

CASE REPORT

Colorectal Leiomyosarcoma – a Rare Tumour in GIST Era

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Summary

Primary malignant mesenchymal colorectal tumours, representing a small fraction of soft tissue sarcomas, are characterised by predominance of gastrointestinal stromal tumour (GIST). After the GIST concept has been implemented in the diagnostics, the incidence of registered leiomyosarcomas has markedly decreased. The scarcity of credible cases embarrasses the analysis of tumour biological behaviour. Here we report well-documented, immunohistochemically proved, surgically treated case of colonic leiomyosarcoma (LMS) in order to broaden the published evidence by our data and to emphasize that the differential diagnosis of mesenchymal gastrointestinal tumours is not limited by GIST.

Key words: leiomyosarcoma, colon, colorectal tumour, differential diagnosis

AIM OF THE DEMONSTRATION

The aim of the demonstration is to report a well-documented case of a rare malignancy – leiomyosarcoma of the sigmoid colon in order to demonstrate the scope of malignant mesenchymal colorectal tumours.

CASE REPORT

A 79-year-old female presented with history of left-sided abdominal pain, which appeared 2 months ago and progressed in few preceding days. The anamnesis was remarkable for breast cancer twenty years ago, treated by mastectomy alone. Patient denied regular use of medications; however, she recalled occasional intake of antihypertensive drugs and non-prescription pain medications. By laboratory investigation, the red blood cell count and haemoglobin level corresponded to mild anemia. The white blood cell count and biochemical blood parameters (ASAT, ALAT, creatinine, sodium, potassium) were within laboratory reference ranges. Abdominal ultrasound evaluation showed an infiltrative left-sided colonic mass. Colonoscopy revealed a circular, stenosing tumour originating 25 cm above the anal verge. Tumour biopsy yielded the LMS diagnosis. Surgical treatment was recommended, and the resection of sigmoid colon was performed 2 months later. The postoperative period was uneventful. The gross examination of surgically resected bowel disclosed an ulcerated, circular mass measuring 15x7.5x4 cm and invading the mesentery. On histological examination the tumour was composed of polymorphous atypical cells possessing elongated nuclei and eosinophilic cytoplasm. Few atypical mitoses were present as well (Fig. 1). Superficial tumour necrosis was found, but there was no invasion in lymph vessels, arteries, veins or nerves. By immunohistochemistry, diffuse, intense cytoplasmic expression of smooth muscle actin, desmin and vimentin was present in the tumour cells. Pancytokeratin, melanosome protein HMB-45, CD31, CD34, CD68, S-100 protein and CD117 were found to be negative (Fig. 2). The proliferation fraction by Ki-67 was high: 52.7%. The radial resection margin was

positive for tumour cells. The mesenteric lymph nodes were free of malignancy (0/5). Thus, the final diagnosis, detected in accordance with recommendations provided by College of American Pathologists (10), was high-grade leiomyosarcoma, pT2bN0MxG2R1.

DISCUSSION

Leiomyosarcoma is defined as soft tissue sarcoma showing unequivocal cellular smooth muscle features (4). Since the development of GIST concept corrected diagnostics of this tumour, primary gastrointestinal LMS became distinctly rare. The infrequent occurrence of true primary gastrointestinal LMS and the fact that the earlier reports have been confounded with GISTs (8) embarrass the analysis of typical demographic characteristics, clinical presentation and pathological features (1,2,11). Therefore we consider important to add our experience to the published evidence.

