Case Report

# Dedifferentiated liposarcoma of the ileal mesentery: Case report

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## ABSTRACT

Primary mesenteric dedifferentiated liposarcoma (DDLPS) is an extremely rare malignancy, usually arising in the retroperitoneum. Its occurrence in the mesentery presents significant diagnostic and therapeutic challenges. We report a 58-year-old female with progressive abdominal distension and left-sided pain for 6 months. Imaging revealed an intra-abdominal mass and exploratory laparotomy identified a large mesenteric tumor, which was completely excised with negative microscopic margins (R0 resection). Histopathology confirmed DDLPS, with immunohistochemical analysis showing MDM2 and CDK4 positivity, DDLPS in the mesentery is challenging to diagnose due to its rarity and diverse histological presentation. Surgical excision remains the primary treatment, but the tumor's high recurrence rate necessitates long-term follow-up and possible adjuvant therapy. Targeted treatments, such as MDM2 and CDK4 inhibitors, may offer additional options. This case underscores the importance of a multidisciplinary approach in diagnosing and managing rare mesenteric malignancies, emphasizing the need for vigilant surveillance and individualized treatment planning.

**Key words:** CDK4, De-differentiated liposarcoma, MDM2, R0 resection, Target therapy

Liposarcoma (LPS) is one of the most common types of soft-tissue sarcoma, originating from mesenchymal tissue. It most commonly arises in the retroperitoneum and deep soft tissues of the trunk and extremities, with gastrointestinal involvement being rare [1]. The World Health Organization classifies LPS into five histopathological subtypes: Well-differentiated, dedifferentiated, myxoid, round cell, and pleomorphic [2]. The dedifferentiated variant (dedifferentiated liposarcoma [DDLPS]) is characterized by the coexistence of both well-differentiated and poorly differentiated components [3]. Diagnosing DDLPS can be challenging, with computed tomography (CT) and magnetic resonance imaging serving as early diagnostic tools, while histopathological examination remains the gold standard [1]. At present, complete surgical resection is the only effective treatment option [3].

Reporting this case is warranted due to the exceptional rarity of primary mesenteric DDLPS, its diagnostic challenges due to non-specific presentation and histologic diversity, and therapeutic dilemmas posed by high recurrence risk despite R0 resection. This case highlights the necessity of multidisciplinary collaboration and contributes to the limited literature on mesenteric DDLPS, aiming to guide clinical decision-making and advance research into targeted therapies such as MDM2/CDK4 inhibitors. Here, we present a rare case of a 58-year-old female diagnosed with primary dedifferentiated mesenteric LPS.

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## CASE REPORT

A 58-year-old Indian woman presented with a 6-month history of insidious onset, persistent, non-radiating left-sided abdominal pain, which was vague in nature and not accompanied by symptoms such as constipation, along with progressive abdominal distension. She had no significant medical, familial, or psychosocial history but reported irregular menstrual cycles.

General physical examination revealed no abnormalities and vital signs were within normal limits. On abdominal examination, a large, well-defined, non-tender, intra-abdominal mass (20 × 14 cm) was palpable in the left lumbar, umbilical, left iliac, and hypogastric regions. The mass was hard, mobile, and without ascites (Fig. 1a).

She was initially evaluated by a gynecologist, and an abdominal ultrasound suggested an intraperitoneal mass of adnexal or bowel origin. Due to inconclusive findings, a contrast-enhanced CT scan was performed, revealing a well-defined, lobulated, heterogeneously enhancing solid lesion (28 × 27 × 16 cm) within the ileal mesentery. The mass displaced bowel loops without early arterial enhancement, suggesting a mesenteric LPS (Fig. 1b and c). Exploratory laparotomy revealed a large,

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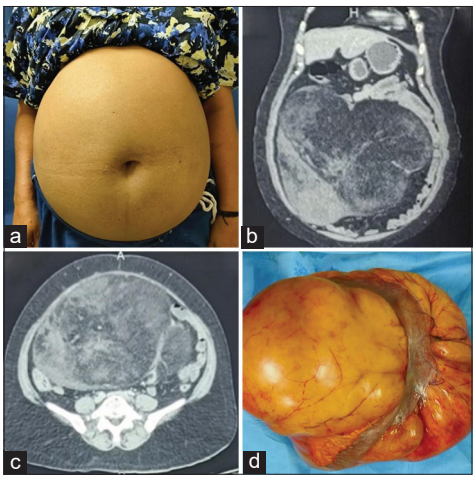


