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CASE REPORT

A challenging diagnosis of mesenchymal neoplasm of the colon: colonic dedifferentiated liposarcoma with lymph node metastases—a case report and review of the literature

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Abstract

Purpose We report a case of primitive colonic dedifferentiated liposarcoma along with lymph node metastases.

Methods The patient's clinical, radiologic, surgical, and histologic data were reviewed, as well as the literature on colonic dedifferentiated liposarcoma with a focus on the incidence of lymph node metastasis in gastrointestinal sarcomas and on the differential diagnosis with other spindle cell tumors in the gastrointestinal tract.

Results A 53-year-old man was referred to our hospital with a 3 year-history of pain on the right back that was refractory to drugs. He performed an abdominal computed tomography scan which revealed a colonic wall thickening in the hepatic flexure and a few serosal nodularities. With these findings, the patient underwent an extended right hemicolectomy. On histopathologic examination, it turned out to be a colonic dedifferentiated liposarcoma with lymph node metastases.

Conclusions The present case was a challenging diagnosis both at presurgical and histopathological level because it strongly mimicked a colonic adenocarcinoma. This was due to non-specific clinical and radiological presentation, to the non-characteristic histologic morphology and to the misleading presence of lymph node metastases. Malignant stromal tumors of the gastrointestinal tract beyond gist are fairly rare entities. Colonic dedifferentiated liposarcoma must be kept in mind and must be considered in the differential diagnosis of gastrointestinal tumors.

Keywords Colonic liposarcoma · MDM2 · Dedifferentiated

Background

Stromal tumors of the bowel account for 1% of all neoplasms [1] and they are mainly represented by gastrointestinal stromal tumors (GIST). Radiologic features can aid in the presurgical identification of these lesions but when the lesion arises from the intestinal wall, it can turn out to be an unexpected finding that is diagnosed only after histopathological examination.

We report a case of colonic dedifferentiated liposarcoma which, at computed tomography (CT) scan, presented as a mass stenosing the intestinal wall and with associated adjacent lymphadenomegalies. The lesion mimicked a common colonic adenocarcinoma. The histopathologic diagnosis was made after excluding other spindle cell neoplasms and confirmed the presence of lymph nodes metastases, an uncommon and misleading finding in case of sarcoma.

Case presentation

A 53-year-old man was referred to the surgery department of our hospital complaining of pain on the right back that had been present for more than 3 years and that was refractory to drugs. A prolactin-secreting pituitary adenoma was present in

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his clinical history. The patient performed an abdominal CT scan which revealed a wall thickening in the hepatic flexure and a few nodularities located in the anterior aspect of the serosa Fig. 1). Based on these findings, the diagnosis of obstructive colon cancer with lymph nodes metastasis was made. The patient underwent surgery.

Surgical findings

Upon inspection of the abdominal cavity, the omentum adhered to the hepatic anterior surface and this process seemed to involve the right colonic flexure, the duodenum, the diaphragmatic peritoneum, the liver, and the renal capsule. Therefore, an extended right hemicolectomy and a marginal resection of the VI liver segment and of the parietal peritoneum were performed. The patient showed good postoperative recover and was discharged on postoperative day 10.

Histopathological findings

Gross examination of the colonic specimen revealed the presence of an irregular thickening of the wall extended for approximately 1.8 cm with whitish septa that crossed the yellowish lobulated adipose tissue for about 4 × 3 cm. The lesion was extensively sampled. Histopathological examination showed a tumor composed of spindle cells (Fig. 2a and c) with moderate cellular pleomorphism and moderate mitotic activity even with atypical mitoses (Fig. 2b). This cellular proliferation involved the colonic wall from the *muscularis propria* to the serosa and was characterized by infiltrating margins to the perivisceral fat. The mucosal and submucosal layers were spared. Two separate nodules showing the same histopathologic features were isolated; in one of them, lymph node tissue could be observed at the periphery (Fig. 2d). Immunohistochemistry revealed negativity to CD117 (C-kit), DOG1, CD34, desmin, cytokeratin, HMB45, Mart1, CD68, and ALK1. Smooth muscle-actin, muscle-specific actin, and S100 were focally positive. Based on these findings, other samples and immunohistochemical assessments were performed. The coexistence of this neoplasm with a PRL-secreting pituitary adenoma had led to the hypothesis of syndromic gastrointestinal stromal tumor (GIST) associated with mutation of the succinate dehydrogenase B (*SDH-B*) gene, a rare CD117-negative subtype: first, because GISTs are the most common forms of sarcoma detected in the gastro-intestinal tract and then, because there are extremely rare forms of hereditary pituitary adenoma associated with *SDH-B* gene mutations. However, SDHB revealed to be negative as well as SOX10 and neurofilaments. There was, instead, positive reaction to TLE (Fig. 2f). New further samples revealed, within the neoplasm, the presence of a few cells with hyperchromatic indented nucleus and multivacuolated cytoplasm (Fig. 2e), just like lipoblast's morphology, although not really convincing. For this reason, MDM2 and CDK4 fluorescence in situ hybridization (FISH) analyses were performed. They highlighted strong MDM2 amplification (MDM2/CEP12 = 7.57) and CDK4 polisomy, without evidence of amplifications (Fig. 3).