The general incidence of soft tissue sarcomas is considered 2.40 – 5.03 per 100 000 person years. However, GISTs and gastrointestinal LMS constitute only 16.5% of these tumours (9) corresponding to the incidence 0.4 per 100 000. Further, in the GIST era, only 1.1% of mesenchymal gastrointestinal tumours are diagnosed as LMS (1). Although 263 colorectal and appendicular LMS have been described in time period 1875 – 1996 (6), an extensive literature search over 12 years revealed only 56 credible gastrointestinal LMS in adults (2). Large series of mesenchymal gastrointestinal tumours registered in 2 large institutions (1970 – 1998) yielded only 10 LMS contrasting with 292 GISTs over the same period (8). Small intestine has been noted as the most frequently affected site (26/56 cases); occasionally, similar or higher number of colonic tumours has been identified (2,8,11). The variations could be attributable to the rarity of such neoplasms. Gastrointestinal LMS occurs mostly between the age of 41 and 76 years (2) with the peak incidence at the age 50 – 59 years (6). Thus, the reported patient is older than most of the previous cases. Similarly to our patient, the affected persons usually present with pain, palpable

abdominal mass, or gastrointestinal bleeding (6). Weight loss, tenesmus, changes in bowel habits, intestinal obstruction, intussusception and perforation also belong to the scope of possible clinical presentations (3). The duration of symptoms can be between 1 month and 1 year, consistent with our experience (6). Histologically, LMS is characterised by spindled cells, eosinophilic cytoplasm and elongated nuclei. The immunophenotype is characterised by expression of actin (71 – 86%), desmin (86%), calponin (71%) and caldesmon (57%) and lack of CD117, CD34, protein kinase C theta and DOG1 [11]. In contrast, GISTs express CD117 (95%), CD34 (47 – 100%) and DOG1 (up to 100%). The expression of actin has been observed in 13 – 47% GISTs while desmin positivity is rare (2, 7, 8). In the described case, the immunophenotype unequivocally justified the diagnosis.

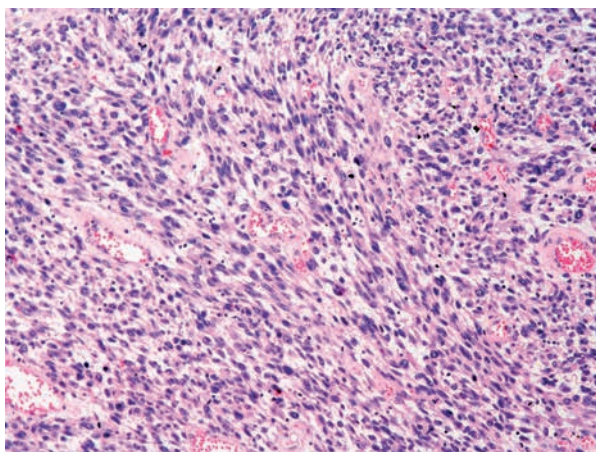
There are few reports of gastrointestinal LMS in the site of previous irradiation (3). However, the history of breast cancer cannot be associated with distant postirradiation tumours. Besides that, our patient denied any other treatment of breast cancer except surgical intervention. Epstein-Barr virus has been implicated in the LMS development in immunosuppressed individuals, e.g., transplant recipients and children with congenital immunodeficiency. Inherited *TP53* mutations have also been reported as a cause (2). Neither of these factors was attributable to our patient. Negative family history and relatively scarce personal oncological history is not suggestive of Lee-Fraumeni syndrome.

Agaimy and Wunsch described gastrointestinal LMS as high-grade infiltrative sarcomas (1). In accordance with this, we observed invasive growth leading also to positive resection lines. The tumour size in our patient also was large exceeding most of the reported cases with the mean diameter 6.3 cm and size range 3.2 – 10 cm (2). Colonic LMS have been characterised as aggressive neoplasms in contrast to rectal tumours (2).

