ABSTRACT

Leiomyosarcoma (LMS) of the colorectal tract is a rare malignant entity with an unfavourable prognosis, and responds poorly to conventional chemo-radiation therapy. Only a few cases of the LMS of colorectum have so far been reported earlier. Here we report two such cases of primary leiomyosarcoma of sigmoid colon and rectum. Due to histological similarity with gastrointestinal stromal tumour (GIST), previously the LMS cases were misdiagnosed as GIST. This is essentially a pathological diagnosis having a similar histomorphological appearance that of GIST, but a different Immunohistochemistry profile, in contrast to GIST. Immunohistochemically LMS are negative for CD34, CD117 and DOG1 and positive for desmin as detected in this report. GIST is curable with surgery followed by imatinib (in intermediate /high-risk patients) while LMS behaves aggressively requiring radical excision of the tumour followed by intensive cytotoxic chemotherapy regimens. Thus it is important to diagnose LMS definitively by immunohistochemical profiling as the prognosis and treatment of these tumours vary from others as mentioned.

KEYWORDS
Leiomyosarcoma, colon, rectum, Immunohistochemistry, Rare case

Background

Primary LMS of colon and rectum are an extremely rare and diverse group of mesenchymal tumours of lower gastrointestinal tract accounting for 0.12 and < 0.1% of all colorectal malignancies, respectively [1, 2]. They are often misdiagnosed as GIST [3, 4]. Primary colorectal LMS is recognized as a distinct entity from GIST due to their dramatically worse prognosis [5]. Due to rarity, only, few cases have been reported related to colorectal LMS in India by Kiran et al. [4] and Kumar et al. [5]. At present, we report two such rare cases of primary LMS of sigmoid colon and rectum from India.

Case report

Case 1

Clinical details: A 58-year-old male patient presented with intermittent and worsening abdominal pain and weight loss was admitted in a private hospital in Ahmedabad in March 2019. His Laboratory tests showed iron-deficiency anaemia, leucocytosis (15,800/mL) and negative tumour markers - CEA and CA19.9. On USG there was a mass in lower abdomen with unclear boundaries. CT Abdomen showed bulky and a continuous bulging, solid enhancing mass measuring 11.0 cm in diameter outside the colonic wall in the sigmoid colon. Colonoscopy showed normal lumen. There was no evidence of metastatic dissemination. Therefore, resection of the tumour was performed by laparotomy.

Gross examination showed a solid whitish nodular tumour in the sigmoid colon forming subserosal mass measuring 12.0 cm in maximum diameter. Luminal mucosa was unremarkable.

Microscopic examination revealed a tumour composed of diffuse proliferation of spindle cells arranged in fascicles forming a whorled pattern. Tumour cells reveal marked nuclear pleomorphism, frequent mitosis and many tumour giant cells. Surgical margins and mesenteric nodes were free of tumour (Fig 1.A).

Desmin is immunoreactive as an indicator for LMS in addi-
Case 2

Clinical details: 62 yr female patient presented with c/o bleeding P/R and constipation. On physical examination, there was a growth in her rectum approximately 6.0 cm from the anal margin. Pelvic magnetic resonance imaging showed a rectal mass with a parietal attachment that invaded the fascia and perirectal soft tissue. We received a biopsy from rectal growth. On gross examination, there were three greyish-white soft tissue bits, in aggregates measuring 2.5 x1.0x0.8 cm, all processed for HP evaluation. Microscopic examination revealed a tumour composed of spindle cells arranged in fascicles with nuclear atypia, frequent mitosis (>10/10 HPF) and mucosal ulceration (Fig 1.E). IHC marker results were also similar to Case 1(Figure 1.F, Table 1).

Discussion

LMS is a malignant mesenchymal tumour arising from smooth muscles. It originates from the muscularis propria layer of the bowel. It is important to distinguish the diagnosis of LMS from other GI mesenchymal tumours, particularly GIST, as the two diseases have different treatments and prognoses [11].

Due to increased incidence and histological similarity with GIST, in past leiomyosarcoma, were misdiagnosed as GIST. It is essential to diagnose LMS definitively by immunohistochemical profiling as the diagnosis and treatment of these tumours vary. Immunohistochemistry is the crux of the diagnosis. GIST stains positive for CD 34, C-kit (CD 117) and DOG1 and stains negative for desmin in contrast to leiomyosarcoma which is positive for desmin and negative for SMA, CD117, CD34, and DOG1 [2] (Table 1).

