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Case Report

# Dedifferentiated Liposarcoma Masquerading as a Recurrent Inflammatory Pseudotumor

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## Abstract

Liposarcoma is a heterogeneous cancer that typically presents at an advanced stage, which leads to a poor prognosis, especially when it is located in the retroperitoneum. Although there are plenty of treatment strategies for liposarcoma, surgery is currently the primary therapeutic choice. Several cases of dedifferentiated liposarcomas that were masquerading as inflammatory pseudotumor have been previously reported, and this contributes to the diagnostic challenge. Many studies have suggested that inflammatory pseudotumor is a type of neoplasm or cancerous process. The use of immunostaining and genetic testing would be very helpful for making a correct diagnosis. Here we present the case of a recurrent tumor located in the retroperitoneum. The patient was initially diagnosed with an inflammatory pseudotumor and then a dedifferentiated liposarcoma following their second presentation.

**Keywords:** Inflammatory pseudotumor, MDM2 amplification, retroperitoneal liposarcoma

## Introduction

Retroperitoneum liposarcomas cause diagnostic and therapeutic challenges due to their deep anatomic location and large size.[1] Up to 40% of liposarcoma cases occur in the retroperitoneum, which is hard to approach and difficult to dissect.[2] Also, it is sometimes very hard for a pathologist to find hallmark lipoblasts or to differentiate between true lipoblasts and lipoblast-like cells to make a correct diagnosis, even after careful, extensive sampling.[3] In this report, we describe the case of a 74-year-old male with a large retroperitoneal tumor, who was initially diagnosed pathologically with an inflammatory pseudotumor. About one year later, a recurrent retroperitoneal tumor over his right lower abdomen was identified and diagnosed as liposarcoma.

## Case Report

A 74-year-old male complained of general malaise and a poor appetite for half a year. On physical examination, a palpable

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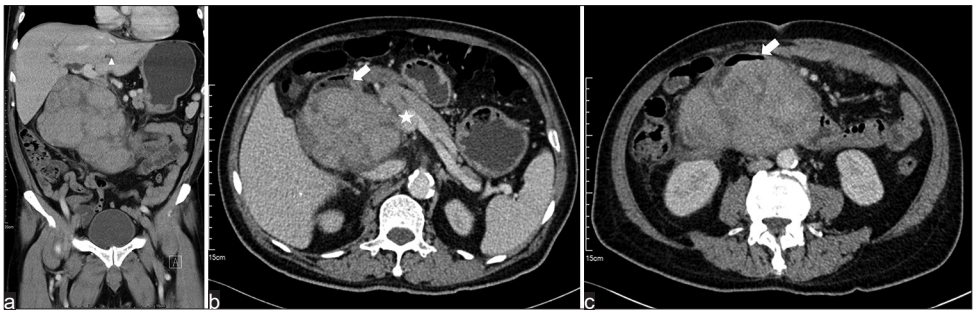

**Figure 1:** (a) A whole abdominal computed tomography that identified a large heterogeneous multi-lobular retroperitoneal tumor, about 17 cm in size, in the duodenal lumen; mass effect caused a dilated intrahepatic duct (white triangle). (b) Dilated pancreatic duct dilatation (white star); (b and c) and flattened duodenum (white arrow)

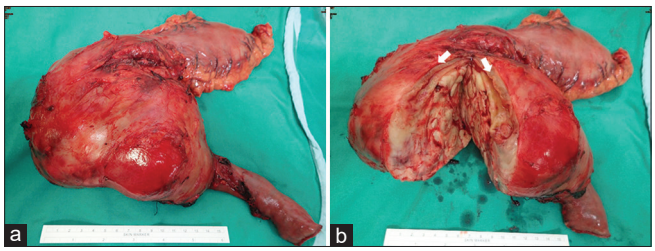

**Figure 2:** Gross appearance of the surgical specimen, including the antrum, duodenum, pancreatic head, distal common bile duct, and proximal jejunum; (a) The large tumor measured about 17 cm in diameter; (b) On cutting a sectional area, a flattened duodenum with swollen walls (white arrow) was noted

mass was found in the protruding upper abdomen. A whole abdominal computed tomography (CT) scan revealed a heterogeneously enhancing mass in the retroperitoneal space measuring about 17 cm in diameter and compressing the duodenum [Figure 1].

The patient underwent a Whipple's operation for radical resection of the tumor because it had invaded the second portion of the duodenum [Figure 2].

During the operation, reactive hyperplasic epigastric and peripancreatic lymph nodes were identified. Histopathology revealed an encapsulated tumor composed of spindle cells with myofibroblastic differentiation in a loose fascicle growth pattern. Many inflammatory cell types had infiltrated the tumor, including lymphocytes, eosinophils, and plasma cells. Immunohistochemical studies showed that the tumor cells were only positive for CDK4, while they were negative for MDM2, CD117, S100 protein, CD34, desmin, and ALK. A diagnosis of an ALK-negative inflammatory pseudotumor was given [Figure 3].