These findings were strongly suggestive of a colonic dedifferentiated liposarcoma associated with lymph nodes' metastases.

Discussion

Liposarcomas involving the gastro-intestinal tract are exceptionally rare. Most are retroperitoneal, well-differentiated, or dedifferentiated liposarcomas that secondarily involve the gut. In the present case, the lesion originated from the colonic wall and adhered to the surrounding structures.

According to the WHO (World Health Organization) Classification of Tumors of the soft tissue [2], five subtypes of liposarcoma can be identified: well-differentiated/atypical lipomatous tumor, myxoid, round cell, pleomorphic, and dedifferentiated. Common to all subtypes is the evidence of lipoblasts (cells characterized by the presence of hyperchromatic indented nucleus and multivacuolated cytoplasm), neoplastic

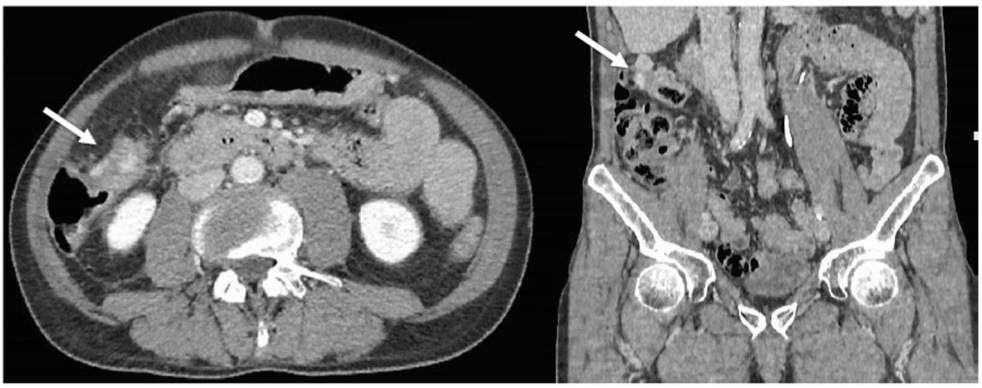

Fig. 1 CT scan revealed a wall thickening in the hepatic flexure and a few nodularities located in the anterior aspect of the serosa

