. Leiomyosarcoma of the sigmoid colon: a rare cause of intestinal intussusception. Journal of gastrointestinal cancer. 2014;45(1):6–9.

30. Yaren A, et al. Primary mesenchymal tumors of the colon: a report of three cases. Turk J Gastroenterol. 2014;25(3):314–8.

31. Granero-Peiró L, et al. Leiomyosarcoma of the ascending colon: a rare tumor with poor prognosis. Revista Española de Enfermedades Digestivas. 2015;107(9):580–1.

32. Janevski V, et al. Leiomyosarcoma of the colon. Medicinski Pregled. 2015;68(11–12):413–7.

33. Kim VM, Goicochea L, Fang SH. Case report: collision tumour of colon leiomyosarcoma and adenocarcinoma. Journal of clinical diagnostic research: JCDR. 2016;10(6):PD03.

34. Akutsu D, et al. A rare case of colonic leiomyosarcoma in association with ulcerative colitis. Intern Med. 2016;55(19):2799–803.

35. Jideh B, Yang T, Turner IB. Rectal bleeding due to leiomyosarcoma. Clinical Gastroenterology and Hepatology, 2017: p. e1-e2.

36. Devriendt S, Leman G, Vanrykel F. Primary leiomyosarcoma of the colon: a case report and review of the literature. Acta Chirurgica Belgica, 2019: p. 1–4.