The typical presentation of leiomyosarcoma of the gastrointestinal tract is in middle-aged patients with a mean age of diagnosis of 50 years. Initial symptoms include abdominal pain, rectal bleeding, intra-abdominal bleeding, weight loss, constipation, diarrhoea, bowel obstruction, tenesmus or fever, which are nonspecific, generally reflect the tumour size and location and can mimic symptoms of colonic adenocarcinoma or other gastrointestinal diseases [3]. LMS of the colorectum was found to be more aggressive compared to other colonic tumours and has a high local recurrence rate and significant haematogenous spread, and rarely lymph node involvement. These tumours are most commonly diagnosed on biopsy obtained during colonoscopy to support our data [1].

Due to the paucity of data, the prognostic factors have been poorly defined and vary by studies. Amongst those identified, poor prognostic factors include age greater than 45 years, necrotic areas within the tumour, dissemination of disease and tumour size as noticed in our cases (Figs 1.A and E). Accurately predicting the patient outcome is difficult due to the rarity of the disease and the short survivals once a diagnosis has been established [1]. Surgery is the main treatment for primary colorectal LMS, as most of the reported cases were diagnosed using surgically resected specimens. While adjuvant chemotherapy and/or radiation are often used in the management of primary colonic LMS, there are conflicting data on their efficacy and impact on overall survival [1]. Currently, the best treatment for leiomyosarcoma of the colon is surgical resection. However, since these malignancies are often not detected until late, outcomes are poor, and there is only a 50–60% success rate. Adjuvant chemotherapy is also used, is typically anthracycline or docetaxel-based and does not significantly improve survival. Radiotherapy has not been shown to be as effective [1].

The optimal treatment modality in patients with rectal leiomyosarcoma remains controversial. Radical surgery, such as anterior resection or abdominoperineal resection, is preferred to wide local excision. In fact, radical surgery is associated with a lower recurrence rate than wide local excision [2]. Khalifa et al., in a review of 135 cases of rectal LMS, found a local recurrence rate of 67.5% with local excision, compared to only 19.5% with abdominoperineal resection, but there were no differences in survival rates between the two surgery modalities [2, 6]. In addition, Anderson et al. and Kiran et al. stated that local excisions of rectal LMS were almost always followed by recurrence no matter what grade of malignancy [4, 7]. Chemotherapy has been generally unsuccessful in treating this tumour. The two most commonly used agents are doxorubicin and dacarbazine [4, 8]. Adjuvant radiotherapy can be proposed by extension of
Table 1. Immunohistochemistry results in comparison to GIST

| Immunostain     | Case 1 (LMS) | Case 2 (LMS) | GIST       |
|-----------------|--------------|--------------|------------|
| Vimentin (DAKO-V9) | Positive     | Positive     | Positive   |
| alpha-SMA       | Positive     | Positive     | Positive/Negative |
| Desmin (Thermo D33) | Positive     | Positive     | Negative   |
| H Caldesmon     | Positive     | Positive     | Negative   |
| CD34 (DAKO-QBend 10) | Negative     | Negative     | Positive   |
| CD117 (Thermo-Polyclonal) | Negative     | Negative     | Positive   |
| DOG1 (Leica K9) | Negative     | Negative     | Positive   |
| S100 (DAKO-polyclonal) | Negative     | Negative     | Negative   |

the management principles of other pelvic tumour types and limb sarcomas, given the absence of randomized clinical trials [2, 9].

Accurately predicting the patient outcome is difficult in our report due to the rarity of colorectal LMS and the short survival after diagnosis. In a recent review of 11 patients with colonic leiomyosarcoma by Aggarwal et al. in 2012 [8], only 2 of the 11 patients survived five years, with an average survival of twenty months [1,10]. Yamamoto et al. reported an estimated 5-year tumour specific overall survival rate of 51.6% [1, 11]. In our cases survival is seemed to be short after diagnosis in light of the above information.

The prognosis and treatment options of this aggressive malignancy in our cases remain unsatisfactory, and amelioration of the prognosis will be achieved as further and more studies are to be carried out.

Conflict of interest

There are no conflicts of interest to declare by any of the authors of this study.

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