

Borderline Sign of A Rare Dedifferentiated Liposarcoma: Report of A Case

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Case Report

Keywords: Dedifferentiation, Liposarcoma, Neoplasm, Histopathology, MR imaging, case report.

Posted Date: July 9th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-40712/v1>

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Abstract

Background: Dedifferentiated liposarcoma (DDLPS) is a unique subtype of liposarcoma, which has obvious histological heterogeneity. Most of them manifested as the dedifferentiation of high-grade histological morphology, but a few could be the dedifferentiation of low-grade histological morphology, or present as some special types of histological or immunophenotypic characteristics. We describe, herein, a case of rare type of dedifferentiated liposarcoma, in which the dedifferentiated components are high-grade and low-grade coexisting with a relatively sharp transition.

Case presentation: A 69-year-old woman with severe abdominal pain lasting for 1 hour presented to our hospital. Physical examination revealed a mobile large left abdominal mass, which was shown on abdominal CT and MRI as a huge retroperitoneal tumor with lipogenic component and solid nonlipogenic components. Tumor resection was performed. Gross examination of the resected specimen showed the gray yellow fatty mass and a round like solid nodule adjacent to the fatty mass, the cut surface of the nodule was gray-white or fish flesh color, and gray yellow in the nodular center. Microscopic examination demonstrated the tumor contains the well-differentiated liposarcoma (WDLPS) component and the DDLPS component. The latter was composed of coexisting high-grade and low-grade components in which multiple focal regions of a sudden transition between the high-grade and the low-grade dedifferentiated component were identified. Immunohistochemistry showed that P16, CDK4, and MDM2 were diffusely positive. The FISH analysis revealed the presence of MDM2 gene amplification in the nuclei of the atypical cells. A final diagnosis of DDLPS was rendered.

Conclusion: In our case, the borderline sign between the high-grade and low-grade dedifferentiated components in the histology may indicate that there can be obvious differentiation lines in tumor dedifferentiation, which is classically and typically abrupt. Low-grade dedifferentiation may be a precursor lesion of high-grade dedifferentiation. MRI images cannot distinguish the two components.

Introduction

Liposarcoma is the single most common soft tissue sarcoma accounting for 20–35% of soft tissue sarcomas^[1,2]. Atypical lipomatous tumor / well differentiated liposarcoma (ALT / WDLPS) and dedifferentiated liposarcoma (DDLPS) have similar genetic characteristics, WDLPS and DDLPS represent a histologic and behavioral spectrum of a single disease entity^[2,3]. Histopathologically, DDLPS may show a markedly heterogeneous morphology. Most manifested as the dedifferentiation of high-grade histological morphology, similar to undifferentiated pleomorphic sarcoma or high-grade myxofibrosarcoma, and a few could be the dedifferentiation of low-grade histological morphology or mixed high-grade and low-grade histological morphology^[4-6]. Low-grade DDLPS may be similar in histology to low-grade myofibroblastic sarcoma, fibromatosis, inflammatory myofibroblastoma, and solitary fibrous tumor^[4, 5, 7]. Distinguishing the various histological types of liposarcoma is not always easy, even for an experienced pathologist, especially when only a small number of samples is available. In this manuscript, we retrospectively analyzed the pathological and imaging findings of a rare case of

DDLPS with mixed high-grade and low-grade dedifferentiated histological features with multiple focal regions of a sudden transition and reviewed the relevant literature.

Case Report

The patient was a 69-year-old woman, who was admitted to the emergency department of our hospital with severe abdominal pain lasting 1 hour in February 2020. The patient accidentally discovered a mass in the left middle abdomen 4 months ago, she began to have abdominal cramps repeatedly in the past 3 months., the abdominal pain was intermittent, and it relieved spontaneously after discharging a large amount of watery stool. On physical examination, a very large soft mass could be palpated in the left abdomen. Laboratory findings were considered as normal, also tumor markers (Carcinoembryonic antigen and CA19-9) were within the normal limits.