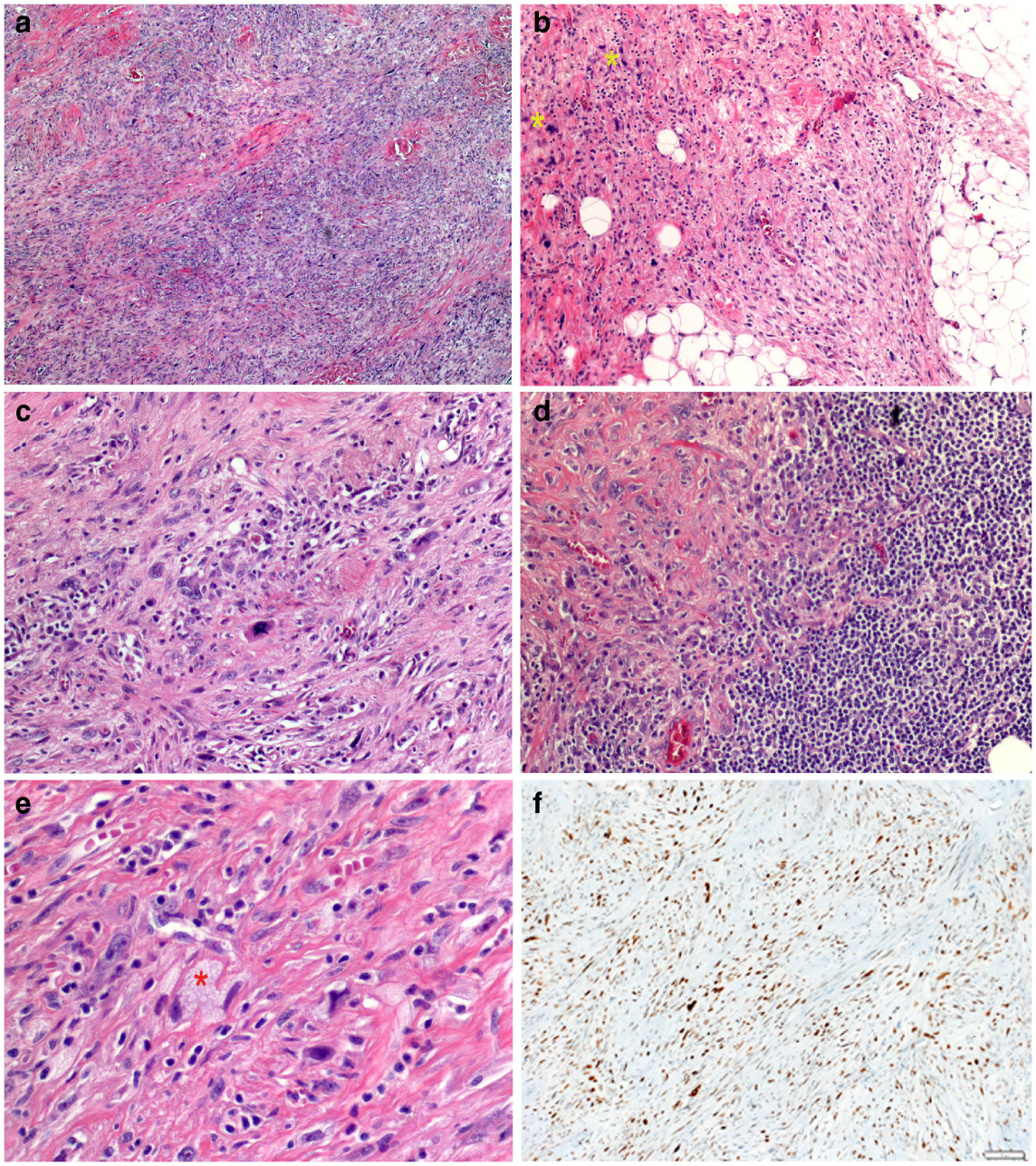

Fig. 2 The lesion was characterized by a hypercellular (**a**, Hematoxylin and eosin stain, × 100 magnification) proliferation of spindle cells that showed an infiltrative growth towards the perivisceral fat (**b**, Hematoxylin and eosin stain, × 200 magnification). There was an evident mitotic activity (**c**, Hematoxylin and eosin stain, × 200 magnification). Lymph node metastasis was present (Hematoxylin and eosin stain, × 200 magnification). Occasional lipoblast-like cells(*) were detected, characterized by with hyperchromatic indented nucleus and multivacuolated cytoplasm (Hematoxylin and eosin stain, × 400 magnification). Neoplastic cells nuclei were immunoreactive to TLE (× 200 magnification)

cells that are assumed to recapitulate, to some extent, the differentiation process of normal fat (adipogenesis) like their potential normal counterpart, (preadipocyte). Lipoblasts [3] may be inappreciable or totally absent in some forms of liposarcomas (atypical lipomatous tumor); consequently, they are not a prerequisite for this diagnosis in the currently used diagnostic system for soft tissue tumors.

The term dedifferentiated liposarcoma [4] is used when non-lipogenic component occurs within an atypical lipomatous tumor or, much more rarely, in a myxoid liposarcoma. The non-lipogenic component can show an appearance that is reminiscent of fibrosarcoma or so-called malignant fibrous histiocytoma. In these cases, it can be difficult to distinguish a dedifferentiated liposarcoma from other high-grade spindle