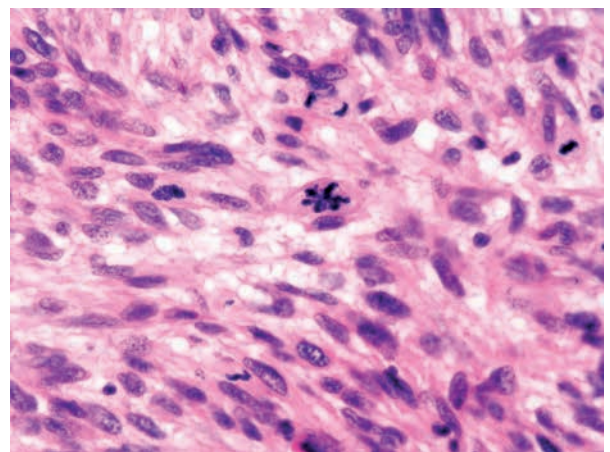
The five year survival of LMS patients ranges 20 – 51.6% (3, 11). Poorer outcome has been reported in colonic LMS: only 2/11 patients survived 5 years. In the pre-tyrosine kinase inhibitor era, LMS patients had better survival than those affected by GISTs. However, nowadays LMS patients are treated with chemotherapy (5), having decreased predictable response that targeted treatment in case of GISTs (2). Surgical treatment is of utmost importance.

In conclusion, colorectal leiomyosarcomas are distinctly rare in the GIST era. However, the entity exists and must be promptly recognised by appropriate immunohistochemical investigation. Invasive growth can be expected in accordance with the malignant biological potential.

Conflict of interest: None

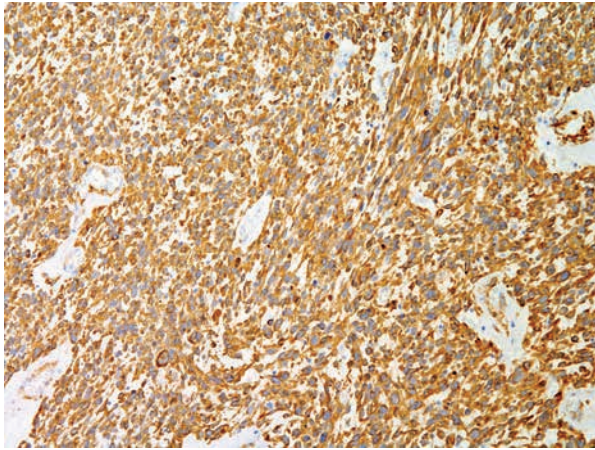


1 A

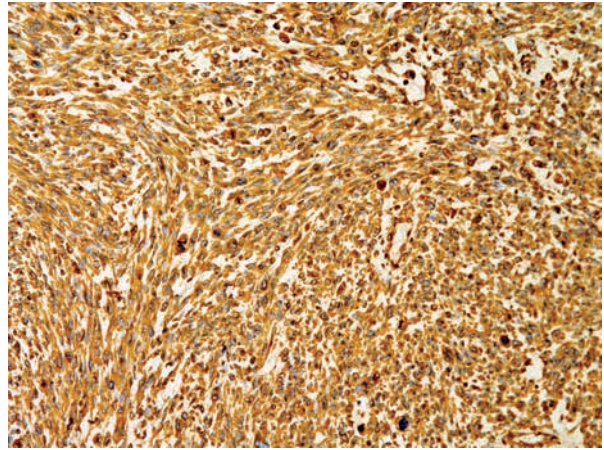


1 B

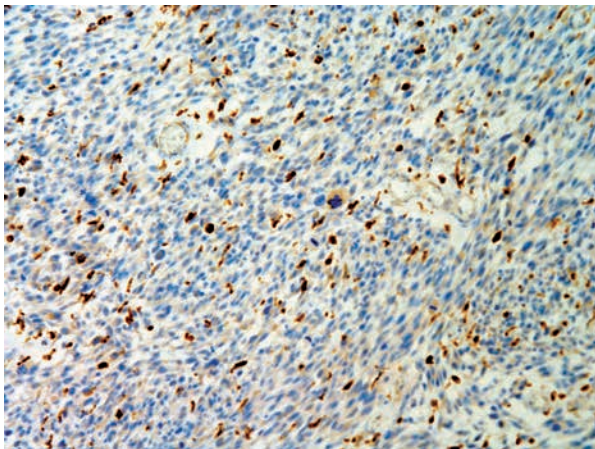
Fig. 1. Leiomyosarcoma of the sigmoid colon. 1A, Overview of the tumour structure; 1B, Atypical mitosis in a neoplastic cell. Haematoxylin-eosin, original magnification (OM) 100x (1A); 400x (1B).