Radiologic findings

Abdominal computed tomography (CT) imaging demonstrated a very large retroperitoneal mass of fat density that was filling the left abdomen cavity, the left colon was seriously compressed by the mass, A huge heterogeneous solid nodule can be seen in the lesion. (Fig.1) Magnetic resonance imaging (MRI) examination showed an 8cm × 13.3cm × 20.9cm mass in the left retroperitoneal cavity, MRI signal intensity of most of the mass was hyperintense on T1-weighted images and T2-weighted images, and drop out on MRI fat-suppressed sequences images. (Fig.2a-2b) A 7.8cm × 10.6cm × 11.2cm solid nodule was seen in the lesion with a heterogeneous signal, T2-weighted images show mixed intensity signal, T1-weighted images show iso-intensity signal, and the signal no dropout on MRI fat-suppressed sequences images. ADC map shows irregular low-intensity signal at the edge of the nodule, the ADC value was 0.913×10^{-3} . (Fig.2c) On contrast-enhanced images, the non-fatty nodule shows irregular peritumoral enhancement and no enhancement in the central region. (Fig.2d)

Surgical and Pathologic features

At laparotomy, the well-circumscribed, lobulated mass underwent complete excision, which located in the left retroperitoneum, about 25cm × 20cm × 22cm in size. The upper part of the tumor was very hard and adhered to the mesocolon of the descending colon; a large amount of brown-yellow fat-like tissue was seen in the lower part of the tumor.

Grossly, the size of the tumor is about 20cm × 16cm × 7cm, and the size of the gray yellow fatty mass is about 9 × 8 × 7cm. A round like a nodule with a complete capsule can be seen adjacent to the fatty mass, which is about 11cm × 9.5cm × 7cm in size. The gray-yellow necrotic area (about 8 × 6 × 5cm) can be seen in the nodular center, the necrotic area is surrounded by crescent-like gray-white and gray-brown tumor, there are brown tumor foci near the capsule, and gray-white or fish flesh color tumor foci in the rest and the boundary between the two is clear. (Fig.3)

Microscopically, there is a sharp transition between ALT/WDLPS and DDLPS. (Fig.4 a-b) Most of the DDLPS are high-grade undifferentiated pleomorphic sarcoma with extensive tumor necrosis, and near the capsule are a low-grade components of DDLPS, Histologically, which are inflammatory myofibroblastic tumor-like (Fig.4 c) and fibromatosis-like features. (Fig.4 e) Multiple focal regions of DDLPS can see a sudden transition between the high-grade and the low-grade dedifferentiated component. (Fig.4 d/f) Immunohistochemical analysis was positive for P16, CDK4, and MDM2. Fluorescence in situ hybridization (FISH) analysis suggested the presence of MDM2 gene amplification. (Fig.5) These findings have supported the diagnosis of DDLPS.

The patient recovered well and was discharged from the hospital on the 7th day after surgery. The patient will receive further treatment, such as chemotherapy, and will be followed up regularly.

Discussion

The definition of dedifferentiated liposarcoma (DDLPS) in WHO classification standard of bone and soft tissue tumor is that atypical lipomatous tumor/highly differentiated liposarcoma (ALT / WDLPS) can be dedifferentiated into a different degree of sarcoma at the same time or at different times with ALT / WDLPS^[2, 8]. Dedifferentiated areas usually consist of undifferentiated pleomorphic sarcoma or spindle cell sarcoma, with high to moderate cellularity and pleomorphism. A minority of DDLPS cases show low-grade sarcoma ingredients resembling fibromatosis or low-grade fibromyxoid sarcoma, this is seen in 10% of cases of DDLPS^[4, 7]. Different from ALT / WDLPS, which has a relatively clear histological subtype, DDL represent a morphologically heterogeneous group. In this case, DDLPS is characterized by the coexistence of high- and low-grade dedifferentiated component, which is rare in clinical work. Therefore, we summarize its pathological features and MRI image findings to deepen the awareness of this rare type of DDLPS.

DDLPS present most frequently in middle-aged and older adults has no gender-prone tendency, and it is extremely rare in children and adolescents. The retroperitoneum is the most frequent site, followed by the limb and spermatic cord / paratesticular area. Rare sites include the chest cavity, mediastinum, and head and neck (such as the larynx or esophagus). Due to the large space for tumor growth in the posterior peritoneal area, ALT / WDLPS in this area can grow for a long time without causing symptoms, and there is dedifferentiation at the time of diagnosis, so there is a high risk (about 28%)^[4, 7].