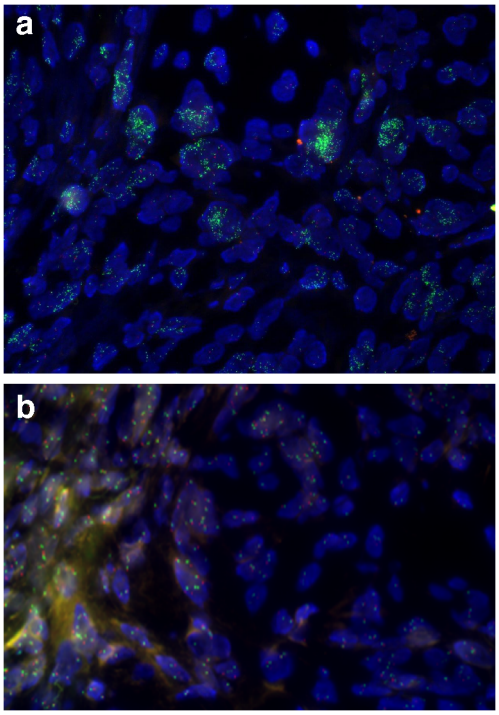

Fig. 3 MDM2 and CDK4 fluorescence in situ hybridization (FISH) highlighted strong (**a**) MDM2 amplification (MDM2/CEP12 = 7.57) and CDK4 (**b**) polisomy, without evidence of amplifications

cell and pleomorphic sarcomas on purely morphologic ground. The evidence of MDM2 amplification (by FISH or immunohistochemistry) is actually considered the most specific diagnostic tool.

Dedifferentiated liposarcoma shares some of the genetic changes occurring in the preexisting well-differentiated liposarcoma (amplification of the 12q13–15 region, which includes *MDM2*, *SAS*, *HMGA2*, and *CDK4* genes), but it often shows additional genetic changes, such as amplifications (e.g., gain of 1q21–24, 6q22–24, 20q13, or 12q24), deletions (e.g., loss of 13q14–21 or 11q22–23), and *TP53* mutation [5, 6].

Pre-surgical radiologic diagnosis is difficult and depends upon the anatomic site and the histologic subtype [7]. CT can be used to effectively characterize tissue components, which is necessary to establish a working differential diagnosis, and CT offers multiplanar reconstructions to easily depict the anatomic site of origin of a mass, as well as its relationship to adjacent organs and vasculature. Dedifferentiated liposarcomas are heterogeneous solid soft tissue masses on CT scan and they classically show a sharp demarcation between well-differentiated and dedifferentiated areas [8].

In WHO blue books [1, 2] and in other pathology textbooks, liposarcoma is not even mentioned as a possible differential diagnosis among spindle cell neoplasms of the gastrointestinal tract. However, less than 25 cases (Table 1, refs. 9–30) of primary colonic liposarcoma have been described in the English language literature. In most cases, they were right-sided and their clinical presentation was non-specific (abdominal pain, abdominal discomfort, diarrhea, weight loss, anemia, constipation, or intussusception) but mostly related to tumor size. The patients' age ranged from 32 to 79 years and the histotype was dedifferentiated, well-differentiated, pleomorphic, and myxoid, respectively in 9, 7, and 3 cases. In one case, more than one histotype was observed. No data were available on the presence of distant metastases. In 7 cases, the neoplasm co-existed with other pathologies (Table 1), most of them related to metabolic syndrome.

Ultimately, once GIST has been excluded, other differential diagnoses [31] should be considered, as leiomyoma of the *muscularis mucosae*, mucosal perineurioma, polypoid ganglioneuroma, and perivascular epithelioid cell tumor (PEComa) that are the most common colonic mesenchymal neoplasms. Each specific diagnosis needs to be confirmed with a carefully chosen immunohistochemical panel and, sometimes, with molecular tests. When none of these hypotheses fit with what is under observation, other possible tumors featuring spindle cell morphology should be examined, like schwannoma, leiomyosarcoma, desmoid fibromatosis, inflammatory fibroid polyp, plexiform fibromyxoma, and clear cell sarcoma-like tumor. However, given the significant frequency with which it can be diagnosed in the colon, as highlighted also by our literature review, liposarcoma should be added to this list.

In our case, two lymph node metastases were present. Historically [32], it has always been considered that lymph node metastases from sarcoma represent a very rare event and that it was associated with specific histotypes. It was shown that the visceral location, malignant fibrous histiocytoma histology, and limited surgery for lymph node metastasis represent the most powerful factors related to poor prognosis in sarcomas. The reported incidence of lymph node metastases varies from 1.6 to 12%. In a recent relevant study of meta-analysis [33], it was shown that lymph nodes are involved by sarcoma in the head/neck, the thorax, and the abdomen/retroperitoneum, respectively in 5.8%, 5.3% and 5.1% of cases, more commonly than in the trunk or extremities (2% of cases). Furthermore, it was observed that the incidence of lymph node metastases was unevenly distributed across histologies (liposarcomas accounted for the greatest number occurring in 22% of cases) and that its impact on overall survival is a prognostic factor only in the absence of synchronous distant metastatic disease.