A palpable mass was found in the right lower abdomen at a follow-up clinic visit 1 year later. Abdominal CT identified three lobular tumor masses in the right lower abdomen, with the largest measuring about 7 cm [Figure 4]. Right hydronephrosis due to invasion of the distal ureter was also observed, as well as right adrenal gland metastasis. The patient subsequently underwent radical resection of the retroperitoneal tumor, including right nephrectomy, right adrenalectomy, and right radical orchiectomy.

Histopathologically, the tumor was composed of many large, pleomorphic cells with hyperchromatic nuclei and notable cellular atypia. The mitotic count was high (>10/10 HFP) and atypical mitosis with many giant tumor cells was also seen. Some lipoblasts were found in the lipomatous area. Immunohistochemical studies showed that the tumor cells were strongly positive for CDK4 and MDM2, which supported the diagnosis of dedifferentiated liposarcoma [Figure 5]. The patient is now scheduled for regular follow-up at Mackay Memorial Hospital in Taiwan and plans to receive targeted therapy with the CDK4 inhibitor palbociclib.

## Discussion

Liposarcoma accounts for 41% of all sarcomas and is one of the most common types to present in the retroperitoneum.[4] Only 12%–15% of soft tissue tumors develop in the retroperitoneum, with liposarcomas representing about 70% of such cases.[5] The major types of retroperitoneal liposarcoma are well-differentiated liposarcoma and dedifferentiated liposarcoma, which account for 40%–50% of all liposarcoma cases.[6] Retroperitoneal liposarcomas have been reported across all ages, with a median patient age of 56 years.[7] Dedifferentiated liposarcomas present most frequently in older adults, with a peak incidence rate in those aged 60–90 years, but without a gender preference.[8]

Retroperitoneal liposarcomas usually present without any symptoms, and they often reach a large size and can compress adjacent organs, as observed in this patient.[9] Dedifferentiated liposarcoma is a higher-grade tumor compared with well-differentiated liposarcoma. It may be primary or dedifferentiated from a preexisting well-differentiated liposarcoma and often has aggressive local growth, a higher risk of local recurrence (40%), and a higher rate of metastasis (15%–30%) and tumor-related death (28%) despite complete gross resection.[10]

Histologically, dedifferentiated liposarcoma is defined by the composition of two distinct components, first a well-differentiated liposarcoma and second a non-lipogenic part, which demonstrates a wide morphologic spectrum with

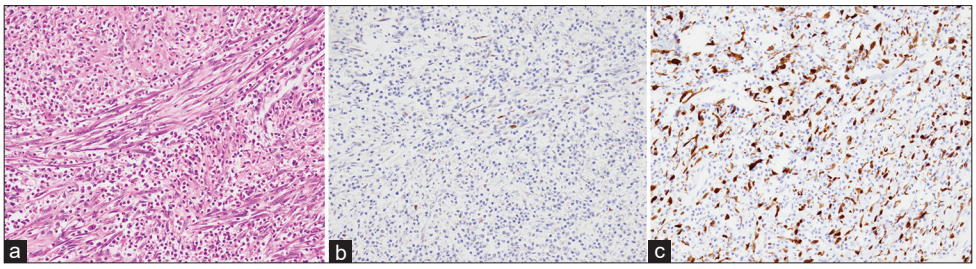

**Figure 3:** (a) Spindle cell proliferation with infiltrating inflammatory cells, including lymphocytes, plasma cells, and eosinophils. (b) The tumor cells were immune-negative for MDM2 staining, (c) while strongly positive for CDK4

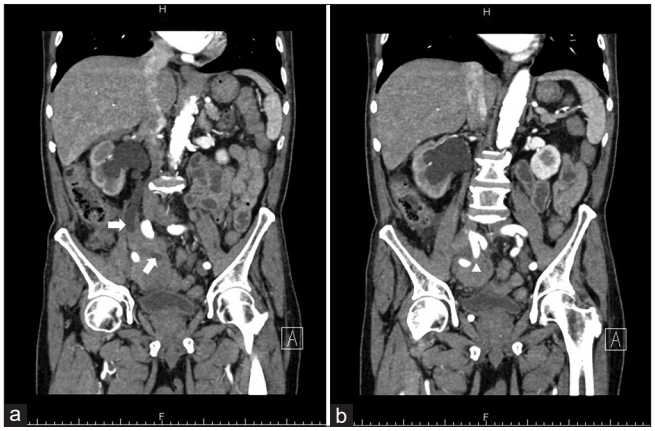

**Figure 4:** Coronal view of a whole abdominal computed tomography scan in the arterial phase. Three lobular tumor masses (about 7, 6, and 4.7 cm) were found in the right lower abdomen and a recurrent tumor was suspected. (a) Right hydronephrosis and proximal hydroureter (white arrow) were observed, possibly due to compression/invasion by the abdominal tumors. (b) A distorted right common iliac artery (white triangle) was noted, possibly due to compression/invasion by the abdominal tumors