The histology of DDLPS usually shows that ALT / WDLPS components are transformed into non-fatty tumor components, and the two components are usually clearly demarcated under the microscope. The histological types of ALT / WDLPS in DDLPS are mainly lipomatous and sclerotic. The retroperitoneal mass seen in this case is huge and contains a lot of WDLPS components. The dedifferentiated components are characterized by the coexistence of low-grade and high-grade dedifferentiated components. The low-grade components account for only 10% of the dedifferentiated tumor, and it is located in the periphery of the high-grade components. The boundary between the two components can be roughly identified in the section of the specimen. Pathologically, there is a sudden transition between

WDLPS and DDPLS or high-grade and low-grade components of DDPLS which showing obvious boundary characteristics. We call it " Borderline sign " here. The " Borderline sign " reflects a certain extent that there can be obvious differentiation lines in tumor dedifferentiation, which is classically and typically abrupt. Besides, the conversion of low-grade DDLPS starts from the periphery of high-grade, low-grade dedifferentiation may be a precursor lesion of high-grade dedifferentiation^[9]. In the central region of the high-grade differentiated tumor, large areas of ischemic necrosis appeared due to poor tissue differentiation and rapid growth. Also, as shown in this case, the low-grade dedifferentiated tissues exhibited with fibromatosis-like and inflammatory myofibroblastoid-like features.

In addition, in the differential diagnosis of other types of fatty tumors other than ALT / WDLPS, the immunohistochemical staining including p16, MDM2 and CDK4 has high sensitivity and specificity for the diagnosis of DDLPS. In this case, well-differentiated liposarcoma components and dedifferentiated liposarcoma components (including high-grade dedifferentiation and low-grade dedifferentiation) all diffusely express P16, MDM2 and CDK4 positive. However, in the differential diagnosis of DDLPS and non-fat-derived tumors, the specificity of the above three markers is insufficient. At this time, the use of fluorescence in situ hybridization (FISH) to detect the amplification of MDM2 gene is highly specific and sensitive for the diagnosis of DDLPS, especially when diagnosed with small biopsy specimens, especially in small biopsy specimens, no typical WDLPS components, low-level dedifferentiation and rare special types of DDLPS, It's even more so^[7, 10]. The amplification of MDM2 gene is generally considered as the gold standard for the diagnosis of ALT / WDLPS and DDLPS.

The diagnosis of DDLPS needs to find two components in the tumor, including lipogenic WDLPS component and cellular nonlipogenic sarcoma components. MRI can easily identify the fat-derived components in tumors through fat-suppressed T2 images or short tau inversion recovery (STIR) imaging^[11], so that WDLPS components in DDLPS can be well found, which is more helpful for diagnosis; however, in some cases, the WDLPS composition can be less and easily ignored. Because DDLPS is the conversion of WDLPS components to non-fat-derived tumor components, the lesions of DDLPS on the MRI images lack signs of lipid characteristics. In addition, the ADC value of DDLPS lesions is low, which indicating poor differentiation of tumor tissue, Dynamic contrast enhancement of MRI can also reflect the blood supply of the active area of the lesion, as well as the extent of necrosis or mucinous cystic changes in the lesion. Although there is a clear boundary between the high-grade and low-grade differentiation components of DDLPS in the case, MRI images fail to distinguish them, the reasons may be as follows: 1. Diffusion-weighted imaging (DWI) can be used to judge the degree of tissue differentiation, but the spatial resolution of DWI images is low and the graphics are easily deformed. 2. The difference in tissues differentiation between high-grade and low-grade dedifferentiated components is not large enough. 3. Compared with high-grade dedifferentiation components, the proportion of low-grade dedifferentiation components in DDLPS is too small.

In summary, for the diagnosis of liposarcoma, whether MRI image or pathology, we should pay attention to the search for typical fat components, but MRI is subject to some limitations concerning the preoperative diagnosis of liposarcoma with lack of fat components or the diagnosis of liposarcoma

subtype; The differential diagnosis spectrum of DDLPS is wide, and there are many diagnostic traps. Extensive sampling of the mass is recommended to avoid missing any component. Sampling should be performed in both non-fatty and fatty tissues. To order avoid misdiagnosis of DDLPS, it is sometimes necessary to combine immunohistochemistry (such as MDM2 gene amplification detection). In addition, the "borderline sign" seen in this case is an important supplement to the rare pathological manifestations of some DDLPS.

Abbreviations

ALT: Atypical lipomatous tumor; WDLPS: Well differentiated liposarcoma; DDPLS: Dedifferentiated liposarcoma; CT: Computed tomography; MRI: Magnetic resonance imaging; ADC: Apparent diffusion coefficient; STIR: Short tau inversion recovery; DWI: Diffusion-weighted imaging

Declarations

Acknowledgements

Not applicable.

Conflicting interest

The authors disclosed no conflicts.