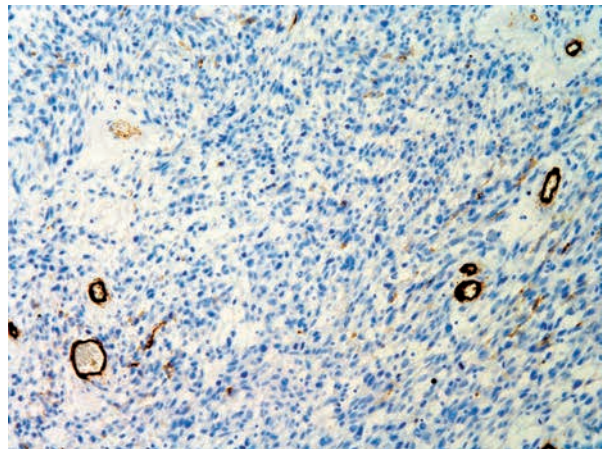
2 A



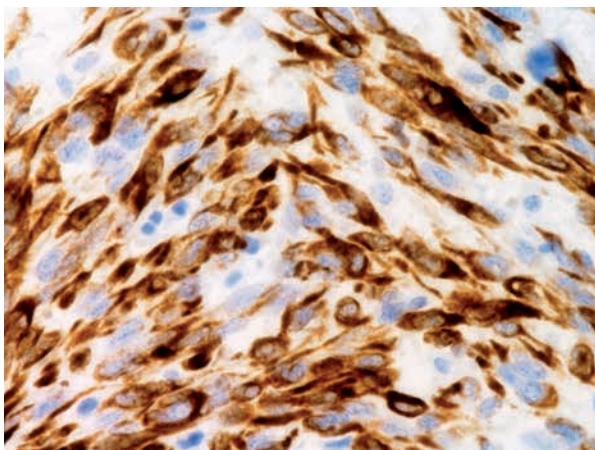
2 B



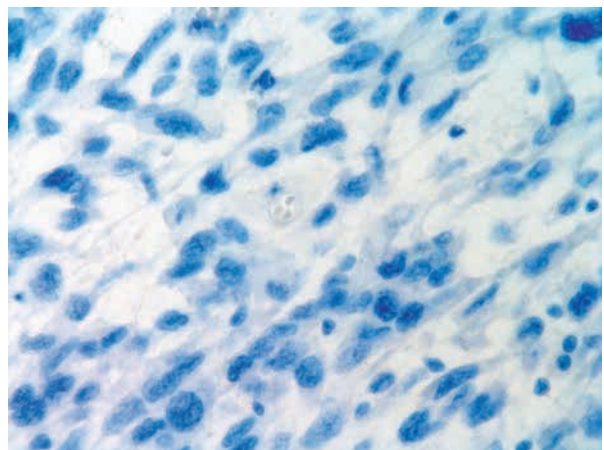
2 C



2 D



2 E



2 F

Fig. 2. Immunophenotype of colonic leiomyosarcoma. 2A, Intense cytoplasmic expression of actin in leiomyosarcoma cells; 2B, Expression of vimentin; 2C, Lack of CD68 in tumour cells; 2D, Absence of CD34 in neoplastic cells. Note the positive reaction in the endothelium; 2E, Positive desmin expression in leiomyosarcoma; 2F, Lack of CD117 in neoplastic cells. Immunoperoxidase, OM 100x (2A,B,C,D); 400x (2E,F).

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