Conclusions

Overall, we present a rare case of colonic dedifferentiated liposarcoma metastatic to lymph nodes, whose diagnosis was hindered both in the pre-surgical phase, due to the non-specific clinical and radiological presentation, and in the histopathological diagnostic phase, due to the non-characteristic

Table 1 The results of the different research examined in the present study

Authors (year)	Ref.	Age (years)	Sex	Clinical presentation	Size (cm)	Site	Histotype	Comorbidities
Wood DL et al., 1989	[9]	62	F	Pain and palpable mass	7.5 × 12	Ileocecal valve	Myxoid	–
Parks RW et al., 1994	[10]	54	F	Lethargy, abdominal discomfort, diarrhea, and 7 kg weight loss	6 × 4	Ascending colon	Pleomorphic	–
Chen KT, 2004	[11]	52	F	Abdominal pain and hematochezia	–	Descending colon	Well-differentiated	–
Gutsu E et al., 2006	[12]	46	M	Abdominal pain	12 × 11	Ascending colon	Myxoid	–
Sasaki Y et al., 2006	[13]	58	M	Abdominal pain	14 × 7	Sigma	Pleomorphic	–
Shahidzadeh et al., 2007	[14]	56	M	Hematochezia	3.5 × 2.8	3.5 × 2.8	Well-differentiated	History of non-Hodgkin lymphoma, chronic obstructive pulmonary disease, and diabetes
Chaudhary A et al., 2007	[15]	66	F	Pain, hematochezia, weight loss, and palpable mass	6 × 3	Descending colon	Well-differentiated	–
Jarboui S et al., 2009	[18]	69	M	Pain, constipation, and weight loss	7 × 6	Descending colon	Dedifferentiated	–
Suzuki S et al., 2009	[19]	53	M	Right upper abdominal palpable mass	12 × 8	Ascending colon	Well-differentiated	–
D'Annibale M et al., 2009	[20]	79	F	Pain, progressive constipation, and weight loss	5 × 5.2	Ascending colon	Pleomorphic	–
Choi YY et al., 2010	[21]	41	M	Pain and palpable mass	20 × 13	Ascending colon	Mixed	–
Takeda K et al., 2012	[22]	71	M	2-month history of abdominal distention	11 × 9	Ascending colon	Dedifferentiated	–
Türkoˇglu MA et al., 2014	[23]	71	F	Abdominal pain and swelling	23 × 19	Transverse colon	Dedifferentiated	–
Kito Y et al., 2014	[24]	84	F	Abdominal pain due to intussusception	10 × 3	Ascending colon	Dedifferentiated	–
Rudnick C et al., 2015	[25]	34	M	Left iliac fossa pain and variable stool pattern	40 × 25	Sigma	Well-differentiated	Metabolic syndrome
Fernandes SR et al., 2016	[26]	32	F	Lower left quadrant abdominal pain	3.5 × 3	Sigma	Well-differentiated	Crohn's disease
Constantinoiu S et al., 2016	[27]	73	M	Abdominal pain and bowel disorders	15 × 10.5	Sigma	Dedifferentiated	Multiple cardiovascular comorbidities
Chou CK et al., 2016	[28]	62	M	Palpable mass in the right lower abdomen	14 × 13	Ascending colon	Myxoid	
Sawayama H et al., 2017	[30]	52	F	No complaints and no abnormalities	6.5 × 4	Ascending colon	Dedifferentiated	History of TBC infection at 22 years age
Hollowoa B et al., 2018	[31]	64	M	Increasing abdominal pain. Cramping and intussusception	4.2	Hepatic flexure	Dedifferentiated	–
Zhang D et al., 2019	[32]	65	M	Abdominal pain	6	Ascending colon	Dedifferentiated	History of non-ischemic cardiomyopathy, mitral valve replacement, diabetes and hypertension
Sultania M et al., 2019	[33]	57	F	Abdominal swelling and pain	Multiple	Ascending colon	Well-differentiated	–
Current case		53	M	3-year history of right back pain	4 × 3	Hepatic flexure	Dedifferentiated	Pituitary adenoma

morphology and to the misleading presence of lymph node metastases. The spectrum of liposarcoma has widened considerably in recent years concerning both its morphological features and its sites of occurrence. This report of an apparently primary example in the colon further widens this spectrum.

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