Funding sources

This work was supported by the fund of Medical and Health Research Projects of Health Commission of Zhejiang Province (No.2018KY247).

Authors contribution

Dr. Yang wen put all data together and wrote the manuscript. Dr. Xianglei He and Dr. Ming Zhao did the pathologic examination and gave the pathologic interpretation. Dr. Yang wen and Dr. Songhua Fang gave the radiologic interpretation.

Availability of data and materials

The data and materials are available upon request.

Ethics approval and consent to participate

This publication is approved by the Research Ethics Committee of Zhejiang Provincial People's Hospital.

Consent for publication

Consent from the patient is obtained.

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Figures

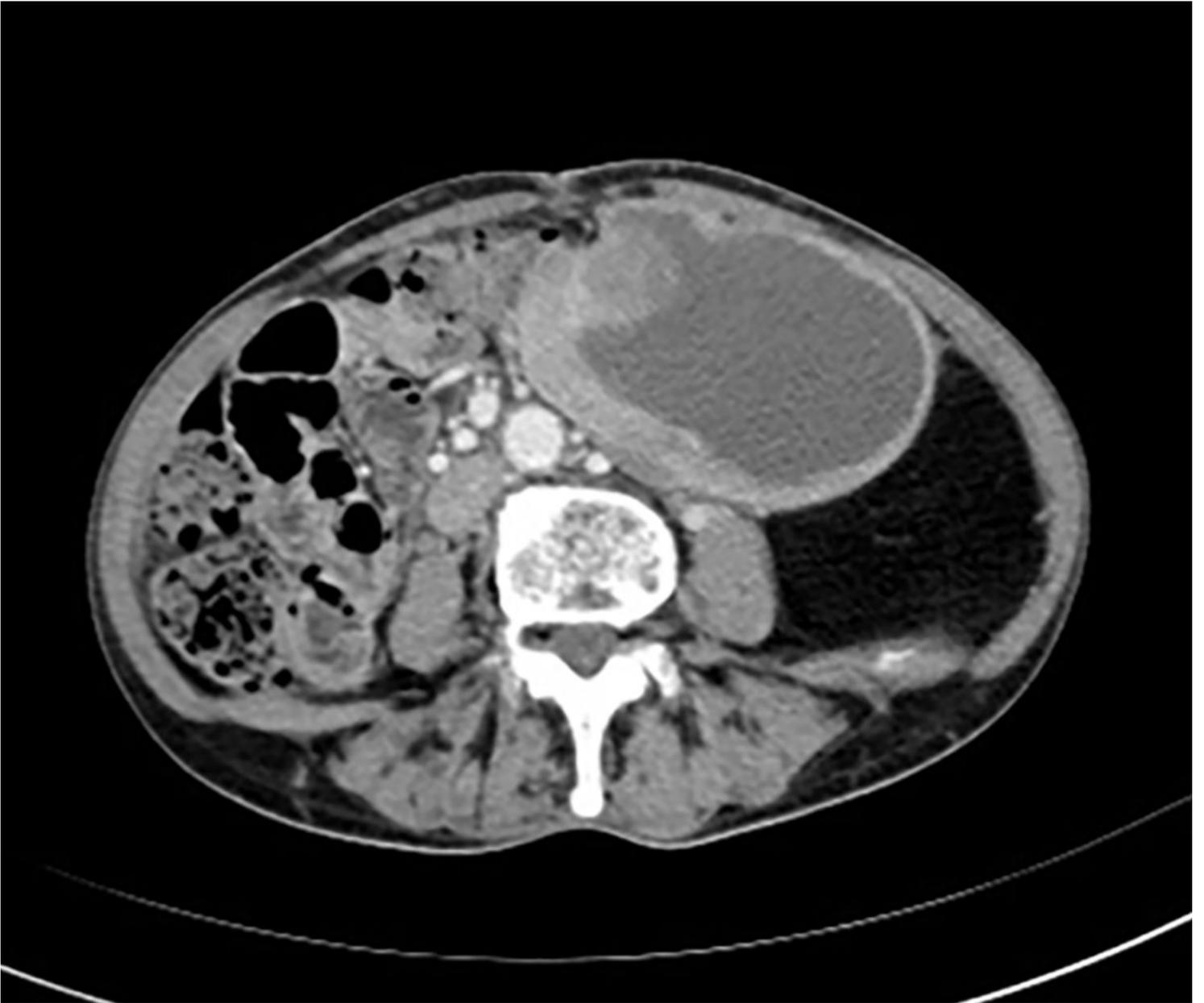


Figure 1

CT images of DDLPS Axial contrast-enhanced CT image shows a giant retroperitoneal fatty mass with huge heterogeneous nodular component.