**Figure 1: Clinical, radiological, and surgical findings of the patient. All images are original images taken from the patient with appropriate consent. (a) Pre-operative clinical image showing a distended abdomen; (b) Coronal contrast-enhanced computed tomography (CT) scan showing a large, well-defined heterogeneous mass occupying the abdominal cavity; (c) Axial contrast-enhanced CT scan; (d) Intraoperative image showing the resected tumor**

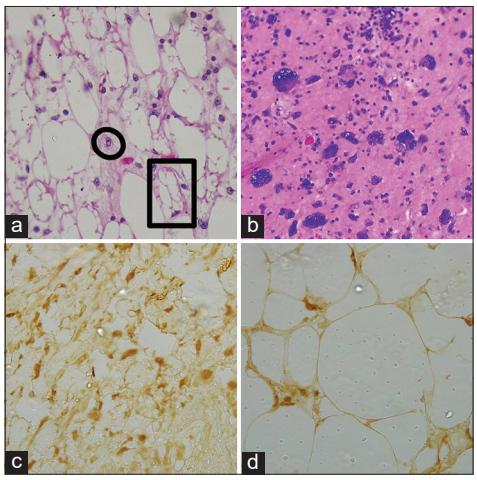


**Figure 2: Histopathological and Immunohistochemical Features of DDLPS all images are original images taken from the patient with appropriate consent. (a) Histopathological section showing liposarcomatous areas with scattered lipoblasts (H&E stain, ×400). (b) Dedifferentiated component exhibiting marked pleomorphism (H&E stain, ×400). (c) Immunohistochemical staining demonstrating CDK4 positivity in tumor cells. (d) Immunohistochemical staining showing nuclear positivity for MDM2 in tumor cells.**

yellowish mass with solid and myxoid areas arising from the ileal mesentery, weighing approximately 5 kg. Complete (R0) surgical resection was achieved (Fig. 1d).

Histopathological examination of the resected tumor revealed a well-differentiated liposarcomatous region, predominantly composed of mature adipocytes with scattered lipoblasts exhibiting intracytoplasmic vacuolations (Fig. 2a). In contrast, areas with marked nuclear pleomorphism, increased mitotic activity, and spindle cell morphology lacking adipocytic differentiation were observed, indicative of the dedifferentiated component and its aggressive biological behavior (Figure 2b). This biphasic pattern is a hallmark feature of dedifferentiated liposarcoma (DDLPS). Immunohistochemistry demonstrated strong nuclear positivity for CDK4 and MDM2, confirming the diagnosis of DDLPS (Figures 2c and d respectively). Given the high recurrence rate and metastatic potential, the patient was referred for oncological evaluation and adjuvant therapy. She is currently stable and remains on regular follow-up.

## DISCUSSION

LPS is predominantly a disease of adults, comprising approximately 12.8% of all soft-tissue malignancies with its peak incidence occurring in the sixth and seventh decades. The term "dedifferentiated liposarcoma" (DDLPS) was first introduced by Evans in 1979 to describe tumors containing a mix of atypical well-differentiated LPS (WDLS) and high-grade non-lipogenic sarcomas, with distinct transitions between these components. DDLPS accounts for 18.5% of all LPS cases and represents a more aggressive variant, typically associated with a poorer prognosis. It most commonly arises in the retroperitoneum. LPS originating in the mesentery, by contrast, is rare [3-5].

The clinical presentation of DDL is often vague in the early stages, with non-specific symptoms. In many cases, early tumors are incidentally detected during radiological imaging. As the tumor grows, it may present as a palpable abdominal lump and cause pressure-related symptoms [3,6]. In later stages, symptoms are largely dependent on the tumor's location. Common complaints include abdominal pain, progressive abdominal distension, weight loss, early satiety, and freely mobile abdominal masses. Literature also describes cases presenting with complications such as bowel obstruction, perforation, intussusception, or symptoms mimicking acute appendicitis and prostatism [6,7]. Our patient presented with chronic pain and progressive abdominal distension.

The tumor exhibits a multinodular external surface with a fleshy, irregular appearance. On the cut surface, it showed a mix of greyish-white and yellow regions. DDLPSs display a diverse range of histological patterns, consisting of both well-differentiated and dedifferentiated areas. The transition between these components is usually abrupt but can occasionally be gradual or mosaic-like. The well-differentiated regions are primarily adipocytic, while the dedifferentiated areas comprise various low- and high-grade tumor types, including pleomorphic sarcoma, fibrosarcoma, inflammatory myofibroblastic-like tumors, myofibrosarcoma, and fibrous histiocytoma [8,9].