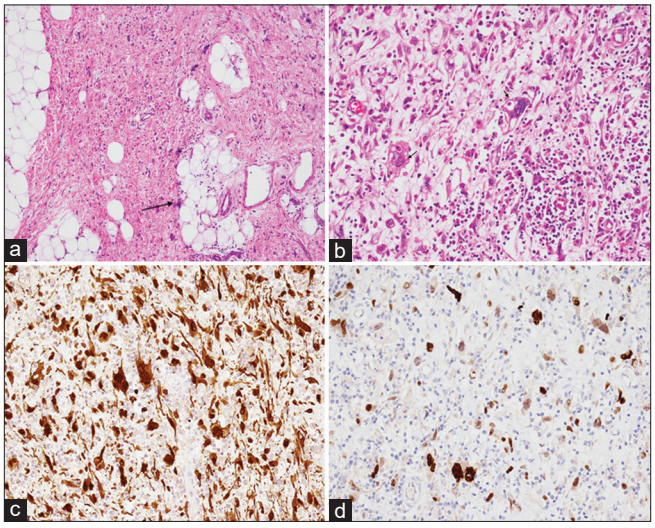

**Figure 5:** (a) Lipoblasts are present in the adipocytes (arrow) and (b) many giant tumor cells show high cellular pleomorphism and nuclear atypia arrow in the dedifferentiated liposarcoma area. Tumor cell nuclei are strongly immune positive for (c) CDK4 and (d) MDM2

moderate-to-high cellularity and pleomorphism.[4] The diagnosis of well-differentiated liposarcoma and dedifferentiated liposarcoma is currently determined by MDM2, CDK4, and p16 immunohistochemical staining, which can differentiate well differentiated liposarcoma/dedifferentiated liposarcoma from benign tumors and other sarcoma types.[11] Dedifferentiated liposarcoma with inflammatory myofibroblastic tumor-like features has been reported in previous studies. It seems to have an increased incidence in the inguinal and retroperitoneum and can lead to a misdiagnosis of benign tumors.[12] Ghatak *et al*.[13] proposed that loss or gain-of-function mutations in TP53 induce dedifferentiation and proliferation of stem cells with damaged DNA leading to the generation of cancer stem cells. Therefore, mutations of TP53 may indirectly result in dedifferentiation. Inflammatory myofibroblastic tumors, commonly known as inflammatory pseudotumors, are usually benign tumors characterized by myofibroblastic spindle cells accompanied by inflammatory infiltrates. They occur more often in children and young adults and are more likely to affect females.[14]

In the current case, the patient was diagnosed with dedifferentiated liposarcoma for the recurrent tumor, but it was initially thought to be an inflammatory myofibroblastic tumor. Kimura *et al*.[15] examined the utility of fluorescence *in situ* hybridization (FISH)-mediated detection of *MDM2* amplification for differentiating well-differentiated liposarcomas/dedifferentiated liposarcoma from other morphologically similar sarcomas and benign lipomatous tumors. They concluded that it is the most accurate diagnostic method and stated that it "cannot be substituted" for the use of immunohistochemistry, especially while a diagnostic challenge exists. Another study by Serguienko *et al*.[16] found that a three-gene signature based on *PNPLA2, LIPE*, and *PLIN1* provided a highly accurate genetic diagnosis with 100% sensitivity and 90% specificity. As in the current patient, it is important to note that FISH-mediated detection of *MDM2* amplification and genetic testing are decisive diagnostic tools that should have been performed for the first tumor to guide the diagnosis. This case was initially diagnosed as an ALK-negative inflammatory pseudotumor/inflammatory myofibroblastic tumor. Sukov *et al*. suggested that the absence of ALK gene rearrangements may be an indicator of true malignant spindle cell tumors such as liposarcoma and leiomyosarcoma and that this should be highlighted within a clinical setting.[17]

## Conclusion

It is challenging to correctly diagnose dedifferentiated liposarcoma because of its variable and pleomorphic pathological features. If a tumor is highly suspected of being dedifferentiated liposarcoma, the FISH-mediated detection of *MDM2* amplification and genetic testing should be performed to confirm the final diagnosis.

### Ethical approval

This case report is approved by the Research Ethics Committee(Institutional Review Board) of MMH with approval number: 20MMHIS106e.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

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