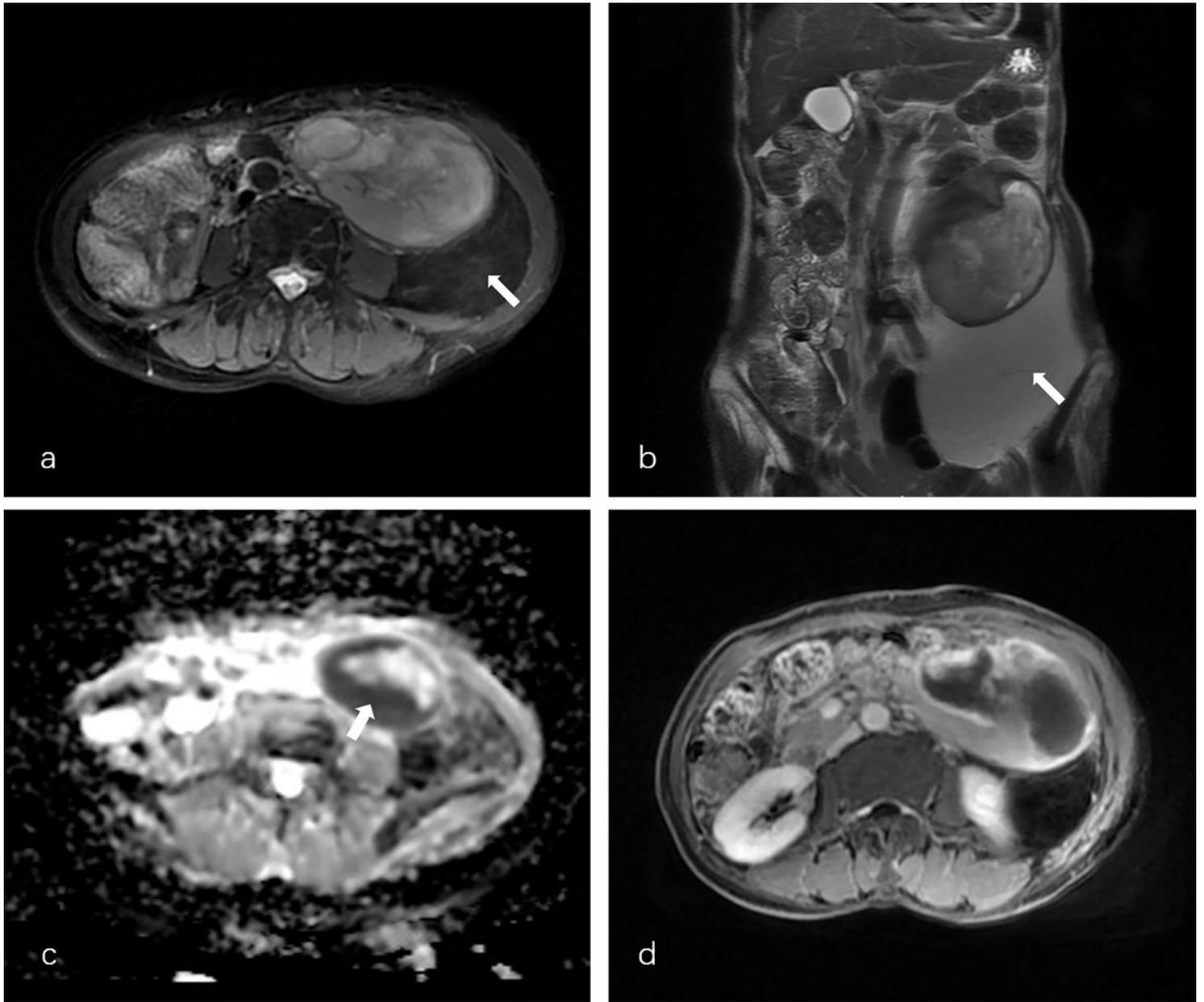


Figure 2

MRI images of DDLPS (a-b) Axial fat-saturated T2-weighted image (a) and coronal T2-weighted image (b) shows a relatively well-defined pure fatty mass (white arrows), and a non-fatty solid mass within the mass. (c) Axial apparent diffusion coefficient map of the non-fatty solid mass shows the edge of the lesion is hypointense (white arrows), the mean ADC value was 0.92×10^{-3} . (d) Axial post-contrast fat-suppressed T1-weighted image shows heterogeneous enhancement of the non-fatty solid mass.