DDLPS shares significant genetic similarities with WDLS or atypical lipomatous tumors, with both exhibiting high amplification of MDM2 and CDK4 oncogenes within the 12q13–15 region. Additional amplifications in 1p31 and 6q23 have also been identified in DDLPS. The 12q13–15 region contains key genes that drive tumor progression. MDM2 promotes p53 degradation, inhibiting its tumor-suppressive function, while CDK4 regulates the cell cycle through interaction with Cyclin D1 (CCDN1), leading to retinoblastoma phosphorylation. Other genes, such as high mobility group at-hook 2 and tetraspanin 31, are co-amplified with MDM2 and play roles

in transcription regulation. YEATS Domain-Containing Protein 4 and carboxypeptidase M (CPM) suppress p53 and contribute to dedifferentiation, while solute carrier family 35 member E3 is co-amplified with MDM2 and CPM. Beyond the 12q13–15 region, DDLPS also exhibits co-amplifications in 1p32 and 6q23. Jun proto-oncogene (JUN), located at 1p32, is part of the activator protein 1 complex and inhibits adipocyte differentiation, while Mitogen-Activated Protein Kinase Kinase Kinase 5, found at 6q23, activates the c-Jun N-terminal Kinase pathway, further enhancing JUN activation and blocking adipocyte differentiation. Amplifications in tyrosine kinase genes, including discoidin domain receptor tyrosine kinase 2, Erb-B2 receptor tyrosine kinase 3 (ERBB3), neurotrophic tyrosine receptor kinase 1, fibroblast growth factor receptor 1, and ROS proto-oncogene 1, suggest a potential role for tyrosine kinase inhibitors in targeted therapy for DDL. Recent studies have also identified novel fusion genes in DDLPS, such as Carboxy-Terminal Domain Small Phosphatase 1- DNM3 Opposite Strand/Antisense RNA (CTDSP1-DNM30S) and CTDSP2-DNM30S, which upregulate microRNAs, contributing to tumor progression and poor prognosis. Unlike many cancers, somatic point mutations are rare in DDL, suggesting that genomic amplifications, rather than specific mutations, are the primary drivers of the disease [6].

A detailed tumor sampling is essential to identify the non-lipogenic component, as it constitutes only a small portion of the tumor. Distinguishing DDLPS from other high-grade tumors can be challenging due to the limited sample size, making post-operative histopathology the most reliable diagnostic method [5]. Imaging helps overcome sampling limitations by guiding biopsies to appropriate areas. Targeting nodules with a Hounsfield unit (HU) >90 or an enhancement >20 HU above the psoas muscle reduces sampling error [10]. CT findings such as the absence of central necrosis, fat content <25%, and an enhancing nodule greater than the psoas muscle exclude DDLPS. Positron emission tomography, the gold standard in metabolic imaging, shows high fluorodeoxyglucose uptake in dedifferentiated components and minimal uptake in well-differentiated areas. A standardized uptake value >4 suggests a higher likelihood of DDLPS [11].

The treatment of DDLPS remains a significant challenge. Surgical resection is the primary approach for localized disease, with achieving an R0 margin being more feasible in extremity DDLPS than in retroperitoneal or primary mesenteric tumors [6,12]. However, even with optimal surgery, the risk of recurrence or relapse within 5 years remains high. Although adjuvant or neoadjuvant chemotherapy is not routinely recommended for soft-tissue sarcomas, it may be considered in cases of rapidly progressive symptomatic disease to facilitate surgical resection. The choice of treatment for each patient depends on various factors, including disease extent, performance status, comorbidities, and symptom burden. Potential toxicities must be carefully assessed, weighing the advantages and disadvantages of different treatment options [12-14]. The systemic treatment landscape for DDLPS has evolved significantly. Conventionally, systemic therapy was limited to cytotoxic chemotherapy agents such as doxorubicin, ifosfamide, gemcitabine, and docetaxel. More recently, targeted therapies have emerged, leveraging the amplified expression of MDM2 and CDK4 found in nearly all DDLPS tumors. CDK4 and MDM2 inhibitors, particularly in combination with conventional chemotherapy, show promise. Clinical trials have demonstrated the efficacy of the CDK4 inhibitor abemaciclib and the nuclear export inhibitor selinexor, supporting further research into anti-MDM2 therapies [15].

## CONCLUSION

DDLPS is a rare, aggressive malignancy requiring multidisciplinary management. Imaging and histopathology enable early diagnosis and differentiation from other soft-tissue tumors, with MDM2/CDK4 immunohistochemistry critical for confirmation. Surgical excision remains the cornerstone of treatment, supplemented by adjuvant therapies in advanced or recurrent cases. Despite advancements, high recurrence rates necessitate long-term surveillance. Further research into disease mechanisms and targeted therapies is essential to improve outcomes and personalize treatment strategies.

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