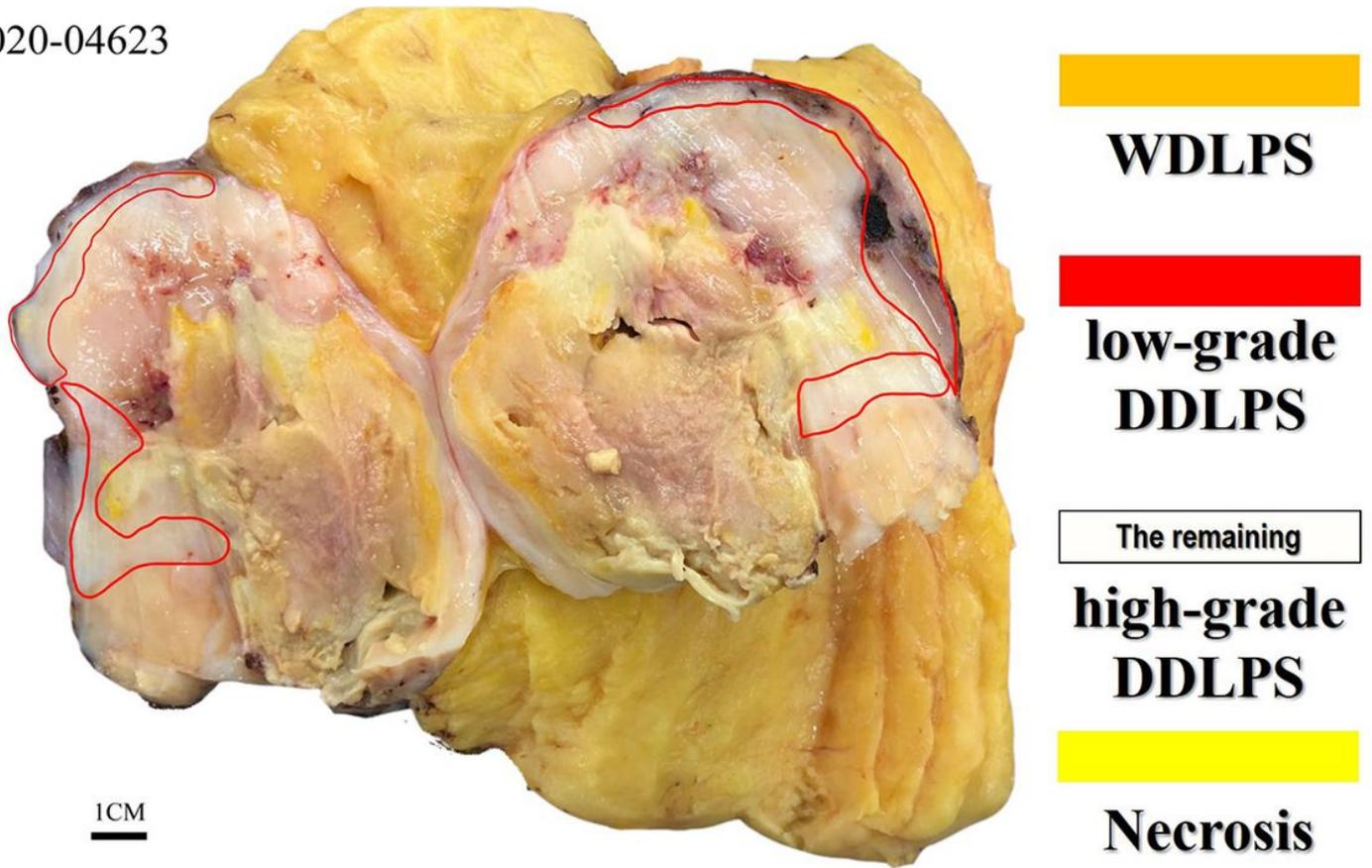


Figure 3

Gross appearance of DDLPS The section of the WDLPS is yellow, the high-grade DDLPS is fish-colored, and the middle necrotic area is pale yellow, the low-grade DDLPS is grey-white, but the local area is Grayish-brown, the boundary between the low-grade dedifferentiation and the high-grade dedifferentiation is visible.

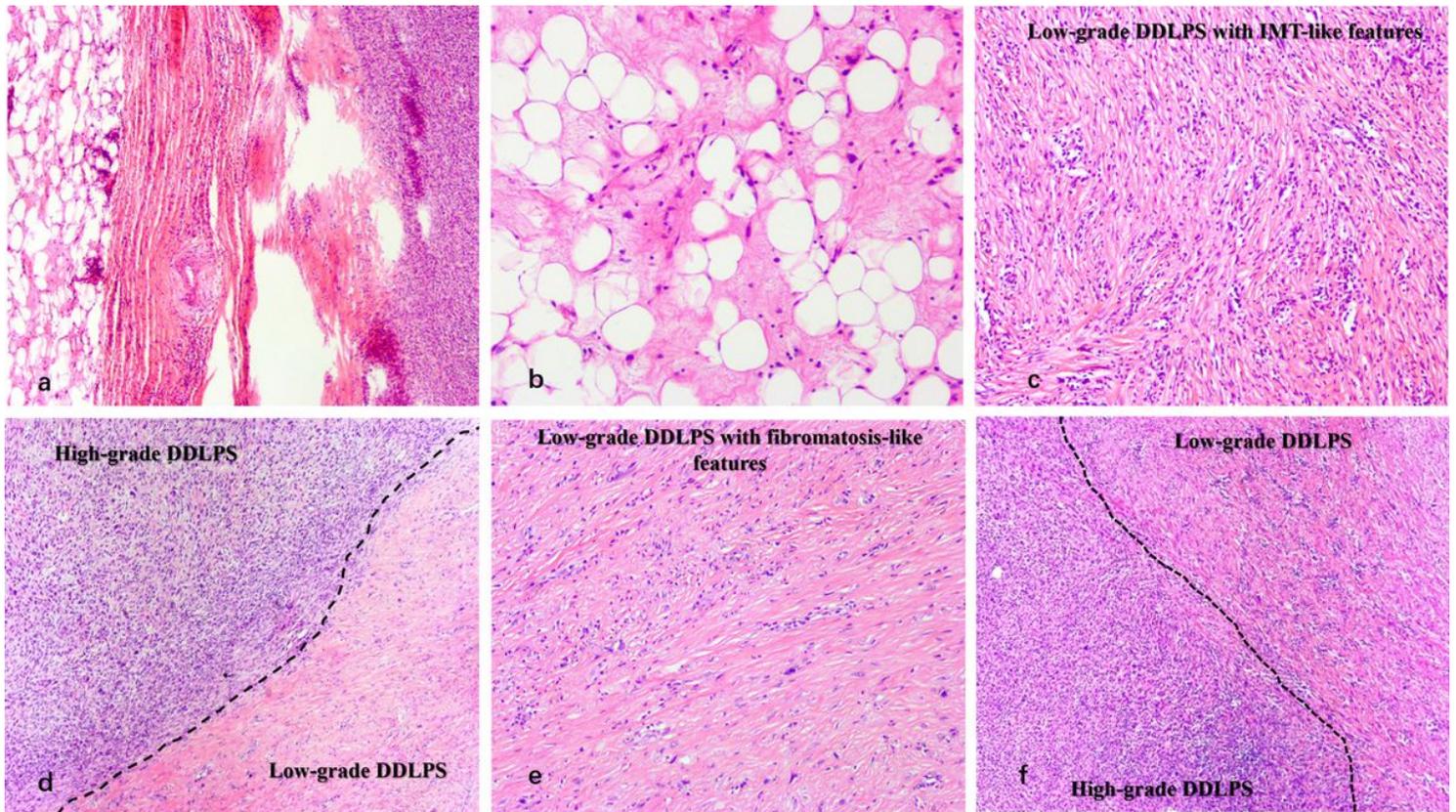


Figure 4

Histologic specimens of DDLPS (a) The highly differentiated component and the dedifferentiated component is sudden transition. (Hematoxylin-eosin stain; $\times 40$) (b) Typical Well-differentiated liposarcoma of the adipocytic/lipoma-like type. (Hematoxylin- eosin stain; $\times 100$) (c-d) Low-grade dedifferentiation with inflammatory myofibroblastic tumor-like features transition to high-grade dedifferentiation with undifferentiated pleomorphic sarcoma features. (Hematoxylin-eosin stain; c $\times 40$) The boundary (dotted line) between them is clear. (Hematoxylin-eosin stain; d $\times 20$) (e-f) Low-grade dedifferentiation with fibromatosis-like features transition to high-grade dedifferentiation with undifferentiated pleomorphic sarcoma features. (Hematoxylin-eosin stain; e $\times 40$). The boundary (dotted line) between them is clear. (Hematoxylin-eosin stain; f $\times 20$)

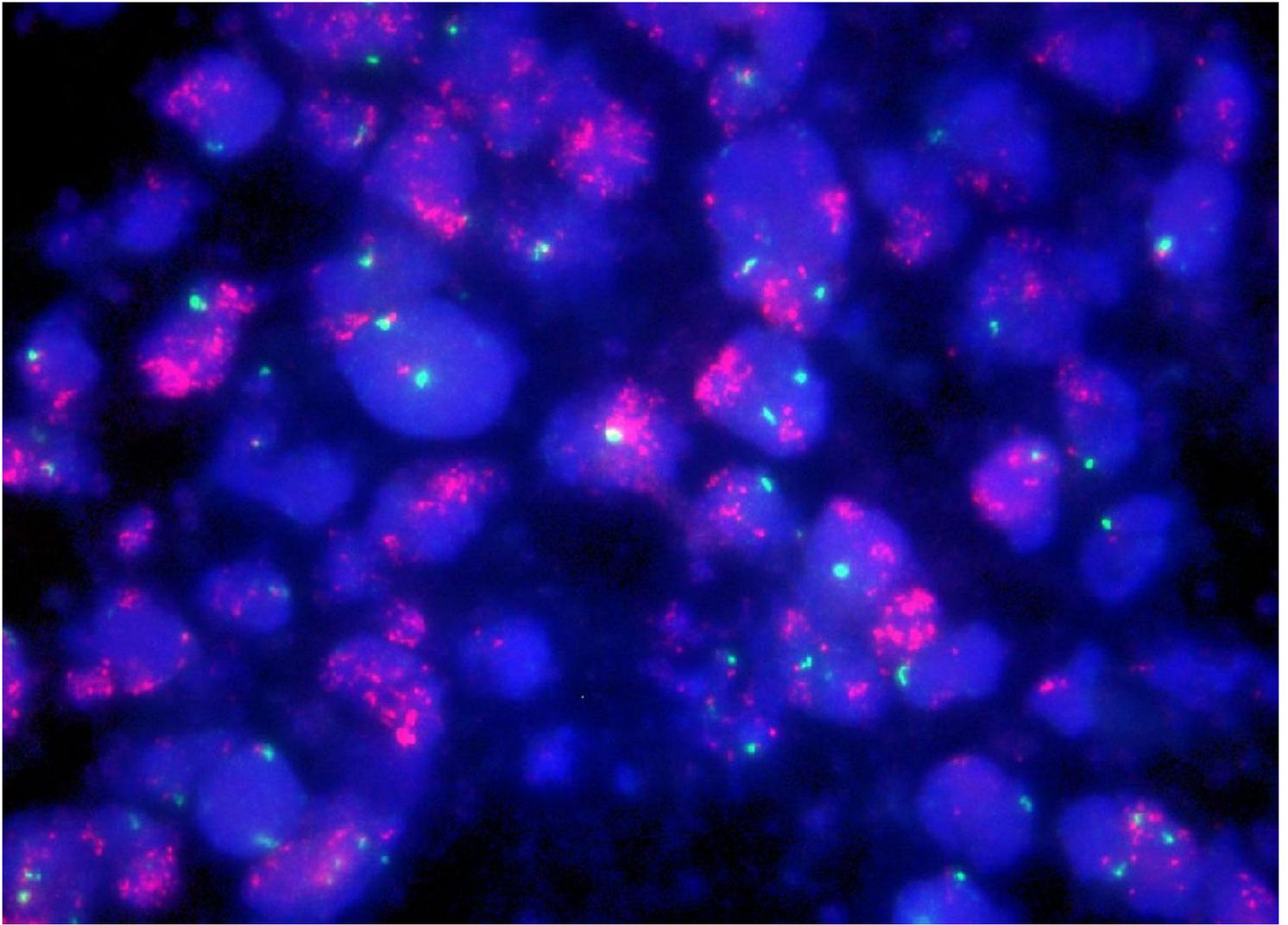


Figure 5

Fluorescence in situ hybridization (FISH) of MDM2 gene FISH analysis confirmed MDM2 gene amplification (Clustering of red signals) in the nuclei of the atypical cells.

Supplementary Files

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